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# TABLE OF CONTENTS

1. An Unusual Case Of Clostridium Difficile Infection In Trinidad & Tobago
   
   Lemar Blake, Patrick Eberechi Akpaka, Adash Ramsubahag, Renea Ali & Asongna T. Folefoc  
   
   81

2. Evolution Of Relationship Between Increased Demand Of Insulin Secretion And Increased Level Of Proinsulin In Blood Of Patient Of Diabetes Mellitus 2
   
   Dr. Madhumati Varma  
   
   94

3. An Assessment Of The Rate And Predisposing Factors To The Development Of Breast Abscess Among Lactating Mothers In The Batibo Health District, North West Region, Cameroon
   
   Akwo Cyril Tabe-Tanyi & Mirabel Ngoin  
   
   101

4. Prevalence Of Ocular Morbidities Among School Children In A Rural Area Of South India
   
   Meundi AD, Athavale AV & Suruliraman SM  
   
   116

5. Article Review On Improvement Of Eustachian Tube Function By Tissue-Engineered Regeneration Of Mastoid Air Cells
   
   Dr. Muhammad Tariq  
   
   126

6. Role Of Dipeptidyl Peptidase-4 Inhibitor In Glycemic Control And Cardiovascular Mortality And Morbidity
   
   Dr. Shaikh Khalid Anwar  
   
   133
<table>
<thead>
<tr>
<th></th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Innovative Proposal Of Cardiac Hawk Eye Technology</td>
<td>Sumukha Prasad U &amp; Prithvi Shankar N</td>
</tr>
<tr>
<td>8</td>
<td>Measles, A Diminishing Threat To Child Development In Northern Region Of Ghana</td>
<td>Dr. Michael Wombeogo &amp; Dominic Abugri</td>
</tr>
<tr>
<td>9</td>
<td>Assessment Of Common Oral And Dental Diseases Among Pregnant Women At Dhaka City In Bangladesh</td>
<td>Mahmud SZ, Begum F, &amp; Uddin MM</td>
</tr>
<tr>
<td>10</td>
<td>Pharmacovigilance-An Emergence</td>
<td>Dr Deven V Parmar &amp; Dr. Dharani Munirathinam</td>
</tr>
<tr>
<td>11</td>
<td>Clinical Understanding Of A Life-Threatening Asthma Help To Improve Pediatric Patient’s Outcomes</td>
<td>Dr. Alain Kabongo</td>
</tr>
<tr>
<td>12</td>
<td>Menstrual Changes Among Hiv Positive Women On Anti-Retroviral Treatment In Southwestern Nigeria</td>
<td>Adebimpe Wasiu, Adebimpe Mujidat, &amp; Adewole Adefisoye</td>
</tr>
<tr>
<td>13</td>
<td>Cardiac Monitoring In Her-2 Positive Elderly Patients Treated With Transtuzumab</td>
<td>Dr. Rajani Sinha</td>
</tr>
<tr>
<td>14</td>
<td>Rare Occurrence Of Enterocutaneous Fistulae Following Onlay Mesh Repair For Incisional Hernia: A Case Series</td>
<td>Shah BC &amp; Degloorkar S</td>
</tr>
<tr>
<td>15</td>
<td>The Effect Of Combined Oral Contraceptive Pills (Cocp) Containing Levonorgestrel And Ethinylestradiol On Kidney Function</td>
<td>Ekhator C.N. Omorogiowa A. &amp; Akpamu U</td>
</tr>
</tbody>
</table>
AN UNUSUAL CASE OF CLOSTRIDIUM DIFFICILE INFECTION IN TRINIDAD & TOBAGO

A Case Study By Lemar Blake¹, Patrick Eberechi Akpaka¹, Adash Ramsubahag², Renea Ali², Asongna T. Folefoc³, Trinidad & Tobago
(Microbiology & Pathology Unit, Department of Paraclinical Sciences, The University of the West Indies, St. Augustine, Trinidad & Tobago¹
Department of Life Sciences; The University of The West Indies; St. Augustine, Trinidad and Tobago²
Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of Calgary, Alberta, Canada³)
Email: peakpaka@yahoo.co.uk

ABSTRACT

AIM: To report the first fatal case of a toxin A positive toxin B gene positive strain of Clostridium difficile that caused pseudomembranous colitis in a patient living in Trinidad & Tobago.

Presentation of case: Patients admitted in a tertiary hospital with history of diarrhea were being investigated and reviewed. A case of a 47-year old Trinidadian of African descent presenting with diarrheal stool at a public hospital in Trinidad and Tobago. The identified patient had his stool sample analyzed using conventional and molecular microbiology procedures to identify the bacteria, toxins and genes produced by the microorganism. The antimicrobial susceptibility was also determined using agar dilutions according to CLSI guidelines.

DISCUSSION: The patient’s stool sample produced positive results for Clostridium difficile toxin. The Quick Check Complete® kit demonstrated the production of toxin and the glutamate dehydrogenase enzyme. This strain exhibits the toxin A and B gene.

CONCLUSION: Clostridium difficile isolated from this patient revealed the presence of toxin A and B gene. This gave a 1266bp and 204bp DNA fragment corresponding to the toxin A and B gene respectively, based on the primers used. The isolated strain was resistant to meropenem, ampicillin, ceftriaxone, cefotaxime and ciprofloxacin. This organism seems to have been responsible for the formation of psuedomembranous colitis in the studied patient. Further
research is needed on similarly detected strains, to better understand their significance in Inflammatory Bowel Diseases and their prevalence in our geographical location.

KEYWORDS

Clostridium difficile, Pseudomembraneous colitis, Polymerase Chain Reaction, Trinidad & Tobago

INTRODUCTION

Clostridium difficile is an anaerobic gram positive bacilli which is the major cause of psuedomembraneous colitis [1]. Infection with this organism may result in a range of presentations including asymptomatic carriage, mild diarrhea, psuedomembraneous colitis and toxic megacolon [2]. Various researches have shown that Clostridium difficile is present in approximately 10% of the normal healthy adult population and is implicated in 20-30% of nosocomial diarrhea. This organism is also the major role player implicated in antibiotic associated diarrhea [3-5].

Acquisition of Clostridium difficile infection often occurs in conjunction with disruption of the normal colonic microflora. Causes for such disruption may include antibiotic overexposure and underlying disease [6]. Clostridium difficile spores and vegetative cells are brought into the body via ingestion. The vegetative cells are destroyed by the low pH of the stomach, however the spores continue on to the small intestine where they germinate upon exposure to bile acids [7]. The proliferating cells move into the colon where they attach themselves, being adequately protected by a polysaccharide layer. In a patient with good IgG response, this colonization leads to asymptomatic carriage; however in patients with poor IgG response toxin production may lead to manifestations of disease [6].

Two major toxins-toxin A and toxin B are produced by Clostridium difficile vegetative cells [8]. Both toxins attach themselves to epithelial cells of the colon and enter the cells via endocytosis. The resulting vacuole has a pH which facilitates the glycosyltransferase portion of the toxin to be released into the cytoplasm. This glycosyltransferase moiety facilitates the transfer of a glucose molecule from uridine diphosphate to Rho, Rac or Cdc-42 molecules which leads to inactivation of these molecules [9]. These molecules are responsible for actin formation, regulation of apoptosis and transcriptional regulation [9]. The mechanism for both toxins is the same; however there are differences in the effect on intestinal cells. Toxin A is enterotoxic; and causes neutrophil infiltration, substance P production, chemokine production, disruption of tight
junctions and apoptosis. Toxin B has more direct (cytotoxic) effects causing disruption of tight junctions and apoptosis. The overall effects are edema and an inflammatory response [9].

There are now evidences of a third toxin known as a binary toxin that is produced by various Clostridium difficile strains; one of such is the NAP 1 strain [10]. This new strain is an actin-specific ADP-ribosyltransferase toxin, that has two dependent proteins; CDTa, which is the catalytic component and CDTb which is the binding component [11]. It is widely accepted that certain strains of Clostridium difficile have the propensity to cause outbreaks, including multiple-state outbreaks in healthcare facilities [12]. Even though toxigenic strains have been sensitive to the widely accepted cytotoxicity assay, its use has become limited and methods such as Enzyme Linked Immuno-Sorbent Assay (ELISA) testing are now routinely used [13].

Molecular analysis has now been added to the algorithm for Clostridium difficile detection. This includes toxin gene detection via simple PCR analysis [14, 15]. This enables researchers and health-care workers to understand the genetic aspect of the organism and how it may be related to where the organism was found. The species-specific internal gene fragment (tpi) for Clostridium difficile, as well as the gene for toxin A and B can efficiently be tested for using specific primers; which in turn can show the pathogenic nature of Clostridium difficile [13].

**PRESENTATION OF CASE**

A 47 year-old Trinidadian male of African descent was admitted to the Eric Williams Medical Sciences Centre (EWMSC) in Mount Hope, Trinidad and Tobago as a referral from his family doctor where he had been seeking medical attention for the past 5 months. He presented with complaints of fever, abdominal cramps, generalized swelling and moderate diarrhea. He had no history of travel abroad. However, he had a 6 month history of rheumatoid arthritis. (Rheumatoid Factor was positive at 720 IU/ml). While in the care of his family physician, he received steroids for persistent swelling of his upper and lower limbs. According to the patient, he visited his family physician because he was having diarrhea and fever after he and a relative consumed substantial amounts of seafood at a weekend social gathering. He stated that they both became sick with symptoms of diarrhea and malaise following the meal. Although his relative recovered, the patient remained ill and was then referred to the medical center by his family physician.

On admission to the EWMSC he was treated for arrhythmia with adenosine; and empirically with ceftriaxone for suspected septic arthritis. Steroid therapy was continued his symptoms dramatically improved and he was subsequently discharged. Four months later he was readmitted with similar complaints – diarrhea, fever, malaise. On physical examination the patient appeared very ill, pale and dehydrated. He was febrile, blood pressure was 115/81 mm/hg and pulse rate was 125 beats/min. He was in mild respiratory distress and had generalized abdominal
tenderness and swelling. The right inguinal lymph node was soft, mobile and enlarged. Rectal examination showed the presence of soft stool mixed with bright red blood on the examining finger.

Blood, stool and urine samples were taken for laboratory investigations. Stool was submitted specifically for identification of ova, cyst and parasite (OCP); as well as for culture. His hemoglobin was 11.1g/dl and his white blood cell count was 25.6 x 10⁹/dl. Blood and urine cultures came back negative; stool was also negative for OCP and culture with Cycloserine Cefoxitin Fructose Agar (CCFA) media. Flexible sigmoidoscopy revealed a pale mucus membrane and edema in the left transverse colon. There were no mucosal lesions visible. Computed Tomography (CT) of the abdomen/pelvis showed a hypodense mass in inguinal canal adjacent to the right iliopsoas muscle. Unfortunately, surgical intervention was not carried out to remove this mass as patient was too ill. The patient was treated with amantadine, levofloxacin, ibuprofen, prednisolone, Celebrex®, Panadol® and metronidazole 500mg intravenously.

His diarrhea persisted, and twelve days later the white blood cell count was 30 x 10⁹/l. A repeat CT scan showed a wedged shaped area in the periphery of the spleen, diffused thickening and mucosal enhancement of the distal ilium and the colon. Flexible sigmoidoscopy was repeated and demonstrated inflammation, jelly-like mucin, an enhanced, yellowish membrane and few mucosal lesions in the transverse colon. Biopsy of the region ruled out malignancy and a diagnosis of pseudomembranous colitis was made. Vancomycin was subsequently added to the treatment regimen; and was given orally at 500mg doses every 6 hours each day. The patient did not respond to treatment and eventually died before surgical procedures were carried out.

**METHOD**

Prior to the patient’s death, a repeat stool samples were collected and tested for the organism using the C.diff Quick Check Complete® from Tech Labs. The stool sample was positive for the Clostridium difficile toxin however the ELISA kit used above did not indicate which toxin was present. The stool sample was cultured anaerobically using Cycloserine Cefoxitin Fructose Agar (CCFA) for 96 hours at 37°C. Culture revealed flat, ground-glass shaped greenish colonies which produced a horse scent; gram stain showed gram positive bacilli. The organism was confirmed as Clostridium difficile using Polymerase Chain Reaction to test for the organism’s house-keeping gene. No additional biochemical tests were carried out in Trinidad & Tobago. This isolate was further analyzed at Foothills laboratory of the University of Calgary, Calgary Alberta, Canada. Here, the isolate was re-cultured and incubated on a CCFA plate where positive growth was obtained (Figure 1). This isolate was also subjected to the Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) test method which is a mass spectrometry
technique that allows for DNA, peptides, proteins and sugars to be analyzed further confirmed the isolate as C.difficile. The ATCC 9686 control strains was analyzed with PCR and similar DNA fragments were obtained.

ANTIMICROBIAL SUSCEPTIBILITY TESTING

Antimicrobial susceptibility of C. difficile was determined by minimum inhibitory concentration obtained by agar dilution method; as recommended by the Clinical Laboratory Standard Institute (CLSI) [16]. A 105 bacteria inocula was prepared by the direct suspension of the bacterial colonies, into 10 ml peptone water, equivalent to a 0.5 McFarlane standard (Biomerieux Vitek Inc, Hazel Hood Missouri). Fresh bacterial colony was taken from that which was grown for a 48-72 hour period on the CCFA agar. The suspended colonies were then inoculated 105 bacteria per spot on the Muller Hinton supplemented with 7% horse blood and a 2 fold increase in varying antibiotic concentration. Antibiotics used were: Metronidazole, Ampicillin, Piperillin-Tazobactam, Meropenem, Penicillin G, Ceftriaxone, Cefotaxime and Ciprofloxacin. A total of 5 concentrations were used for each antibiotic according to the CLSI standard for anaerobes. Inoculated plates were used for each antibiotic according to the CLSI standard for anaerobes. Inoculated plates were used for each antibiotic according to the CLSI standard for anaerobes.

PCR ANALYSIS

PCR analysis for the toxin A gene was carried out using the NK11 (5_TGATGCTAATAATGAAATCTAAAAATGGTAAC-3_) and NK (5_CCACCAGCTGCAGCCATA_3). For toxin B gene NK104 (sequence-5_GGTGACAAATGAAATGCACTTTAGC-3_) and NK105 (sequence-, 5 CACTTAGCTCTTTGATTGCTGCACCT-3_), were used as previously reported [17].The house keeping gene (tpi) which is specific for Clostridium difficile was also assessed to further confirm the organism using the primer set tpi-F 5 AAAGAAGCTACTAAGGGTACAAA-3 and tpi-R 5_CATAATATGGGTCTATTCCCTAC-3 [14].

PCR conditions were as follows: the PCR mixtures were denatured (3 minutes at 95 °C), and then a touchdown procedure was implemented, consisting of 30 seconds at 95 °C, annealing for 30 seconds at temperatures decreasing from 65 °C to 55 °C during the first 11 cycles (with a 1 °C decremental steps in cycles 1 to 11), and a final extension step of 72 °C for 30 seconds. A total of 45 cycles were performed following methods previously described by [13]. PCR was performed using Promega GoTaq Green® master mix.
RESULTS

Patient stool C. difficile isolate produced positive PCR result for toxin A, B and the housekeeping gene. The C. difficile isolate was subjected to antimicrobial susceptibility testing using agar dilution and revealed that the isolate was resistant to ampicillin, ceftriaxone meropenem, cefotaxime and ciprofloxacin. However it was sensitive to metronidazole, piperclillin-tazobactam, and penicillin G.

The Quick direct kit demonstrated the production of toxin and the glutamate dehydrogenase enzyme. All test procedures (isolation, ELISA and molecular) were repeated before making any conclusions. However, no toxinotyping, ribotyping or cytotoxicity tests were carried out. The ATCC 9686 C. difficile strain reveals the presence of two major toxin genes A and B, (figure not shown) and was used as a positive control. The DNA fragment from the isolate is shown in lane 1 of figures 2 and 3, both toxin A and B gene fragments were shown respectively; a 1% agar gel and 1kb ladder was used for analysis.

DISCUSSION

Clostridium difficile has two major virulent factors toxin A and toxin B [18]. Clostridium difficile is the main etiological agent linked to pseudomembranous colitis, and is responsible for over 90% of all cases [19]. Patients usually present with fever, abdominal pain, diarrhea, loss of appetite and fatigue [20]. Clostridium difficile-associated diarrhea seems to be on the increase and is implicated in 20-30% of all antibiotic associated diarrheal cases [21]. Toxin A and B have enterotoxic and cytotoxic effects respectively; which have now been reported to show synergistic capabilities in their virulent processes [9]. These may lead to fluid infiltration, inflammation, disruption of tight junctions, psuedomembrane and mucus formation in the colon [5].

Psuedomembranous colitis is a mucosal disease, recognizable by numerous yellow plaques which are 0.2-2.0 cm in diameter; these attach themselves to varying lengths of the colon [22]. Patients with psuedomembranous colitis are normally treated based on the stage of the disease. Metronidazole and vancomycin are the two major drugs used [23]. In mild to moderate cases, supportive therapy along with the withdrawal of the offending drug is the first step to recovery [23].

For patients with severe psuedomembranous colitis, vancomycin is the preferred treatment and is given at 125 mg qds for 10-14 days [24]. A colectomy is carried out for patients who have megacolon consisting of a diameter >10 cm [25].
In this case the patient proved to be positive on culture which is indicated by the presence of the organism in an amount greater than 2000 of 10 X 1010 bacteria present per gram of wet feces. The isolated organism produced the enzyme glutamate dehydrogenase and a toxin, both of which were detected using the C.diff Quick Check Complete Kit® (Tech Labs). However this test was unable to differentiate if the toxin produced was A, B or both. The test is described to be 87.8% sensitive and 99.4% specific [26].

The DNA from the organism was positive for the confirmatory housekeeping tpi gene (not shown). Previous studies have shown strains of similar gene fragment lengths [10]. Non-toxigenic Clostridium difficile strains have been shown to adhere far less frequently to intestinal mucosa than toxigenic strains [19]. It has also been shown that the adhesions produced by toxigenic strains binds to gut, mucosa and cells more frequently than non-toxigenic strains [19]. This ability of the cell may cause increased colonization and an enhanced ability to carry out its toxigenic effects.

As stated in the case presentation, the patient clearly stated during interview that he had consumed substantial amounts of seafood at a weekend social gathering. This indicates that the patient may have been infected in a community setting after ingesting contaminated seafood. Re-infection may have occurred later at a similar event since seafood is a popular dish in Trinidad & Tobago. Consideration should also be given to the patient’s past medical history which includes a diagnosis of rheumatoid arthritis. It is known that increased risk factors for the acquisition of C.difficile associated diarrhea include the severe underlying diseases and a faulty response to the toxins [27]. This has important implications for this patient because of the production of abnormal immunoglobulin G and formation of immune complexes in rheumatoid arthritis. Patients at greatest risk for severe disease are those who have had surgical intervention and or have been treated with immunosuppressive therapy since such patients cannot mount an adequate response [27]. This patient, while having not received surgical intervention, had been maintained on steroid therapy for rheumatoid arthritis.

**CONCLUSION**

This case demonstrated that the toxin A and B positive strain have a role in the formation psuedomembranous colitis and that possible resistant strains are present in the population. Further research is needed on similarly detected strains, to better understand their significance in Inflammatory Bowel Diseases.
ACKNOWLEDGEMENTS

Nursing staff of the EWMSC and technical staff of the microbiology department for their support. Part of the funds for this study was provided by the Campus and Research Fund, School of Graduate Studies, The University of the West Indies, St. Augustine.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

AUTHORS’ CONTRIBUTIONS

Both authors designed the study. LB collected, analyzed the data and drafted the manuscript. PEA supervised and coordinated the project. Both authors read and approved the final manuscript.

CONSENT

Authors declare that written informed consent was obtained from the patient and hospital authority for publication of this case report. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

The ethics committee of the Faculty of Medical Sciences, the University of the West Indies, St. Augustine gave approval for this study.

REFERENCES


7) Clinical and Laboratory Standard Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Information Supplement 2012; M100-S22; Vol 31 No.1


22) Persson S, Torpdahl M, Olsen K. New multiplex PCR method for the detection of Clostridium difficile toxin A (tcdA) and toxin B (tcdB) and the binary toxin (cdtA/cdtB) genes applied to a Danish strain collection. *Clin Microbiol Infect* 2008; 14(11), 1057-1064.


24) Sharp SE, Ruden LO, Pohl JC, Hatcher PA, Jayne LM, Ivie WM. Evaluation of the C. Diff Quik Chek Complete Assay, a new glutamate dehydrogenase and A/B toxin combination lateral


FIGURE 1

Figure 1 A fatal case of Clostridium difficile infection from Trinidad & Tobago. Isolate was grown on a Cycloserine Cefoxitin Fructose Agar (CCFA) plate before being subjected to Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) test and it confirmed the isolate as Clostridium difficile.
**FIGURE 2**

Figure 2 of PCR products of a fatal case of Clostridium difficile infection from Trinidad & Tobago. The isolated strain revealed the presence of the toxin A genes as indicated in lane 1. The patient produced a 1266bp band on a 1% agar gel, using a 1kb ladder.

**FIGURE 3**

Toxin A gene fragment approximately 1266bp

Toxin B gene 204bp fragment
Figure 3 of PCR products of a fatal case of Clostridium difficile infection from Trinidad & Tobago. The isolated strain revealed the presence of the toxin B genes as indicated in lane 1. The patient produced a 204bp band on a 1% agar gel, using a 1kb ladder.
EVOLUTION OF RELATIONSHIP BETWEEN INCREASED DEMAND OF INSULIN SECRETION AND INCREASED LEVEL OF PROINSULIN IN BLOOD OF PATIENT OF DIABETES MELLITUS 2

Article Review By Dr. Madhumati Varma, India
(DNB Family Medicine, MMSc in Diabetology Student of Texila American University)
Email: - madhumativarma@gmail.com

SOURCE


REVIEW OF LITERATURE

The Insulin resistant triggered by high proinsulin to insulin ratio which is associated with NIDDM( 1 ). Elevated intact proinsulin seems to indicate an advanced stage of β-cell exhaustion and is a highly specific marker for insulin resistance. It might be used as arbitrary marker for the therapeutic decision between secretagogue, sensitizer, or insulin therapy in type 2 diabetes( 2 ).
In DM2, insulin processing deficient. There is an increased proinsulin:insulin ratio( 3 ). Changes in proinsulin levels are associated with diabetes.

Random proinsulin levels and the proinsulin-to-C-peptide ratio represent dynamic markers of the state of β-cell function that complement immune markers in identifying relatives who are at high risk of contracting type 1 diabetes( 4 ). Proinsulin is a very sensitive marker of beta cell exhaustion and may therefore be useful for therapeutic decision-making in type 2 diabetes ( 5 ).
IDDM in humans and in non-obese diabetic (NOD) mice is a T-cell–dependent autoimmune disease in which the β-cells of the pancreatic islets are destroyed.

Several putative β-cell auto antigens have been identified, but insulin and its precursor, proinsulin, are the only ones that are β-cell specific.(6), his assay allows for a pathophysiological
staging of type 2 diabetes based on beta-cell secretion. It could be confirmed by a large epidemiological study (IRIS-2, 4,265 patients) that intact proinsulin is a highly specific marker for insulin resistance. It could also be shown in other studies that successful resistance treatment with insulin or glitazones led to a decrease in elevated proinsulin levels and, thus, to a decrease of cardiovascular risk, while the levels remained high during sulfonylurea therapy.

Therefore, patients with increased fasting intact proinsulin values should be treated with a therapy focusing on insulin resistance. Assessment of beta-cell function by determination of intact proinsulin may facilitate the selection of the most promising therapy and may also serve to monitor treatment success in the further course of the disease.(7).

**KEYWORDS**

Insulin, Proinsulin ratio, Endocrinology, Ampullary Cancer, Venous Blood, Immune System

**INTRODUCTION**

In a healthy population, glucose is controlled by Insulin. When secretion of Insulin increased on in circumstances like stress, operation, resection of some part of pancreas with resection and B cells, destruction of due to auto antigens, increase release reserve insulin form of proinsulin which increase resistance of periphery of receptor of insulin on cells which prohibits enter glucose in cell for utilization and this develops Insulin resistance other name called Diabetes type 2.

This study was done after pancreatectomy where reduced mass of pancreas but not effect to increase level of proinsulin but when increase demand of insulin secretion of increases that time increase level of proinsulin in blood and increase ratio of Proinsulin on Insulin which indicate Insulin resistant Diabetes Mellitus 2,Proinsulin is immature insulin precursors and insulin is mature .after somatostatine infusion improves Hyperproinsulinemia and ratio of proinsulin to insulin and also in .

Diabetes type 2 show advance stage of B cell exhaustion and marker of insulin resistance and indicate treatment of sensitizer therapy or insulin. Proinsulin, a major β cell protein, is the only autoantigen that is almost exclusively expressed in β cells
ARTICLE SUMMARY

The study shows that when reduces b cell mass which results decreased insulin secretion but increase proinsulin concentration both total and intact results impairment of insulin secretion an action of insulin. Proinsulin ratio increase mostly in obese patient and high risk of DM 2. The proinsulin increase when increase demand of secretion of insulin in DM 2.

This study show three principle pointes

1) There is absolute or relative increase of proinsulin in blood with patient of secondary Diabetes.

2) When the function of b-cell declines level of proinsulin increases in blood, it is measured by HOMA index camper to B-cell area

3) There is not strong relation between Insulin resistance and proinsulin level in blood.

Proinsulin Insulin ratio improves after Somatostatin, Metformin, Thizoliinedione, relative reduction of proinsulin level but increase proinsulin/insulin ratio after sulphonylureas. The study shows lower proinsulin level indicate HOMA index improvement but b-cell mass negligible. There is positive relationship between proinsulin and insulin resistance. The fasting insulin level in both Matsuda Index of insulin sensitivity and HOMA index of insulin résistance moch close to proinsulin based parameter. Hyperproinsulinema is more close to functional defect rather than b-cell mass.

ARTICLE STRUCTURE

The article was initiated with Abstract in which clearly mentioned introduction, Patients and methods, Results, Conclusions. Idea well formed which author wanted to explain that Hyperproinsulinaemia is has direct relation with defects in insulin secretion rather than reduction in b-cell area. Introduction explained about mature insulin and immature proinsulin. Ratio of Proinsulin/insulin normal in healthy people and increased ratio in secondary diabetes or in insulin resistance and DM type 2 but not related to mass of pancreas reseated.

Next explained types of taken spacemen and patients with diseases of pancreas which done resection of pancreas like chronic pancreatitis, pancreatic carcinoma, pancreatic adenoma or ampullary cancer and number of patient. There was paragraph of experimental procedures where clearly mention how to take a sample of venous blood for glucose tolerance.
The was next heading patients and methods, study design, pancreatic tissue processing, morphometric analysis, calculations and statistical analysis where explained kit of ELISA for proinsulin C-peptide and taken sample for histopathology and seen in microscope. Calculations and statistical analysis explained HOMA index was calculated for b-cell function linear or non-linear regression functions correlation analyses carried.

There was presented result between different type of patent proinsuline in graph form and quantitative analysis. Finally main objective of proinsulin/insulin ratio increase in insulin resisttanc Diabetes type2 rather than reduce b-cell mass discussed in discussion paragraph. At the end declaration of interest, funding, acknowledgements, references are written clearly.

AUTHORITY

This article published in European Journal of Endocrinology (2010). It is authentic journal and Thomas G K Breuer worked up this project in Ruhr-University Bochum, 44789. This article is authentic article and several references used which showed it unbiased authenticity. Author has academic background I working in university. There work in academic qualified study on patient in with patient and laboratory. It is valuable. This article as authority very strong academic of nature because is related to University of Germany and funded by authentic source and acknowledged.

ACCURACY

Source of information on study carried out I academic University of Germany is correct and accurate. But there is no literature review, conclusion mentioned in article. There is clear and good explanation about methodology, discussion, introduction. There are reference which shows accuracy. This project funded by Deutsche Forschungsgemeinschaft (DFG grant no. Me2096/5-1 to J J Meier) and the Ruhr-University of Bochum (FoRUM grants to J J Meier and acknowledged by Birgit Baller, Kirsten Mros, Heike Achner and Gudrun Muller.

PERIOD

Article Received on 21 June 2010. Accepted at 2 August 2010 so it is recent article.
It is published in European Journal of Endocrinology (2010). Which as resent article. This study is 4 years earlier published but received in June 2010. It shows is resent article.

**RELEVANCY**

This study done with a group of academic specialist in University. It is more relevant as done with funding and acknowledgement of authorized body and in academic and university level. There is references which interlinked and correlated to each other and study well organized relevant as done in University and academic level and published in relevant authentic journal of Endocrinology.

**OBJECTIVITY**

The article gives information is evidence based due to reference provided to use in study. There is no literature review. There objectivity clearly mentioned and acknowledge. This is very nicely explained objectivity to proinsulin and relation with Diabetes type 2.

Stability- About the stability of the article based on its publication. This is the source of academic database of the University and that is why it is stable database.

Analysis of graph/Image/Table – Brief analysis of the Graph/image/table

Following graphs and chart explain nicely

- Correlation analyses between the fasting insulin

- Concentrations and the Matsuda index of insulin sensitivity, Correlation analyses between total proinsulin

- Intact proinsulin, Correlation analyses between total proinsulin

- Correlation analyses between total proinsulin,

- Plasma concentrations of total proinsulin
RECENT ADVANCES RELATED TO THE TOPIC

When glucose increases, it simulate proinsulin formation by increasing PC3 biosynthesis. This is endopeptidase that regulate proinsulin secretion while insulin resistance in DM type 2 increase obesity and increase resistance of insulin on periphery. In type 1 diabetes (T1D), there is an intense inflammatory response that destroys the β cells in the pancreatic islets of Langerhans, the site where insulin is produced and released.

A therapy for T1D that targets the specific autoimmune response in this disease while leaving the remainder of the immune system intact, has long been sought. Proinsulin is a major target of the adaptive immune response in T1D. We hypothesized that an engineered DNA plasmid encoding proinsulin (BHT-3021) would preserve β cell function in T1D patients through reduction of insulin-specific CD8+ T cells.

CONCLUSION

The reviewed article ‘Proinsulin levels insulin secretion rather than pancreatic b-cell area’ has introduction, methodology, discussion and conclusion. The article has good academic background and stable article and accurate, but there is no literature review and conclusion. In a healthy population glucose is controlled by Insulin. When secretion of Insulin increased on in circumstances like stress, operation, resection of some part of pancreas with resection and B cells, destruction of due to auto antigens, increase release reserve insulin form of proinsulin which increase resistance of periphery of receptor of the insulin on cells which prohibits and enter glucose in cell for utilization and this develops Insulin resistance other name called Diabetes type 2.

There are study was done after pancreatectomy where reduced mass of pancreas but not effect to increase level of proinsulin but when increase demand of insulin secretion of increases that time increase level of proinsulin in blood and increase ratio of Proinsulin on Insulin which indicate Insulin resistant Diabetes Mellitus 2, Proinsulin is immature insulin precursors and insulin is mature .after somatostatine infusion improves Hyperproinsulinemia and ratio of proinsulin to insulin and also in .Diabetes type 2 show advance stage of B cell exhaustion and marker of insulin resistance and indicate treatment of sensitizer therapy or insulin. Proinsulin, a major β cell protein, is the only autoantigen that is almost exclusively expressed in β cells.
REFERENCE


5) http://care.diabetesjournals.org/content/27/3/682.abstra

6) www.raymondcheong.com/DB33%20-%20Diabetes,%20Insulin%20A

AN ASSESSMENT OF THE RATE AND PREDISPOSING FACTORS TO THE DEVELOPMENT OF BREAST ABSCESS AMONG LACTATING MOTHERS IN THE BATIBO HEALTH DISTRICT, NORTH WEST REGION, CAMEROON

A Case Study By Akwo Cyril Tabe-Tanyi ¹, Mirabel Ngoin ², Guyana

(¹ Assistant Professor-Microbiology; Texila American University Georgetown, Guyana
² St Louis University Institute of Health and Biomedical Sciences, Bamenda, Cameroon)

Email Id: - faculty.microblgy@tau.edu.gy

ABSTRACT

Lactation breast abscess is a painful, debilitating condition that if inappropriately managed, may lead women to discontinue breastfeeding prematurely. This study assessed the rate and predisposing factors to development of breast abscesses among 100 women in the Batibo Health District.

A structured questionnaire was used to collect socio-demographic and other data which was analyzed using the Statistical Package for Social Sciences (SPSS), version 16.0; SPSS inc. 38 of the 100 women were found to have had breast abscess giving a rate of 38%. Premature cessation of breastfeeding, refusal to breastfeed, excessive weight gain during pregnancy, and abrupt method of weaning were the major predisposing factors identified. Thus, breast abscesses occur among lactating mothers in the Batibo Health District.

KEY WORDS

Breast abscess, Lactation, Breast feeding, Predisposing, Weaning
INTRODUCTION

Breast abscess is a relatively rare but serious complication of mastitis that may occur during breastfeeding particularly in primiparous women. These abscesses can be clinically difficult to detect and to distinguish from mastitis especially when the abscess is small or when it is located deep within the breast (Cunningham et al., 1997).

Lactation mastitis is a painful debilitating condition that can adversely affect mothers in their effort to breast-feed their babies. Despite being a relatively common complication of lactation, surprisingly few studies documenting the incidence of and risk factors for the condition have been reported. Studies of inflammatory processes of the breast during lactation show an estimated incidence of between 2% and 33% (Foxman et al., 2002).

Some researchers have reported that delayed treatment of mastitis by antibiotic therapy is the major risk factor for the development of breast abscess (Marchant, 2002). Other researchers however suggest that this may not be the case because mastitis may be a self limiting disease in many cases (Fetherson, 2001).

The common problems that may arise during the breastfeeding period are breast engorgement, plugged duct, breast infection and lactation failure or insufficient milk supply and these are due to inadequate emptying of the breast, incorrect techniques, not frequent breastfeeding, breastfeeding on scheduled times, and use of food supplements. Absence of suckling due to various reasons is the most common for abandoning breastfeeding, which ultimately leads to lactation failure. Other reasons are glandular tissue problems, prior breast surgery and Sheehan’s syndrome (Mather, 1992).

Although seldom overtly referred to in ancient or modern texts on child birth, it may be assumed that child birth and the subsequent nutrition of the infant have been of the greatest political importance to all societies, reason being that without new well-nourished members, the societies ceases to exist.

The knowledge of breastfeeding practices embedded within ancient civilization was the knowledge gained through observation and cognition and its philosophy was the philosophy of nature. The knowledge of women was passed from generation to generation by the rhetoric which has been identified as the oldest and the most important tradition of human sciences (Kjorup and Torhell, 1999).

During the end of the 19th century, modern pediatry emerged as a medical specialty based primarily on its expertise in artificial feeding (Brosco, 1999). By the middle of the 20th century, the preparation of breast milk substitutes (Formula) had become an industry in which much research and monetary funds were invested. During this period, Benjamin Spock became a world
authority on all aspect of infant care. In his famous text, (Spock and Lowenberg, 1955), he seems to struggle with his convictions, passing backward and forward between allowing the baby to determine its feeding time and allowing the mother to make the decision whether to offer her baby the breast or not.

Breastfeeding problems appear to have been with humanity since mothers first put their babies to the breast (Fildes, 1986) including sore and damaged nipples, insufficient milk and stagnation of milk in the breast. This discomfort may be one of the major reasons for a mother to make a decision to wean her baby from the breast (WHO, 2000).

Towards the end of the 1990s, WHO and UNICEF brought to focus the problem of falling rates of breast feeding all over the industrialized world and the effect that this would inevitably have on the breastfeeding rate of the developing countries and thus on infant mortality rates (WHO and UNICEF, 1989). Thus WHO with its BFHI and ten steps to successful breastfeeding united research institutions in breastfeeding pedagogy and breastfeeding has become an important public health issue worldwide (Palma, 2004).

**BREASTFEEDING PRACTICES AND RISK OF BREAST ABSCESS DEVELOPMENT**

International agencies recommend breastfeeding initiation within less than 2 hours after delivery. According to Hartmann et al. (1985), following birth, the breast produce a thick yellowish fluid which is primarily colostrum which differs from mature milk; protein, fat soluble vitamins and minerals are present in higher concentration while fat and lactose are present in lower concentration. ADA notes that feeding colostrum reduces the risk of gastroenteritis, diarrheal disease, and respiratory disease.

WHO and UNICEF (1992) describe breastfeeding “on demand” as “mothers of normal babies who are breastfeeding should have no restriction placed on the frequency or length of their babies’ breastfeeds, they should breastfeed their babies whenever they are hungry or as the baby wants”. In their review of the available evidence, Weighert et al. (2005), note that milk production is dependent on a physiological feedback mechanism determined by the rate at which the breast is emptied. If the infant is breastfed according to a rigid schedule rather than on demand, the breast may be emptied less often leading to problems as breast engorgement, sore nipple and even to the development of breast abscess.

WHO, (2009), estimates that the incidences of breast abscess vary between 2.65% to 33%. The prevalence globally is approximately 10% in lactating women. In India, incidence of lactation breast abscess ranges from7-11%. The incidence of lactation failure was 15%, among them, 11%
had secondary lactation failure and 4% had primary lactation failure (Cregan, 2002). A study was conducted to assess the incidence of breast abscess among lactating women.

A structured telephone interview was conducted among 1193 primiparous women. The result showed that 207 (95% CI=0.14-0.98) women experienced mastitis and 150 (95% CI=1.6-6.7) women developed breast abscess. The study concluded that 72.4% of women with mastitis will develop breast abscess and the incidence of lactating breast abscess appear to be higher than reported in the past (Amir et al., 2004)

A study was conducted to assess the current status and causes of breast abscess. The samples were 299 Nigerian women whose medical records were analyzed and reviewed. The results revealed that lactation breast abscess constitute 95% while non-lactation breast abscess constitute only 5%. The high evidence of lactation breast abscess corresponded to low level of personal hygiene. The study concluded that the lactating women are more prone to breast abscess and should be educated about the importance of personal hygiene during breastfeeding periods (Efem, 1995).

Another study was conducted to assess the contributing factors and prevention of puerperal breast abscess among nursing women over a two year period during which 176 nursing women with breast infection was followed. Around 20.4% had breast abscess (P ≤ 0.05) and 18.8% had a history of cracked nipples prior to the infection. The study revealed that milk stasis due to inadequate emptying of the breast lead to breast abscess formation. The study concluded that early identification would prevent breast abscess formation (Devereux, 1970).

A study was conducted to assess the association between excessive weights gained during pregnancy with early termination of breastfeeding. Around 2,783 women were included in the study. Their medical records were reviewed and categorized on BMI. less than 19.8/m2 was considered as underweight, 19.8-26 kg/m2 as normal, 26.1 to 29 kg/m2 as overweight and >29 kg/m2 as obese.

The result revealed that 30% women were underweight (P < 0.05), 30% were overweight (P < 0.05), 20% were obese and 20% were normal. So women who were overweight and obese had lactation failure (P < 0.01) which led to earlier termination of breast feeding. Thus, the study concluded that excessive weight gain during pregnancy led to lactation failure and hence women must be educated in weight management (Hilson and Rasmussen, 2006).

A prospective study was conducted to assess the incidence and causes of lactation failure among primigravid women. The study included 956 primigravid women and was given a leaflet explaining the objectives of the study and questionnaire was used to fill the data. The results revealed that out of 956 women, 788 had normal breast (80.3%), 188(19.7%) had breast problems like flat or inverted nipples, fissured nipples, breast surgery, tubular breast deformity
were the recognized causes. The incidence of lactation failure among women with these abnormalities was 9.8% (P≤0.005). The study concluded that nipple and breast abnormalities were recognized causes of feeding problems leading to lactation failure and intervention should be taken to identify and correct abnormalities of nipple or breast abnormalities in antenatal period (Sajeewa, 2006).

The recommended management of lactation failure is usually conservative with key recommendations being that mothers continue to breast feed frequently from the affected breast or expressed milk from the affected breast in an effort to clear blocked ducts and engorgement (WHO, 2000). However, one in every ten affected women were advised inappropriately either to stop breastfeeding from the affected breast or to stop breastfeeding all together. Despite being a relatively common complication of lactation, surprisingly few studies documenting the incidence of and risk factors for the condition have been reported.

The incidence of mastitis following delivery also depends on the frequency of breast-feeding. In the geographical area of a study carried out by the national board of health and welfare, breast-feeding is nearly 95% of the mothers’ breast-feeding at the time their infant is two months old. All these factors are present in the area of study thus there is a need to carry out a study on the rate and predisposing factors to breast abscess in the area.

STATEMENT OF THE PROBLEM

Incidence of breastfeeding is declining in almost all parts of the world despite all its nutritional and immunological benefits. Breast infection most commonly occur during pregnancy and lactation which may or may not be cyclical and may or may not be associated with nodules. Breast infection is a common problem among lactating mothers and has a wider spectrum ranging from localized cellulitis to abscess formation. WHO estimated that incidence of breast abscess vary between 2.65%-33% with prevalence globally about 10% in lactating women indicating a decline in breastfeeding practices in the urban area of developing countries.

Research into breast inflammation during lactation has drawn attention to the fact that scientific evidence for the best care of these mothers is lacking. Empirical evidence is very limited and there are suggestions that breast abscess during lactation may occur without a forgoing episode of breast inflammation/mastitis. Despite being a relatively common complication of lactation, surprisingly few studies documenting the incidence of and risk factors for the condition have been reported. This result shows that although breast-feeding may be widespread in Cameroon, there is a big need to provide accurate information on proper breast-feeding practices and weaning.
MAIN OBJECTIVE

To assess the rate and predisposing factors to the development of breast abscess among lactating mothers in the Batibo Health District.

SPECIFIC OBJECTIVES

1. To assess the rate of occurrence of breast abscess among lactating mothers in the Batibo Health District.
2. To evaluate the predisposing factors to breast abscess among lactating mothers in the Batibo Health District.

HYPOTHESIS

Breast abscesses occur in lactating mothers in Batibo Health District.

SIGNIFICANCE OF THE STUDY

- Identification of factors other than current breast-feeding practices may increase understanding of the etiology of the disease and suggest more preventive measures for specific groups of women.
- It aims to improve the knowledge of breastfeeding on the part of nurse practitioners enabling them to be more explicit during education.
- To health departments in charge of sensitization of the public about breastfeeding and its relationship to breast abscess in that more information will be set out to enable people especially lactating mothers becoming aware and so put in measures to prevent it.

STUDY AREA AND DESIGN

The research design was a descriptive cross sectional study among lactating mothers in the Batibo Health District, with Batibo District Hospital being the hosting hospital for the research. The Batibo Health District is made up of 71 000 inhabitants and 22 health centers. It shares boundaries with Bali (Mezam), Widikum, Njie, and Mbengwi (Momo) in the North- West region; upper Bayang (Manyu), Wabane (Lebialen) in the South- West region. The main activity
here is farming with others including palm wine tapping and palm oil production of which they export 70% of it.

**STUDY POPULATION**

This study included lactating mothers attending the Batibo District Hospital. Targeted population was 71 lactating mothers of which 100 lactating mothers were recruited and involved in the study.

**DATA COLLECTION**

A well structured pre-tested questionnaire with close ended questions was filled up for data collection by interviewing on various socio-demographic variables and breast-feeding attitude. Data was keyed into data log book and later transferred to excel worksheet for analysis.

**DATA ANALYSIS AND PRESENTATION**

Data were analyzed that is compiled, edited and presented by frequency distribution table using the software the Statistical Package for Social Sciences (SPSS for Windows version 16.0 by SPSS Inc). Significance of variables was established using Pearson Chi-square test with p value calculated with 95% CI and those less than or equal to 0.05 considered statistically significant.

**CRITERIA FOR THE SELECTION OF PARTICIPANTS**

**Inclusion Criteria**

Mothers who;
- Were from selected health areas in Batibo urban
- Were willing to participate
- Were available at the time of data collection
- Answered questionnaire

**Exclusion Criteria**

Mothers who;
- Were not from selected health areas in Batibo Urban
- Were not willing to participate
- Were not available at the time of data collection
- Did not answer questionnaire
Ethical considerations

- A written permission from the school authority was obtained prior to the study.
- Permission was also obtained from the authority of the hospital
- Consent was taken from the clients before conducting the study
- Confidentiality of the subjects was maintained

RESULTS

This study assessed the breast abscess rate and predisposing factors among lactating mothers in Batibo Health District. During this study, 100 breast feeding mothers were identified. Of these, 38 women had breast abscess giving a rate of 38%.

<table>
<thead>
<tr>
<th>n=38</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breastabscessyes</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>no</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1 Distribution according to the rate of breastabscess occurrence.

DISTRIBUTION OF WOMEN WITH BREAST ABSCESS ACCORDING TO DEMOGRAPHIC DATA OF PARTICIPANTS

38 women with breast abscess were of the adulthood age group. Majority of women with breast abscess were married (79%) while 21% of the women with breast abscess were single. This difference was however not statistically significant (p<0.05). Also, majority ended at the primary level of education (68.4%) while only 5.3% had attained tertiary level of education. This difference was also not statistically significant (P>0.05). Out of the 38 women with breast abscess, the majority 18 (47.4%) were primiparous, 9 (27.7%) had two children while 11 (28.9%) had three children. This difference was statistically significant (p=0.023).

<table>
<thead>
<tr>
<th>n=38</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Person chi-square test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Adulthood</td>
<td>38</td>
<td>100.0</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married</td>
<td>30</td>
<td>79.0</td>
</tr>
<tr>
<td></td>
<td>Single</td>
<td>8</td>
<td>21.1</td>
</tr>
<tr>
<td>Level of education</td>
<td>Primary</td>
<td>26</td>
<td>68.4</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>10</td>
<td>26.3</td>
</tr>
</tbody>
</table>
Majority of the women generate their income from farming (65%) followed by business (28.9%) then government employed (5.3%). The difference was statistically significant (p=0.041).

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Frequency</th>
<th>percentage</th>
<th>Person chi-square test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farming</td>
<td>25</td>
<td>65.8</td>
<td></td>
</tr>
<tr>
<td>Business</td>
<td>11</td>
<td>28.9</td>
<td>0.041</td>
</tr>
<tr>
<td>Civil servant</td>
<td>2</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Distribution of women with breast abscess according to socioeconomic factor

DISTRIBUTION OF WOMEN WITH BREAST ABSCESS ACCORDING TO BREASTFEEDING ATTITUDE

Majority 20 (52.6) of the women with breast abscesses do not breast feed their child frequently and on demand while 18 (47.4%) did. This difference was not statistically significant (p>0.05). Also, majority of the women with breast abscess 20 (52.6%) gained excessive weight during pregnancy while 18 (47.4%) did not. This difference was not statistically significant (p>0.05). Majority initiated weaning at four months and above 24 (63.2%) while 14 (36.8%) initiated weaning at less than three months. Also, this difference was not statistically significant (p>0.05). Most of the women with breast abscess stopped breast feeding on a single day (57.9%) and 2 (5.3%) continued breastfeeding while introducing solid food. This difference was not statistically significant (p>0.05). Most of the women with breast abscess did not continue breastfeeding in case of an inflammation 27 (71.1%) while 11 (28.9%) continued breastfeeding. This difference was also not statistically significant (p>0.05).
DISCUSSION OF RESULTS

Breast abscess is a condition in which there is a collection of pus in the breast due to infection with *Staphylococcus aureus* with common signs and symptoms being an elevated temperature either estimated or measured as being >38°C, one or more of the constitutional symptoms of fever, body aches, headache and chills.

This study was done to determine the rate and predisposing factors to the development of breast abscess giving a rate of 38%. This rate is similar to that of 33% reported by WHO, 2009 but very different from 72.4% reported by Amir *et al.* (2004). This difference could be due to the fact that this and other earlier studies probably underestimated the incidence due to limitations in case ascertainment and the short time period that women were followed.

In general, incidence rates for mastitis are below 10% when medical records and women seeking medical advice are used as a source of data whereas incidence rates at around 20% and above are seen in studies where diagnosis based on self-reported symptoms (Fetherson, 1997).
An assessment of the demographic characteristics was done where in all participants (100%) in this study were of the adulthood age group of which majority of them were less than 24 years (63.2%) with the mean age of participants being approximately 26 years (range of 19-39 years).

According to Mathir et al. (1992), maternal age had a clear effect on abscess formation. They showed that, least risk of breast abscess was seen amongst mothers who were ≤ 24 years and a significantly increased risk amongst mothers ≥ 30 years. Kaufmann (1991), also notes that breast abscesses more prevalent among first time mothers and mothers over thirty years of age. He states that the advent of a new child always gives cause for the restructuring of one’s lifestyle.

It is possible that younger women are less set in their ways and more receptive to the babies demands to be fed at varying intervals and for varying lengths of time. Majority of the women with breast abscess ended at the primary level of education (68.5%) as such, failed to report to the hospital early enough for possible prevention of abscess formation but preferred self and traditional treatment including chewing of bitter cola reported by them where by failure of resolution resulted to seeking of medical care while already presenting with abscess.

Most of the women with breast abscess were first time mothers (44.4%). This is in line with the study of Sajeewa (2006), of which 80% first time mothers had breast problems like inverted nipples, fissured nipples, breast surgery resulting to lactation failure and breast abscess of which early identification during antenatal period would prevent the occurrence of the condition.

An assessment of breastfeeding attitude was also done of which majority of the women with breast abscess (52.6%) do not breast feed their children frequently and on demand. Weighert et al. (2005), noted that milk production is dependent on a physiological feedback mechanism determined by the rate at which the breast is emptied. Breast feeding the infant according to a tight schedule rather than on demand empties the breast less often leading to problems as breast engorgement, sore nipple and even to the development of breast abscess.

Most of the women with breast abscess gained excessive weight during pregnancy (52.6%). This is in line with Hilson and Rasmussen (2006), who reported that women who were overweight and obese (50%) had lactation failure which led to earlier termination of breast feeding resulting in breast abscess hence, educating women in weight management during pregnancy is important.

Also, a greater number of the women with breast abscess initiated weaning at four months and above (63.2%). This result is in line with that of Srivastava et al.(1994), who reported that 73% of mothers established breast feeding successfully but 27% of mothers terminated breastfeeding due to reasons like lactation failure and breast infection. Though majority initiated weaning at four months and above, majority stopped abruptly and on a single day (57.9%). Weighert et
al.(2005), noted that milk production is dependent on physiological feedback mechanism determined by the rate at which the breast is emptied.

Stopping breast feeding abruptly without gradually signaling the brain through reduced rate of sucking the child leads to continued milk production as though the child was still breast feeding. This results to milk stasis from inadequate emptying as stated by Devereux (1970), making abscess formation unavoidable. Majority of women with breast abscess stopped breast feeding in case of an inflammation (71.1%) of the breast presenting reasons such as once the breast is inflamed; the milk automatically becomes infected and bad for the health of the child since it will cause the child to be sick. This is opposed to the findings of Vogel et al. (2008), in which 89% of women with lactation mastitis continued breastfeeding.

CONCLUSION

Breast abscess occurs in lactating mothers in Batibo Health District. The findings of this study suggest that one in three women may develop lactation breast abscess giving a rate of 38%. Major predisposing factors identified include premature cessation of breastfeeding, refusal to breast-feed in case of inflammation of the breast, of which mothers unnecessarily deprive their infants of the known nutritional and immunological benefits of breast milk, excessive weight gain during pregnancy, and abrupt weaning from the breast.

RECOMMENDATIONS

Governments should implement programs through which regular seminars could be organized to enable health workers become aware of conditions that interfere with maternal and child health directly linked or not such as breast abscess to ensure that they educate these women extensively so that they are able to put in measures that will help reduce the incidence.

The hospital should endeavor to organize breast-feeding clinics through which they can better explain to these mothers the importance of breast-feeding as well as good breast-feeding attitudes so as to curb the occurrence of breast-feeding problems as engorgement, mastitis and breast abscess. This will also enable the hospital best capable of keeping track records on the incidence of the condition through which action to reduce it can be put in place based on their records.

Mothers should put in efforts in taking control of their health and that of their children by ensuring that they heed to the advice offered in the hospital and by reporting to the hospital for clarifications when in doubt for early correction of the doubt avoiding complications that may impair health.
LIMITATIONS OF THE STUDY

Firstly, women identified as cases through interview were only identified if they answered yes to having had breast abscess specifically. They were not asked if they had experienced any symptoms suggestive of breast abscess.

This study does not determine the overall rate of breast abscess among lactating women since only those who reported to the hospital for management were included in the study.

We relied only on the women’s judgment of gaining excessive weight during pregnancy since not all the women were admitted in the post natal ward as such; their BMI could not be gotten to confirm weight gain.

REFERENCES


32) WHO Global strategy on infant feeding, 2002.

PREVALENCE OF OCULAR MORBIDITIES AMONG SCHOOL CHILDREN IN A RURAL AREA OF SOUTH INDIA

A Case Study By Meundi AD, Athavale AV, Suruliraman SM, Anjan S, Gururaj MS, Dhabadi BB, Rekha R, India

(Department of Community Medicine, KVG Medical College, Sullia, D.K.District, Karnataka State, India)

E mail: anandmeundi@yahoo.com

ABSTRACT

Schools are ideal setting to implement screening services for eye healthcare program. We conducted a study in schools around the Primary Health Centre Sampaje which is under the KVG Medical College, Sullia with objectives of appraising various ocular symptoms in the children and studying the prevalence of refractive errors, squint, vitamin A deficiency, conjunctivitis and color blindness among the children.

This was a cross sectional study conducted between July and October 2009 using a predesigned structured questionnaire and ocular examination on a total number of 1938 students attending 30 schools in the Sampaje Primary Health Centre (PHC) area. Prevalence of total ocular morbidity was 20.12% of which Refractive errors constituted 17.1%. (Myopia 16.9% and Hyperopia 0.20%), Squint 2.1%, Vitamin A deficiency 0.6%, Conjunctivitis and Color blindness 0.5%. An alarming prevalence of ocular morbidity of about 20% was demonstrated in the present study.

Also, since majority of children (76%) with ocular morbidity in the present study were asymptomatic, the need for active screening of all school going children for the various ocular morbidities is imperative.

KEYWORDS

Ocular symptoms, Refractive errors, Rural school children, India
INTRODUCTION

A large proportion (approximately 41%) of the over 1 billion population of India is aged younger than 16 years. Blindness and visual impairment in children is now recognized as a priority by blindness control programs including VISION 2020—The Right to Sight initiative. An estimated number of 200,000 to 300,000 children in India suffer from severe visual impairment or blindness. This represents only a small percentage of the estimated 5 million blind in India but it is significant in terms of ‘blind person years’.

Childhood blindness and visual loss will have an impact on the child’s development, education, future employment opportunities and quality of life leading to serious social & economic consequences on the family and the society. Fifty percent of all childhood blindness in India is preventable or treatable. Knowledge of the prevalence and causes of visual impairment and blindness is required especially in rural India. School is an ideal setting to implement screening services for eye healthcare program, especially in rural areas. Hence, this study was conducted to estimate the prevalence of ocular morbidity among rural school children.

METHODS

A cross-sectional study was conducted among school children of Sampaje Primary Health Centre area of Kodagu District (Karnataka State, South India) from the months of July to October 2009. The total population of Sampaje PHC is approximately 18,800. Languages spoken by the locals are Tulu and Kannada. There are 30 schools (27 Government and 3 Private). Out of 2090 students registered in all the schools, 1938 students who were present on the day of examination were included. The local district literacy rate is 82.5% and school enrolment proportion is 99%.

A pre-designed structured questionnaire based on the review of literature was used to interview the school children. The questionnaire included questions on detailed history about present and past ocular problems and treatment, history of any other medical or surgical treatment and family history. Questions were administered in Kannada, the local language, by trained medical interns. The questionnaire was pilot tested for comprehension on a group of 50 school children. For children between 5-7 years, parents were contacted for confirming the history given by the child. A standard examination procedure was used for each study subject.

Ocular examination included assessment of visual acuity for distance with Snellen’s chart at room illumination and for near with near vision test types. A pinhole test was followed by refraction under cyclopegia by an ophthalmic assistant to confirm presence of refractive error.
Ishihara’s chart was used to identify presence of color blindness and Axis deviation (squint) was assessed by torch light examination. Vitamin A deficiency diagnosis was made if child had history of night blindness, or on examination there were signs of conjunctival xerosis, Bitot's spots, corneal xerosis or keratomalacia. Examinations of the students were conducted after obtaining consent from the respective school authorities and parents.

All children identified with ocular morbidities were provided appropriate management through an ophthalmic assistant and/or an ophthalmologist. Ethical committee clearance was obtained from the ethics committee of KVGMc, Sullia (Institutional Review Board). Investigations were performed according to the guidelines of Declaration of Helsinki. Interviews were conducted before all ocular examinations. Statistical analysis was performed using SPSS Version 11.5. Chi-square test was used as test of significance of difference between proportions at 95% significance level.

RESULTS

A total of 1938 children attending 30 schools were screened. The age of children was in the range of 5 to 17 years. There were 1024 (52.8%) male children while 914 (47.2%) were females. The distribution of children by gender and education level is given in Table 1. Ocular symptoms were found only in 93 children (93/1938, 4.8%). However, a greater proportion of children (390/1938, 20.12%) presented with one or combination of ocular morbidities. Two hundred and ninety seven students who were identified with one or more ocular morbidities were asymptomatic (297/390, 76.1%). However a significantly greater proportion of children with ocular morbidity presented with symptoms (Table 2). The most common symptom (Table 3) was persistent headache (32/1938, 1.7%) followed by watering of eyes (29/1938, 1.5%).

Refractive errors were the commonest ocular morbidity and were seen in 17.3% (336/1938) of students, followed by squint, Vit. A deficiency, conjunctivitis and color blindness (Table 4). Out of the 336 children presenting with refractive errors, myopia was predominant (332/336, 98.8%) compared to hyperopia (4/336, 1.2%). Myopia was unioocular in 88 and binocular in 244 children (Table 5). Refractive errors did not differ significantly between the genders. Only a small proportion of myopics were symptomatic (16/332, 4.8%).

DISCUSSION

In all, 1938 school children were examined out of which 390 children were found to have one or the other ocular problems showing an ocular morbidity rate of 20.12%. Lower rates of ocular
morbidity has been reported by Kuruvilla et al10 (12.5%) in rural coastal area of Karnataka. Chaturvedi et al11 showed an ocular morbidity prevalence of 40% among school children in rural parts of Delhi whereas Madhu Gupta et al4 showed 31.6% in urban areas of Shimla. The present study showed lower prevalence of ocular morbidity compared to other studies done in north India.

It was observed that, of all the ocular morbidities, refractive error was the most common with a prevalence of 17.3% which is lower than the findings by Madhu Gupta et al4 (Shimla), Sethi et al12 (Ahmedabad) and Desai et al13 (Jodhpur) where the prevalence of refractive error was 22%, 25.31% and 20.8% respectively. The prevalence of squint as reported by Madhu Gupta et al4 (Shimla), of 2.5% is comparable to 2.1% prevalence in this study. However, higher (7.4%)14 and lower (0.215& 0.19%16) rates of squint have been reported from studies done in other parts of India. Vitamin A deficiency up to an extent of 5- 10.6%6, 11, 15 has been reported in various studies as compared to 0.6% in our study.

The lower rates may be due to better utilization of Vitamin A prophylaxis program and better nutrition (people in this region routinely consume green leafy vegetable called “basale” which is rich in vitamin A). Higher prevalence 3.27% of conjunctivitis has been seen in the past in a study conducted by Singh S et al16 in Patiala but a recent study2 showed a prevalence of 0.8% comparable to 0.5% in this study. In the present study, color blindness showed a prevalence of 0.5%. Identification of color vision defects in school children with concurrent vocational counseling can save the child the frustration later on and help him to choose a suitable vocation.

Apart from testing for refractive errors, (for which screening is already being done routinely in schools under the yearly medical examination in India) comprehensive ocular examination should be done at regular intervals and should be a prime component of school health program. The teachers have to be trained in recognizing common ocular symptoms among children so that they can be referred for further treatment.

CONCLUSIONS

In the present study, refractive error was the most common ocular disorder. The present study demonstrates a prevalence of ocular morbidity of about 20% among rural school children which is disturbing. However, the present study documented lower prevalence of various ocular morbidities compared to the other studies especially vitamin A deficiency and conjunctivitis. Majority of school children (76%) with ocular morbidity were asymptomatic. Therefore symptoms may not be good criteria to screen children for a detailed ophthalmic examination. School health programs should focus on early recognition of the ocular disorders by active screening of locally important ocular morbidities including refractive errors by trained teachers.
Ethical approval: Ethical approval was taken from the ethics committee of KVG Medical College. Informed consent was taken from school authorities.

Funding: None

Competing interests: None

Acknowledgements: None

REFERENCES


LEGEND FOR TABLES

TABLE 1. Distribution of the study population by gender and education.

TABLE 2. Proportion of children with ocular morbidities who were symptomatic in the study population.

TABLE 3. Prevalence (%) of ocular symptoms among total study population and symptomatics.

TABLE 4. Prevalence of ocular morbidity in the study population.

TABLE 5. Proportion of children having myopia and hyperopia in the study population.
### TABLE 1. Distribution of the study population by gender and education.

<table>
<thead>
<tr>
<th>Education levels</th>
<th>Total children N = 1938</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female n = 914(%)</td>
<td>Male n = 1024(%)</td>
</tr>
<tr>
<td>Primary school</td>
<td>376 (41.2)</td>
<td>366 (35.7)</td>
</tr>
<tr>
<td>Middle school</td>
<td>322 (35.2)</td>
<td>355 (34.7)</td>
</tr>
<tr>
<td>High school</td>
<td>216 (23.6)</td>
<td>303 (29.6)</td>
</tr>
<tr>
<td>Total</td>
<td>914(100)</td>
<td>1024(100)</td>
</tr>
</tbody>
</table>

### TABLE 2. Proportion of children with ocular morbidities who were symptomatic.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Ocular morbidity</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (%)</td>
<td>Absent (%)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>39(41.9)</td>
<td>54(58.1)</td>
</tr>
<tr>
<td>Non-symptomatic</td>
<td>351(19)</td>
<td>1494(81)</td>
</tr>
<tr>
<td>Total</td>
<td>390(20.1)</td>
<td>1548(79.9)</td>
</tr>
</tbody>
</table>

\( p < 0.01; \ X^2 = 28.913 ; \ df = 1 \)
TABLE 3. Prevalence (%) of ocular symptoms among total study population and symptomatics.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. Of children in the group</th>
<th>Among all children N=1938</th>
<th>Among symptomatics n=93</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent headache</td>
<td>32</td>
<td>1.7</td>
<td>34.4</td>
</tr>
<tr>
<td>Watering of eyes</td>
<td>29</td>
<td>1.5</td>
<td>31.2</td>
</tr>
<tr>
<td>Difficulty in reading blackboard</td>
<td>20</td>
<td>1.0</td>
<td>21.5</td>
</tr>
<tr>
<td>Difficulty in reading text book</td>
<td>9</td>
<td>0.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Redness of eyes</td>
<td>8</td>
<td>0.4</td>
<td>8.6</td>
</tr>
<tr>
<td>Difficulty of vision at night</td>
<td>1</td>
<td>0.05</td>
<td>1.1</td>
</tr>
</tbody>
</table>
### TABLE 4. Prevalence of ocular morbidity in the study population.

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 1938</td>
</tr>
<tr>
<td>Refractive errors</td>
<td>336 (17.3)</td>
</tr>
<tr>
<td>Squint</td>
<td>41 (2.1)</td>
</tr>
<tr>
<td>Vat. A deficiency signs</td>
<td>11 (0.6)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>10 (0.5)</td>
</tr>
<tr>
<td>Color blindness</td>
<td>10 (0.5)</td>
</tr>
</tbody>
</table>
**Table 5.** Proportion of children having myopia and hyperopia in the study population.

<table>
<thead>
<tr>
<th>Refractive errors</th>
<th>No. of children (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=1938</td>
<td></td>
</tr>
<tr>
<td><strong>Myopia</strong></td>
<td></td>
</tr>
<tr>
<td>Uniocular (88)</td>
<td>332 (17.1)</td>
</tr>
<tr>
<td>Binocular (244)</td>
<td></td>
</tr>
<tr>
<td><strong>Hyperopia</strong></td>
<td>4 (0.2)</td>
</tr>
</tbody>
</table>
ARTICLE REVIEW ON IMPROVEMENT OF EUSTACHIAN TUBE FUNCTION BY TISSUE-ENGINEERED REGENERATION OF MASTOID AIR CELLS

An Article Review By Dr. Muhammad Tariq Alvi, Saudi Arabia (Diploma in Otolaryngology, MS-ENT Student of Texila American University)
Email: kanemaru@ent.kuhp.kyoto-u.ac.jp

SOURCE:
Link: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3599483/

KEYWORDS
Eustachian tube, Mastoid cell, Function, Patient, Mastoidectomy, Regeneration therapy

INTRODUCTION
The review is a critical analysis of the article” Improvement of Eustachian Tube Function by Tissue-Engineered Regeneration of Mastoid Air Cells” published in the Laryngoscope.

In the review of this article, first to summarize it, then to analyze its print structure, keeping in view its layout and reader friendly ease. Lastly the review aims towards a critique analysis of the article evaluating its authority, currency, accuracy, objectivity and coverage. Any tables, graphs, diagrams and illustrations will also be analyzed.

ARTICLE SUMMARY
The purpose of this article is to assess the ability of regenerated mastoid air cells (MACs) to restore normal gas exchange function and helps to improve poor Eustachian tube (ET) function
in patients with chronic otitis media (COM) by using tissue engineering method [1]. This article comprises a prospective randomised control study of Seventy-six patients with COM, who received tympanoplasty with mastoidectomy and MAC regeneration therapy in a two-stage. During first stage artificial pneumatic bones were implanted and in second stage, a nitrous oxide (NO2) gas study was performed, both in patients with good MAC regeneration and with poor MAC regeneration to measure middle ear pressure (MEP). For the control group, MEP was also measured in patients with good MAC development during cochlear implantation or facial nerve decompression.

ET function was measured twice in each patient, once before the 1st operation and 6 months after the second operation. Recovery of mastoid aeration and regeneration of the pneumatic air cells were assessed by performing high resolution computed tomography (HRCT) scan images taken before and then 6 months after the operations, respectively [2]. Statistical analysis was carried out using SPSS software.

Results were analyzed using Chi- square test. P < 0.05 was taken as a level of statistical significance. The discussion include that most cases of COM shows poor development of MACs and poor ET function. Although tympanoplasty with mastoidectomy is presently the best operative treatment for COM but recurrence is very common even after operation. MEP is regulated not only by the ET but also by MACs. This article summarizes that tissue-engineered regeneration of MACs improves ET function and gas exchange in the middle ear and MEP increased in the group with good MAC regeneration after administration of N2O gas[3].

ARTICLE STRUCTURE:

The article is available as PubReader; ePub (beta) & PDF (629K)

The article was introduced with an Abstract including an Objective, Study design, Method, Result and Conclusion. The operative method for MAC regeneration has been described in details. The result has been elaborated by use of tables. The discussion on importance of MAC regeneration and its outcomes on ET function is promising. The online article links included Pubmed, MedGen and related citations. The full text version is free to users including PDF format printout. Previously one article on same topic, had also been published in same journal: Regeneration of mastoid air cells in clinical applications by in situ tissue engineering. Kanemaru S, Nakamura T, Omori K, Magrufov A, Yamashita M, Ito J. Laryngoscope. 2005 Feb; 115(2):253-8 [4].
ARTICLE CRITIQUE

AUTHORITY

Established in 1896, for more than 100 years, otolaryngologists, clinicians, and researchers around the world have read The Laryngoscope to keep pace with and learn how to take advantage of the most important advances in the diagnosis and treatment of head and neck disorders. This journal is the first choice among otolaryngologists to publish their most important findings and share their own successful techniques with their colleagues. This is the highest ranked otolaryngology journal, published monthly[5]. ISI Journal Citation Reports © Ranking: 2012: 7/44 (Otorhinolaryngology); 72/121 (Medicine Research & Experimental). Online ISSN: 1531-4995 [6].

The editor in chief include Prof Michael G. Stewart( MD, MPH). The assistant editor includes Prof Robert C. Kern, MD and others.

The author Shin-ichi Kanemaru has another publication in Journal of Tissue Engineering Regenerative Medicine named “Glottic regeneration with a tissue-engineering technique, using acellular extracellular matrix scaffold in a canine mode.“ recently published on January 8, 2014

ACCURACY

The article reveals that it is a prospective randomized control study. A prospective study is a cohort study that follows over time a group of similar individuals (cohorts) who differ with respect to certain factors under study, to determine how these factors affect rates of a certain outcome [7] and randomized control trial (RCT) name only for trials that contain control groups, in which groups receiving the experimental treatment are compared with control groups receiving no treatment (a placebo-controlled study) or a previously tested treatment (a positive-control study).

In prospective cohort study investigators begin enrolling subjects and baseline information is collected, after this subjects are then followed "longitudinally," i.e. over a period of time, usually for years, to determine if and when they become diseased and whether their exposure status changes. In this way, investigators can eventually use the data to answer many questions about the associations between ”risk factors” and disease outcomes. Prospective cohort studies are typically ranked higher in the hierarchy of evidence than retrospective cohort studies[3] and can be more expensive than a case–control study.
CURRENCY

This paper was presented at the Triology Annual Meeting, San Diego, California, U.S.A., April 18–22, 2012 and accepted on July 9, 2012. It was printed online on October 19, 2012. The research it describes is current and article cites references in body of text ranging from 1997-2010. The article has also been cited in the Laryngoscope February 2013; 123(2): 472–476.

RELEVANCE

This was a scientific journal on a scientific database. It was written to inform otolaryngologists and clinical researchers in visual science rather than to entertain, advertise or promote a particular brand. The article is of particular interest to any general otolaryngologist but particularly to a worker in the field of mastoid ear disease. This is an easy article to read and will be relevant to post graduate students of otolaryngology. This article will also be of special interest to the health workers in otolaryngology who deals many cases of intractable COM on daily basis, where simple tympanoplasty with mastiodectomy show poor development of MACs and poor ET function.

OBJECTIVITY

This article provides information of the latest evidence relating to the understanding of COM and its complications, current treatment strategies, their limitations, new areas of research regarding the importance of mastoid cells regeneration in management of the patients. The author’s further dwell upon two stage procedure for the development of MACs via by artificial pneumatic bone implantation followed by NO2 gas study. The article not only shows good MAC regeneration, but also correlates closely with recovery of ET function and gas exchange function. The information was well supported and with adequate sample size and with all evidence acknowledged and referenced. There is no evidence of bias, a fact that is reinforced by the recognition and inclusion of the article in one of the most prestigious peer reviewed journals of the subject.

STABILITY

The article with its source an internationally acclaimed scientific journal on an academic data base is stable as a resource. The article is also being cited in further research papers. The results
from the study undertaken are also fairly impressive and the trial was endorsed by an university of international repute.

**RECENT ADVANCES RELATED TO TOPIC**

A recent study “Development of a porous poly(DL-lactic acid-co-glycolic acid)-based scaffold for mastoid air-cell regeneration” done by Gould TW in the Division of Drug Delivery and Tissue Engineering, University of Nottingham, University Park, Nottingham, United Kingdom and published in the journal of Laryngoscope in Dec 2013[8]. This study related to in vitro development of a temperature-sensitive poly(DL-lactic acid-co-glycolic acid)/poly(ethylene glycol) (PLGA/PEG) scaffold for mastoid air-cell regeneration. This study demonstrates similar structural features to human mastoid bone, support cell growth, and display sustained antibiotic release. These scaffolds may be of potential clinical use in mastoid air-cell regeneration. But further in vivo studies are required to assess the suitability of PLGA/PEG-alginate scaffolds for this application.

**CONCLUSION**

This review has both, summarized and critically reviewed Shin-ichi Kanemaru article “Improvement of Eustachian Tube Function by Tissue-Engineered Regeneration of Mastoid Air Cells. The introductory links, structure, strength, accuracy and relevance of the article were analyzed and critiqued.

This article provides a review of the latest evidence for current treatment strategies, for intractable COM by the regeneration of mastoid air cells with tissue engineering methods. As this the most common cause of significant morbidity, and a leading cause of deafness all over world [9]. Although regenerated MACs can perform gas exchange function in the middle ear and improves ET function, besides that their function cannot reach the level of normally developed MACs. It is considered that mutualistic relationship exists between MAC function and the ET.

**REFERENCE:**


7) en.wikipedia.org/wiki/Prospective_cohort_study

8) www. laryngoscope.com

9) www.ncbi.nlm.nih.gov/…erm=Laryngoscope%5BJournal%5D
ROLE OF DIPEPTIDYL PEPTIDASE-4 INHIBITOR IN GLYCEMIC CONTROL AND CARDIOVASCULAR MORTALITY AND MORBIDITY

An Article Review By Dr. Shaikh Khalid Anwar, India
(PG Diploma in Diabetes, MMSc in Diabetology Student of Texila American University)
Email: drkhalids@gmail.com

SOURCE

KEYWORDS
Glycemic cycle, DPP-4, Amori, inhibitors, hypoglycemia, diabetes

REVIEW OF LITERATURE
DPP-4 inhibitors are one of the newer class drugs which have been claimed to have more efficacy and varied effect not only on the glycemic cycle but also on cardiovascular mortality and morbidity and weight control. There are many types of DPP-4 inhibitors but the commonly used ones are Sitagliptin, Vildagliptin and Saxagliptin each of them have different metabolism, dosage and excretion.

Studies have shown showed a variable reduction in HbA1c levels between 0.4 to 1.4 with different DPP-4 inhibitors. A study done by Amori et al showed a decrease of 0.74% in HbA1c with these drugs. This result proved that sulfonylureas were slightly more effective than DPP-4 inhibitors while being as effective as metformin and thiazolidinediones in reduction of blood glucose. In studies where DPP-4 inhibitors and metformin were used as a single tablet, the results were much better for two reasons, firstly, metformin has an positive regulating effect on the level of GLP-1, and hence it augments the effect of incretin on DPP-4 inhibitors. The second probable explanation for the positive results of the combined drug is that the patients are more compliant taking a single oral tablet instead of two.
Boschmann et al added that DPP-4 when inhibited accentuate the postprandial lipid causing it to be mobilized and oxidized it by activating the sympathetic system causing an indirect effect on the metabolic status. Matikainen et al explained that treatment with vildagliptin for 4 weeks improves the postprandial triglyceride and the apolipoprotein B-48 which contains triglyceriderich lipoprotein particle after taking a meal rich in fat in type 2 diabetes patients who were drug-naive patients.

Studies with DPP-4 inhibitors and its effect on patient weight showed variable results but in general they are weight neutral.

Commonly seen adverse effects in clinical trials were naso-pharyngitis, headache and upper respiratory tract infection. Pancreatitis is one suspected side effects of DPP-4 inhibitors. Sitagliptin causing pancreatitis has not been proved yet. Though, diabetes in itself is one of the risk factor for pancreatitis.

INTRODUCTION

I shall review this article mainly for its action on blood glucose levels and the cardiovascular system. In this article the author has elaborated only on three drugs namely Sitagliptin, Saxagliptin, and Vildagliptin.

Saxagliptin, Vildagliptin and Sitagliptins are different in their metabolism (Saxagliptin and Vildagliptin are metabolized in the liver while Sitagliptin is not metabolised in liver) their recommended dosage, excretion, and the daily dosage for effective treatment. But when compared to their efficacy regarding lowering the safety of the drug its HBA1c lowering effect and patient tolerance, all are almost same.

I shall look into the different studies which the author has taken as references to impress the usefulness of DPP-4 inhibitors in not only influencing the glycemic cycle but also the cardiovascular system and the weight neutrality.

I shall look into the different studies used as references by the author to prove his point.

A study done by Hsieh et al showed that inhibition of DPP-4, or increasing of GLP-1 receptor (GLP-1R) signaling, causes a decrease intestinal secretion of triacylglycerol, apolipoprotein B-48 and cholesterol. Further the endogenous GLP-1R signaling is required for the control of secretion and biosynthesis of intestinal lipoprotein.

These studies with other similar ongoing studies used by the author have impressed that the DPP-4 inhibitors group of drugs will has a beneficial effect not only on the glycemic control but also on cardiovascular system.
ARTICLE SUMMARY

DDP-4 are few of the newer generation of drugs which are showing effectiveness in not only controlling blood sugars but also having reasonable effect on cardiovascular system, blood pressure and other metabolism of the body.

Management of diabetic patients with these drugs from the incretin family is one of the latest addition in the group of oral anti diabetic medication which is as efficient as the other oral anti diabetic drugs, it is safer to treat with a DPP-4 inhibitor rather than a sulfonylurea when compared to the incidences of hypoglycemia. It can be used as a single drug or in combination with metformin. When wanting to choose between the GLP-1 analogues and the DPP-4 inhibitors, the physician should take into consideration the patient’s age, weight, compliance, the time from initial diagnosis of diabetes, and financial status.

In the older population the author has recommended the use of DPP-4 inhibitors for their confined effect in blood glucose lowering and no effect on caloric intake so less negative effect on the total body protein mass and the muscle. In young patients who have been newly diagnosed type 2 diabetes, abnormal metabolic profile, abdominal obesity, the physician should consider treating with a GLP-1 analogs as it will have a better effect in improving metabolic profile and weight reduction. DPP-4 inhibitors when used in low doses are safe for managing patients with moderate to severe renal failure, while GLP-1 analogs are contraindicated in these patients.

ARTICLE STRUCTURE

The author has presented this article and its relevant references and study in a very simple and narrative manner though with not much of visual statistics like graphs tables etc. but he has managed to impress upon the beneficial use of the three drugs Sitagliptin, Vildaglitin and Saxagliptin.

The author introduces the drugs when they were introduced in different part of the world and touches upon the metabolism and excretion. He further moves on to the effects of these three drugs on the glycemic cycle, cardiovascular action and weight reduction all of which he has authenticated by different studies.

The author has mentioned different studies which show the effect on HBA1c and that DPP-4 inhibitors are a little less effective than sulfonylureas but equally effective as thiazolideones and metformin in reducing blood glucose. But in studies where a combination of DPP-4 inhibitors and metformin in one tablet were used, the results were better.
Studies with regard to weight, DPP-4 inhibitors showed variable results but are usually considered to be neutral though some studies have shown a loss of weight for almost up to 1.8 kilogram.

Mistry et al. showed that sitagliptin had small but significant reductions statistically in systolic blood pressure varying between 2–3 mmHg and diastolic between 1.6–1.8 mmHg in a 24-hour blood pressure measured acutely in ambulatory patients on day 1 and on day 5 it showed a steady state in non-diabetics patients with mild to moderate hypertension.

Boschmann et al explained that DPP-4 inhibition increases postprandial mobilization and oxidation of lipid by activating the sympathetic system but not by a direct effect on metabolic status.

He has concluded with a comparison between DPP-4 and GLP-1 analogs where he has proved that GLP-1 analogs are a drug of choice in younger patients especially newly diagnosed while DPP-4 inhibitors are better suited for older patients.

ARTICLE CRITIQUE

AUTHORITY

The author Dror Dicker is working in Tel Aviv, Israel with Hasharon Hospital.

This publication is influenced on the presentations discussed in the 3rd World Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy).

The Congress itself and the publication were made in part by grants from Boehringer Ingelheim, Astra Zeneca, Daiichi Sankyo, Bristol-Myers Squibb, Eli Lilly, Ethicon Endo-Surgery, F. Hoffmann-La Roche, Janssen-Cilag, Generex Biotechnology, Johnson & Johnson, Medtronic, Pfizer and Novo Nordisk.

DOI: 10.2337/dc11-s229 © 2011 by the American Diabetes Association.

Dror Dicker has published many papers few of them are:

1. Increased Epicardial Adipose Tissue Thickness as a Predictor for Hypertension: A Cross-Sectional Observational Study by Dror Dicker, Eli Ata et al

2. Metabolic Syndrome Controversy by Dror Dicker - ESIM 2011
ACCURACY

The article has used different studies in the form meta-analysis, retrospective study, clinical trials and long-term prospective trial, this gives it substantial evidence based backup and enough weightage to be considered as an authentic article.

The author has used as references these studies from 2006-2009. The very fact that it is published in Diabetes Care which has a strong preview structure to publish any article in this journal. The authenticity is verified and only then it is published thus giving this article and the author a sort of authority on this topic.

So in conclusion it can be said the article is reasonably accurate.

WHETHER THE ARTICLE IS OLD / CURRENT

This article was published in the diabetes care issue of 2, May 2011 which is around 2 and a half year from now. DPP-4 has become one of the most popular drugs used in diabetes for its multicentric action. Though much work has been done on DPP-4, the studies and references used by the author in his article still holds good and there is no denial that these are evidence based which are supporting this article to prove its point. In recent years the cost effectiveness of this drug compared to a sulfonylurea or other oral hypoglycemic agents have been matter of discussion.

RELEVANCY

The title of DPP-4 Inhibitors and its Impact on glycemic control and cardiovascular risk factors does justify the information shared by the author. Though besides giving the different studies which have proved the actions and efficacy of DPP-4 inhibitors on glycemic control and cardiovascular effects he has also touched upon the weight loss or neutrality of these drugs.

He has compared DPP-4 inhibitors with GLP-1 analogs their effectiveness in different age groups ie younger and newly diagnosed show better response to GLP-1 analogs while older group benefit more with DPP-4 inhibitors and the reason behind their action which he has seconded by different studies. Though there is no reference of GLP-1 analogs in the title.

OBJECTIVITY

The author has objectively used different studies to prove his point about DPP-4 inhibitors and to some extent GLP-1 analogs. He has proved the usefulness of DDP-4 inhibitors in the glycemic cycle, cardiovascular action and weight effects with the use of different studies. It does not appear to be biased article though as mentioned by the author that this publication “on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)” was based on the presentations at the 3rd World Congress. Grants were given to the Congress and also for the
publication of this supplement from different pharmacological companies which could have been an influence.

**STABILITY**

The article has used recognised studies, references for describing DPP-4. He has mentioned that there is no conflicts of interest with regard to this article. Diabetes Care is one of the most respected journals in the field of diabetes and the article being published here gives it stability.

**ANALYSIS OF GRAPH/IMAGE/TABLE**

Not applicable.

**RECENT ADVANCES RELATED TO THE TOPIC**

An article published by Claire McDougall, Miles Fisher, Gerard A McKay-Fisher, Drugs for Diabetes: Part 5 DPP-4 Inhibitors in Medscape Br J Cardiol. 2011;18(3):130-132 showed that managing patients having type II diabetes, needs balancing potential benefits of controlling hyperglycaemia on microvascular and macrovascular complications, with possible side effects of treatment and possible harm from over intensive control of glycaemia.

In diabetes hypoglycaemia and weight gain are the undesirable side effects. The adverse effects of sulphonylureas, glitazones and insulin are all associated with weight gain, while metformin is good with causing slight weight loss. Meanwhile the DPP-4 inhibitors are weight neutral, causing neither weight loss nor weight gain.

Usually patients with type 2 diabetes are overweight or obese, thus DPP-4 inhibitors has a potential advantage over other drugs, and now DPP-4 inhibitors are being used as a second-line therapy in addition to metformin in overweight and obese patients who are unable to achieve glycaemic control with metformin monotherapy. The negligible incidences of hypoglycaemia are an additional advantage in the elderly patients or patients living alone.

Another article published by Sell, Henrike et al titled: Adipose Dipeptidyl Peptidase-4 and Obesity, Diabetes Care Issue: Volume 36(12), December 2013, p 4083–4090 showed a correlation with insulin resistance and depot-specific release from adipose tissue in vivo and in vitro has impressed upon DPP-4 an adipokine has a higher release from VAT that is particularly pronounced in obese and insulin resistant patients. The authors suggested that DPP4 maybe a marker for insulin resistance, visceral obesity and metabolic syndrome.

Most experts at the World Diabetes Congress 2013 have agreed that patients with type II diabetes who in the high risk for or who already have heart failure should not be precluded from receiving
DPP-4 inhibitor glucose-lowering agents, rather, they should be supervised closely for the initial 6 months of treatment, because the Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus — TIMI 53(SAVOR-TIMI 53) trial, reported that heart-failure was associated with the use of saxagliptin, appeared to occur in the initial 6 months of use of the drug(3).

CONCLUSION

This article brings home a very positive usefulness of DPP-4 inhibitors as one of the leading oral hypoglycemic agents available presently. The incretin family is choice in the management of diabetes. This treatment equally efficient as the other known oral anti diabetic drugs, further it is much safer than sulfonylurea with regard to hypoglycemia and hence can be used as a single drug theraopyrin combination with metformin. When choosing a drug to between a GLP-1 analogs and a DPP-4 inhibitors, one must consider different parameters such as the age of the patient, body weight, the time lapse from initial diagnosis of diabetes, financial status and compliance. Also one should consider that DPP-4 inhibitors in low doses can be safely used in patients with renal failure - moderate to severe, while GLP-1 analogs should be avoided in these patients.

The author has compiled different studies which are a mix of meta-analysis, retrospective studies and other references to prove his point about the efficacy of DPP-4, but still there is scope for more research to actually see the benefit of this drug.

The GLP-1 analogs are another newer group of drugs which are almost equally effective though even these needs more research.

Further the cost-effectiveness of DPP-4 is still a topic of discussion.

REFERENCE


INNOVATIVE PROPOSAL OF CARDIAC HAWK EYE TECHNOLOGY

An Article Review By Sumukha Prasad U & Prithvi Shankar N, India (B.E, (M Tech) in RVCE)
Email: - sumukhaprasad@gmail.com

SOURCE
The increase in death rate due to heart diseases is the main motivation for us to choose the cardiac field and propose a instrument which is easy to use and of low cost which helps in early detection of such diseases

ABSTRACT
Proposal mainly concentrates on the core problem on the early screening of cardiovascular diseases. With presently available instruments diagnosis of the heart diseases is possible, but the constraint that idea is focusing on, is the cost-effective method to be implemented in rural sector. The diagnosis method presently available is ECG, which cannot give the prior information of the disease but only depicts the present status and also for the analysis of the ECG signal a specialized doctor is required. Taking into consideration of disadvantages in the current instruments, a new proposal of module, which can overcome these problems being portrayed.

KEYWORDS
ECG, Cardio Vascular, Ultrasound, Doppler Effect.

INTRODUCTION
We are mainly concentrating on the core problem on the early screening of cardiovascular diseases. With presently available instruments diagnosis of the heart diseases is possible, but the constraint that we are focusing on, is the cost-effective method to be implemented in rural sector. The diagnosis method presently available is ECG, which cannot give the prior information of the disease but only depicts the present status and also for the analysis of the ECG signal a
specialized doctor is required. Taking into consideration the disadvantages in the currently present instruments we propose a new module, which can overcome the problems being faced.

Dibrid technology: The ECG is related to electrical activity of the heart any prominent changes can be observed only when heart is abnormal. In Doppler technology we can detect even minor blockages even before heart reaches abnormality. Based on the above facts we have decided to concatenate the above two working principles in our module which provides a better confirmed report based on the artificial intelligence algorithm.

The added advantage of this module is that we are able to bring in the history of the subjects status (thro’ ECG) and also the present scenario (thro’ Doppler image mapping) together which makes the database more stable for predicting the future.

EXISTING SOLUTIONS/PRIOR ART

For the detection of Cardiovascular diseases, the existing solutions being Electrocardiogram(ECG), Echocardiogram, Cartogram, Computerized Tomography Scan, Magnetic Resonance Imaging, CT Angiogram & Biomedical tests. (Most of these higher end systems use gamma rays, which are ionizing radiations that are very much harmful to the cardiac cells) ECG provides the net effective electrical activity of the heart.

Cardiogram, Cartogram, CT scan, MRI and others are imaging techniques used to obtain the topology of the heart. The implementation of these above mentioned sophisticated technique needs a specialist and highly skilled doctor who also needs a well equipped infrastructure in multi specialty hospitals.

PRIOR ART

Doppler Ultrasound (Echocardiography)

*Hardware Type:* Imaging Systems, Measurement Devices, Cardiovascular.

*Hardware Description:* An echocardiogram is a test that uses high-frequency sound waves (ultrasound) to create an image of the heart. Doppler is a special part of the ultrasound examination that assesses blood flow (direction and velocity). In contrast, the M- mode and 2-D Echo evaluates the size, thickness and movement of heart structures (chambers, valves, etc.). During the Doppler examination, the ultrasound beams will evaluate the flow of blood as it makes its way through and out of the heart. This information is presented visually on a monitor.
PROBLEM DEFINITION

When we look to the market statistics for technology the instruments are virtually unaffordable by common man. Nearly 1.2 million people lose their life suffering to cardiovascular diseases according to WHO statistics. In 2001 alone, some 7.1 million deaths were attributed to ischemic heart disease, 80% of which were in relatively poor countries. Medical and public health professionals expect that in developing countries, there will be a 137% and 120% increase in the disease for males and females, respectively, whereas these predictions lie in the 30% to 60% range for developed countries.

Cardiovascular disease is the world's leading killer, accounting for 16.7 million or 29.2 per cent of total global deaths in 2003. In India in the past five decades, rates of coronary disease among urban populations have risen from 4 per cent to 11 per cent. The World Health Organization (who) estimates that 60 per cent of the world's cardiac patients will be Indian by 2010. India lost more than five times as many years of economically productive life to cardiovascular disease than did the U.S., where most of those killed by heart disease are above retirement age. Cardiovascular diseases are not like spurs that suddenly emerge. They are the result of prolonged encroachment of heart territories by anti-cardiac materials.

Hence a prior knowledge of degree of encroachment can help in predicting future implications and also can guide us with precautionary measures. For all these early screening and regular monitoring of the subject is very much essential.

In problem statement for screening of cardiovascular diseases, the present existing technologies being blood tests, Stethoscope & blood pressure, ECG recorders are commonly available tools with practitioners by which we cannot come to the perfect conclusions so as to which part of the heart is affected. So as to find out the perfect infected mapping, sophisticated design tools are used in super specialty hospitals in urban area, whereas the implementation of these techniques are mere impossible in rural areas (which constitute more than 50% of the population as of now!).

The reason being, modern well equipped instruments fail as it needs specialist doctors, well established infrastructure lab facilities, high power consumption & very expensive treatment. Problems like Myocardial infarction, Valves abnormalities, Arteries blockage, Ischemic conditions needs to be screened at early stages for saving life.

Cost effective, accurate, low skilled manpower, unreliable infrastructure, time restraining capability and future predicting facility are some of the pre-requisites that have to be considered while designing an innovative module to be implemented in rural sector. By achieving the above qualities early detection of infections will be possible. The existing Doppler module is capable of
scanning the whole body but for the problem under consideration an overview of heart is sufficient.

**CASE STUDY**

Through this case study we are trying to explain the problem encountered in the existing technology. This heart problem was diagnosed by ECG only when the patient complained about uneasiness, chest pain and breathlessness.

The report of this case is produced below:
PROPOSED IDEA

Considering the pre-requisites highlighted in the problem statement a new model is proposed here. Dual technology of Image processing and Signal processing is the best fit Engineering idea for this problem statement. This technology provides an accurate method for the early screening of cardiovascular diseases. A handy module which processes on the simpler artificial intelligence algorithm, estimates the output based on the supportive methods of image and signal processing, this makes the analysis of heart more accurate.

THE MODULE DESCRIPTION

The module is embedded with a gigahertz processor which handles the signal computation of both domains and can make the comparative analysis of the infected heart with the regular condition by using the artificial intelligence algorithm implementation. The lateral tube in the module is provided with a gel fluid for the frictionless scanning process. Backside of the module is mounted with 3-Dimensional color Doppler sensors which can scan the heart within few seconds by physically moving on the chest region. Simultaneously the 6 wireless chest leads and 4 wireless limb lead electrodes are used to collect the net electrical activity of the heart and blood pressure.

The parallel analysis computing of image and electrical activity of heart will come to an accurate conclusion by the processor. The result is compared with the regular normal heart parameters by
implementing it through artificial intelligence algorithm. The response of AI software will point the exact problem location in the heart and it will be displayed on the flip screen monitor.

**THE PROPOSED IDEOLOGY OF THE MODULE SHOWN AS ALGORITHM**

*Step 1:* Image acquisition using 3D image color Doppler sensor (Transducer) providing input signal to the processor for computation.

*Step 2:* Simultaneously Net electrical signal acquisition using wireless electrodes, parallel computing as one more input signal for the processor.

*Step 3:* Comparative study of acquired signals with regular standard patterns and processing of the signal by the gigahertz processor.

*Step 4:* Artificial intelligence comparative processing and followed by simple yes-no questioning based on the history, physical features, habits of smoking and alcoholism, appearing on the flip monitor.

*Step 5:* Based on the percentage infection of cardiac in early screening method is displayed on the screen which is in the regular understandable format for the layman.

*Step 6:* Upgradation of this scheme on to the going forward plan is extension of making the output transmitting it to the nearest cardiac care centers (Telemedicine) and help for further treatment.

**THE PROPOSED IDEOLOGY OF THE AI ALGORITHM**

*Step 1:* The processed signal is the input feed for the simulation AI logic.

*Step 2:* The data comparison between the processed data and the standard pattern, giving the conclusion of response based on the major abnormalities declaring it as a ‘Critical Cardiovascular disease’.

*Step 3:* If there are limited section variations with the parameters of heart signals, continuing the logic with simple yes-no questionings related to history of person, Body mass index, blood pressure, stressful life, symptoms based, geographical area.
**Step 4:** Based on the reasoning’s of the individual the final report is proposed by our AI algorithm.

**Step 5:** Confirmed report is displayed on the screen.

**Interpretation of artificial intelligence algorithm:**
NOVELTY OF IDEA

The response of the existing technology instruments fails as signal needs backend processing consuming more time to give its analysis report, and also result needs to be certified by a cardio specialist. These disadvantages of existing systems stacks up as major failure, finds very difficulty in implementing in rural sector with limited set of facilities or even no facility sometimes. The proposed model can be a replacement for all impediments mentioned above. The need for fewer infrastructures, accurate results within no time, cost effectiveness makes the module novel from the existing modules. Cardiac Hawk Eye Instrument is a customer friendly device which discards the need of a skilled technician for its operation. This aspect of the module enhances its novelty.
DIFFERENCES BETWEEN PROPOSED SOLUTIONS AND EXISTING SOLUTIONS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Proposed Solutions</th>
<th>Existing Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Domain analysis</td>
<td>Combinational method of image and signal processing.</td>
<td>Any single domain analysis.</td>
</tr>
<tr>
<td>Early screening of cardiovascular diseases</td>
<td>It is designed for the same purpose.</td>
<td>It is designed for later stage purpose.</td>
</tr>
<tr>
<td>Time efficient</td>
<td>It’s very much fast as it uses gigahertz processor, very much time saving.</td>
<td>It needs more time for the diagnosis.</td>
</tr>
<tr>
<td>Reliable screening for large population</td>
<td>As it is a hand held device, which is reliable to screen large population.</td>
<td>As the device structures are complex, not possible to screen large population.</td>
</tr>
<tr>
<td>Cost effective</td>
<td>The module is handy and simple, which is cost effective to be implemented in rural sectors.</td>
<td>The module cost is very much expensive to afford and meet the requirements of rural.</td>
</tr>
<tr>
<td>Skilled Manpower</td>
<td>No need of specialist skilled people. Low-skilled manpower is sufficient.</td>
<td>Expertise and specialist Manpower is very much essential.</td>
</tr>
<tr>
<td>Infrastructure (Electricity, Lab facilities)</td>
<td>Low infrastructural facility. The module is battery operated, and no need of much equipped lab facility.</td>
<td>High sophisticated infrastructural facility is needed.</td>
</tr>
<tr>
<td>Equipment design</td>
<td>Simpler module design.</td>
<td>Complex module design.</td>
</tr>
<tr>
<td>Rural sector implementation</td>
<td>Best fit solution for implementation in rural.</td>
<td>Difficult for rural implementation as of now.</td>
</tr>
<tr>
<td>Accuracy in early screening of diseases</td>
<td>More accurate result for the early symptoms.</td>
<td>Most accurate for the whole treatment process.</td>
</tr>
</tbody>
</table>
ADVANTAGE OF OUR INNOVATIVE MODULE USING A COLOR DOPPLER IMAGE ACQUISITION TECHNIQUE OVER EXISTING

A Doppler sensor (transducer) evaluates BP as it scans through the blood vessels. It helps consumer to evaluate blood flow through the major arteries and veins of heart. It can show blocked or reduced blood flow through narrowing in the major arteries. It also can reveal blood clots in veins that could obstruct and block blood flow. Doppler test may be used to look at blood flow in an unborn baby as well.

During Doppler test, a handheld instrument (transducer) is passed lightly over the chest region. The transducer sends and receives waves that are amplified. The waves bounce off solid objects, including blood cells. The movement of blood cells causes a change in pitch of the reflected waves (called the Doppler Effect). If there is no blood flow, the pitch does not change. Information from the reflected waves can be processed by a processor to provide graphs or pictures that represent the flow of blood through the blood vessels of heart, which also take parameters such as size of heart chambers, septum defects, bundle blockages, abnormal backward flow of blood through valves.

FEASIBILITY OF IDEA

The automatic comparative report study of the images and electrical activity of heart gives more justified accurate analysis. The image captured from the Doppler transducer is processed and compared with the regular, healthy heart parameters. These physical features comparisons will detect directly if there are any abnormalities such as; Enlargement of heart cavities, valves or arteries abnormalities, bundle blockages. The above impediments can be collectively depicted by the blood pressure and net electrical variations of heart. So both the image and signal
processing methods acts as a supportive accurate technology for detecting early symptoms of diseases.

The signal computation in the processor is based on the Artificial Intelligence algorithm, which will give directly confirmed report of early symptoms, if any. If there exists an ambiguity then passed on to the parameter questionings: history of person, Body mass index, blood pressure, stressful life, symptoms based, geographical area.

Based on the report of both the implementations a final confirmed conclusive report is obtained on the screen of the monitor. If the condition is more critical, all the heart parameters are transmitted wirelessly to the nearest cardiac care centers (implementation of tele-medicine), so easing for the early treatment of any such sensitive cardiac diseases.

The commercial risks for the time being are the success rate of the module design response and publicity features in rural sector. As the module design uses the lumped elements, replaceable processors with low-skilled can be achieved. The module is also easily replicable for the manufacturing so there is a less chance of service/maintenance risks.

**POTENTIAL IMPACT**

As mentioned the device is very much simple to handle and monitor, even a low-skilled person can operate on his own to check his own early diagnosis of his heart. The panel screen mounted on the top of the module will give all checked parameters in an understandable format for a common man so that he can contact the specialist doctors for his next stage of treatment. This is a “Life Saving” method which can be implemented in rural, so that he can change is diet and regular life style preventing him from suffering cardiovascular diseases in future. The technology supports “Prevention is better than Cure”.

**CUSTOMER VALUE / COMMERCIALIZATION**

As the module is implemented with the processor technology with more justified results of problem prone area of heart, the analysis is cost-benefit in the commercial point of view. On large scale production of this analysis module costs less, which is the basic equation of economics.

This medical instrument has replaceable processors, so maintaining the product/service is not at all a big task. Since the module uses a present technology gigahertz processor, manufacturing is same as other products. The module is operated with chargeable batteries and mounted on top
with a flip open monitor screen for the display of the response of analysis. The testing circuits are given for each stage of circuit design, so that it’ll be easy for verifying the connectivity of each stage. The parallel processor, co-support is provided for standby condition and the processor is easily replaceable. Battery operated technique can be extended for solar charging.

**FUTURE SCOPE**

The implementation of this technology module can be extended for transmitting the processed signal to the nearest cardiac care centers or primary health care centers in rural for further treatment of the infection.

With slight modification in our module, interfacing with the printer is possible, by which the medical report having sophisticated parameters can be taken out for further reference (expert consultation). Key factor in implementation of this proposed technology for saving life within few minutes by early screening is justified. With the implementation of a buffer and a database management system, customer’s history can piled on. This can later be produced before the doctor for better interpretation of the symptoms. For security issue biometrics’ can be incorporated.

The same module can be upgraded to diagnose defects throughout the entire body.

**CONCLUSION**

The key aspect of our module is early screening method of cardiovascular diseases which uses a dibrid technology and gives more reliable analysis.

The most important conclusion is that the instrument is handy, reliable, cost-effective, time restraining, accurate, low infrastructure which meets all the requirements to be implemented in rural sector. The fundamentals which we considered were ECG and echocardiography which had defects in their own domains were rectified to highest degree by our module. The proposed module design is especially designed for the premature diagnosis of the cardiovascular symptoms, which has a mapping quantified method particularly applicable for the chest region. “If wealth is lost, nothing is lost – if health is lost, everything is lost, Health is wealth”. This innovative cardiac hawk eye is for “Helping and saving mankind and society”. 
ACKNOWLEDGEMENT

We greatly acknowledge the support of Dr. C.G. Prahalada Rao and Dr. N. Sriram, who have been source of motivation for us throughout the conduction of this research work in the health care. We also acknowledge with a deep sense of reverence, our gratitude towards Dr. Bharathi Bhat, Retired Professor, IIT Delhi who has been source of inspiration to choose research area.

REFERENCES


MEASLES, A DIMINISHING THREAT TO CHILD DEVELOPMENT IN NORTHERN REGION OF GHANA

A Case Study By Dr. Michael Wombeogo, Dominic Abugri, PhD, FWACN, MSc PH, Ghana
(Faculty at School of Medicine and Health Sciences, University for Development Studies)
Email:- mwombeogo@gmail.com

ABSTRACT

AIM: This research is aimed at assessing the level of threat measles infection has on child development in northern region of Ghana and its impact on child health in recent times.

METHODS AND SAMPLING: A sample size of 20 health professionals, comprising 15 Public Health Nurses and 5 Family Physicians were used. A convenient and purposive sampling method was used to gather data through interviews and from primary information sources. Data was analysed using Microsoft excel and word processing.

RESULTS/FINDINGS: The results show that the threat of measles infection in northern region is significantly reduced, recording three confirmed cases in 2011. The diminishing trend was acclaimed to be attributable to high level of cooperation from parents’ willingness to send their children out for vaccination and improved living standards of many Ghanaians, among others. These reasons notwithstanding, measles infection is still fluctuating from year to year.

CONCLUSION: Though the disease is fast diminishing, it still has a potential to escalate given that it shot from zero confirmed cases from 2010 to three confirmed cases in 2011.

KEYWORDS

Measles, Child Development, Diminishing, Threat, Northern Region
INTRODUCTION

Measles is ubiquitous, highly infectious disease affecting nearly every person in a given population by adolescence in the absence of immunization program. Measles is transmitted primarily from person-to-person. Measles can lead to widespread infection. This occurs in overcrowded families with infected member, early contact with the virus in high dosages through large respiratory droplets (Waterston, in Paget, 2003). In developed countries, complications occur in 10-15% of cases while in developing countries; up to 75% of cases may have one or more complications. The major causes of high case fatality are pneumonia and diarrhea. Measles can lead to lifelong disabilities including blindness, brain damage and deafness. High complications and fatality rates are associated with malnutrition, including vitamin A deficiency, poor sanitation and poor management of complications (WHO, 2009).

According to the World Health Organization (WHO, 2009), measles is a leading cause of vaccine-preventable childhood mortality. Worldwide, the fatality rate has been significantly reduced by a vaccination campaign led by partners in the Measles Initiative notably, the American Red Cross, the United Nations Foundation, UNICEF and the World Health Organization (WHO). Globally, measles fell 60% from an estimated 873,000 deaths in 1999 to 345,000 in 2005. Estimates for 2008 indicate deaths fell further to 164,000 globally, with 77% of the remaining measles deaths in 2008 occurring within the South-East Asian region (WHO, 2009).

Ghana developed a five-year rolling plan of accelerated control of measles in accordance with the WHO/AFRO EPI 5-year strategic plan (2001-2005), with a focus on reducing measles mortality to near zero. As at the third quarter of this year Ghana has recorded up to 246 confirmed cases of measles, forming an incidence rate of 1.81/100 0000 of target population. In 2011, Ghana as a country recorded 344 confirmed measles cases but dropped to 234 out of 646 suspected cases in 2012 (WHO, in Mohammed, 2013), indicating a significant drop of 46.75% within a period of one year.

WHO (2010) during its 63rd World Health Assembly placed a premium on a global target of 95% reduction in measles mortality by 2015 from the level seen in 2000 and towards eventual eradication after then. However, no specific global target date for eradication has yet been agreed upon.

The sole objective of this work is:

To assess whether or not measles infection as a vaccine preventable cause of child mortality still remains a threat to child development in the northern region of Ghana.
MATERIALS AND METHODS

STUDY DESIGN AND SAMPLING TECHNIQUE

This was a cross sectional survey aimed at proving that the quantum of threat measles in infection in northern of Ghana has been on a diminishing trend from 2005 to 2011. The study covers twenty districts of the northern regional health directorate. However, not all districts have public health physicians manning them. Out of the total of ten districts known to have district health directors who are public health physicians, five were purposively selected for convenience to take part in this study with their corresponding public health nurses. Therefore the sampling method adopted in this direction was a convenient and purposive sampling. The composition of the sample was 5 public health physicians and 15 public health nurses who were interviewed about the measles infection, its prevention and effects on child development in the northern region of Ghana. The data on measles infection was sourced from the annual reports of Ghana Health service (GHS) and World Health Organization (WHO) in the northern region of Ghana.

DATA COLLECTION

The data for the study was gathered by means of structured face to face interviews of public health physicians and nurses, reviews of annual reports of GHS and partners, notably WHO.

DATA ANALYSIS

The data collected was processed and entered into Microsoft excel and Word for statistical analysis. The analysed results were presented on tables and graphs as indicated below.

RESULTS

Table 1 below shows the results of the data collected on the annual surveillance of measles cases from 2005 to 2011. The figures on the table indicate that it was only in Chereponi that three measles cases were confirmed in 2011 in the whole of the region. It also shows that out of six suspected cases in the Tamale metropolis zero case was confirmed as indicated below (Table 1).

Table 2 and figure 1 below illustrate the pattern of discrepancies between suspected and confirmed cases from 2005 to 2011. Based on the above indicators, it can be deduced that suspected cases were relatively high across the years with corresponding confirmed cases much lower than the suspected cases. However, in the years 2008 and 2009 the confirmed cases were high as compared to the other years. The year 2009 recorded the highest of 38 confirmed cases than previous years. In 2007 and 2010, 29 and 41 were recorded as suspected cases. None of the
suspected cases in 2007 and 2010 was confirmed. 2011 recorded the list (20) in terms of cases suspected. Out of this, 3 of them were confirmed (Table 2)

Table 3 and figure 2 below illustrates a deep concern from all the respondents that despite the diminishing trends of the disease, it is still far from being eradicated and should be given the necessary serious attention. It equally shows that measles infection is no longer a serious threat but is still common among the people of the northern region (Table 3 and figure 2)

Table 4 and figure 3 below indicate that 100% of family physicians and over 90% public health nurses attribute the diminishing trend of measles threat in northern region to increased vaccination coverage, while 40% or less of both physicians and public health nurses think that improved living standards have contributed significantly to the fall in measles infection in the northern region of Ghana.

One important observation from figure 3 is the high level of cooperation from parents (between 60-80%) of both categories of respondents admitted that parents sent their children out for vaccination. This might have accounted for the significant increase in the vaccination coverage during the period in the region.

Despite the seemingly positive consensus on the downward trend of measles infection attributive to various factors, as high as 18-20% of total respondents intimated that possibly measles could have been a forgotten disease in the region had it not been the supply and use of low potent vaccines as indicated on the figure below (Table 4 and figure 3) Discussion

Cases were confirmed using IgM ELISA assays detection process to isolate anti measles IgM antibody in the patient’s blood. From the analysis of the data, suspected cases are high with very few corresponding confirmed cases except in some few years when a good number were confirmed.

It is inferred therefore that there might be a new condition similar to or mimicking measles. It could also be that there were no effective or enough diagnostic equipments to isolate the measles virus. This therefore calls for further research.

As evidenced on table 2 above, in the years 2008, confirmed cases shot up significantly from zero to 22 and in 2009 it rose from 28 to 38 while suspected cases in 2008 stood at 79, in 2009, it fell to 71. Since Ghana developed a five-year rolling plan of accelerated control of measles in accordance with the WHO/AFRO EPI 5-year strategic plan (2001-2005), the focus has been to reduce measles mortality to near zero.

Despite this initiative, the incidence of measles in the northern region of Ghana continues to experience diminishing but fluctuating trends. In 2009, confirmed cases shot up from 22 (27.8%
suspected cases) in 2008 to 38 (53.7% of suspected cases). However, in 2007 and 2010, there was no single confirmed case registered. This confirms the high coverage of target population vaccinated against the measles infection. High patronage of immunization days as illustrated on table 2 above, effective and efficient health education have contributed greatly to the dramatic decrease in confirmed cases.

However, as amply evidenced on figure 3 above, between 18 and 20 percent of respondents concurred that use of inactive vaccines might have accounted for the emergence of the few confirmed measles cases in 2011. One important deduction could be that the laboratories used were not well resourced to detect and confirm the measles cases. This also calls for further investigation.

**CONCLUSIONS**

The distribution of the suspected and confirmed cases shows great fluctuations in the incidence of measles infection despite the preventive measures put in place by the GHS to eradicate the disease. The findings however demonstrate that measles infection is fast diminishing its threat to child development in the northern region of Ghana. This notwithstanding, measles transmission is still possible and can affect unvaccinated children if not fully eradicated.

Despite the downward trend of measles infection, 2011 recorded 20 suspected cases with 3 of them confirmed. This development shows that in order to completely eradicate measles in the country, there is need for a shared responsibility. By this, everyone including health personnel must embark on health education on the effects of measles on child development and the benefits of measles vaccination to all people in Ghana, particularly at the rural areas. In addition, the cold chain system in transporting the vaccines should be improved upon to ensure that potent vaccines are continually inoculated into the children.

Batches of vaccines and the manufacturers should be duly noted so that expired vaccines are called back or changed to ensure that potency is not compromised. Records keeping should be properly adhered to since some information could be lost if proper documentations are not done.

**ACKNOWLEDGEMENTS**

I acknowledge the commitment and dedication of my former level 400 nursing students within Tamale for assisting me gather the data for this study. The regional Directorate of the Ghana Health Service, Northern region, Tamale and WHO regional office in Tamale, for providing material resources for this research. I am especially indebted to all health workers who
participated in the interview schedules to make this work a success. Above all I am grateful to God for His blessings.

CONFLICT OF INTEREST

I declare there is no any competing financial interest in relation to the work described. It is purely an academic work and a contribution to the body of knowledge.

TABLES

Table-1: Annual surveillance of measles cases from 2005-2011

<table>
<thead>
<tr>
<th>MEASLES SURVEILLANCE IN NORTHERN REGION</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
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<td>0</td>
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<td>9</td>
<td>5</td>
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<td>0</td>
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<td>2</td>
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<td>2</td>
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<td>1</td>
<td>2</td>
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<td>1</td>
</tr>
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<td>49</td>
<td>16</td>
<td>29</td>
<td>0</td>
<td>79</td>
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</table>

GHS Annual reports, northern regional health directorate, 2011
Table-2: The distribution of suspected and confirmed measles cases from 2005-2011

<table>
<thead>
<tr>
<th>Year</th>
<th>Suspected cases</th>
<th>Confirmed cases</th>
<th>% of confirmed cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>40</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>2006</td>
<td>49</td>
<td>16</td>
<td>32.7</td>
</tr>
<tr>
<td>2007</td>
<td>29</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2008</td>
<td>79</td>
<td>22</td>
<td>27.8</td>
</tr>
<tr>
<td>2009</td>
<td>71</td>
<td>38</td>
<td>53.5</td>
</tr>
<tr>
<td>2010</td>
<td>41</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2011</td>
<td>20</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

Table-3: Respondents’ views on whether or not measles infection is a threat to child development in northern region of Ghana

<table>
<thead>
<tr>
<th>Type of responses</th>
<th>Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Public Health Nurses</td>
</tr>
<tr>
<td>Measles infection is no longer common in the region</td>
<td>13</td>
</tr>
<tr>
<td>Measles infection is common in the region</td>
<td>1</td>
</tr>
<tr>
<td>Measles infection is still a threat to child development</td>
<td>6</td>
</tr>
<tr>
<td>Measles infection is no longer a serious threat</td>
<td>9</td>
</tr>
<tr>
<td>Measles infection must be given serious attention</td>
<td>14</td>
</tr>
<tr>
<td>Measles has been eradicated in northern region</td>
<td>0</td>
</tr>
</tbody>
</table>

Source: Author’s construct, 2013
Table-4: Respondents’ reasons given on whether or not measles infection is a threat to child development in northern region of Ghana

<table>
<thead>
<tr>
<th>Reasons given</th>
<th>Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Public health Nurses</td>
</tr>
<tr>
<td>Higher number of target population (0-14 yrs)</td>
<td>14</td>
</tr>
<tr>
<td>receive vaccinations</td>
<td></td>
</tr>
<tr>
<td>High potent vaccines</td>
<td>10</td>
</tr>
<tr>
<td>Low potent vaccines</td>
<td>2</td>
</tr>
<tr>
<td>High level of cooperation from parents</td>
<td>12</td>
</tr>
<tr>
<td>Quality health care provision</td>
<td>8</td>
</tr>
<tr>
<td>Improved living standards of Ghanaians</td>
<td>5</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
</tr>
</tbody>
</table>

Source: Author’s construct, 2013

FIGURES

Figure-1: Distribution of suspected and confirmed measles cases from 2005-2011
Figure-2: Respondents’ views on whether or not measles infection is a threat to child development in northern region of Ghana

![Bar chart showing respondents' views on whether or not measles infection is a threat to child development in northern region of Ghana.]

Figure-3: Respondents’ reasons given on whether or not measles infection is a threat to child development in northern region of Ghana

![Bar chart showing respondents' reasons given on whether or not measles infection is a threat to child development in northern region of Ghana.]

- Measles eradicated
- Measles needs attention
- Measles not a threat
- Measles still a threat
- Measles common
- Reduced infection

- Vaccination coverage
- High potent vaccines
- Low potency vaccines
-Parents' cooperation
- Quality Health care provision
- Standards
- Improved living

- Family Physicians
- Public Health Nurses
REFERENCES


ASSESSMENT OF COMMON ORAL AND DENTAL DISEASES AMONG PREGNANT WOMEN AT DHAKA CITY IN BANGLADESH

A Case Study By Mahmud SZ¹, Begum F³, Uddin MM²; Bangladesh

¹Dr. Shaikh Zakir Mahmud, BDS, MPH, Senior Medical Officer (Dental Surgeon), Ibrahim General Hospital-Mirpur, Dhaka, Bangladesh
²Dr. (Lt Col) Mohammad Mesbah Uddin, BDS, Consultant Dental Surgeon, Saba Dental Care, DOHS Baridhara, Dhaka, Bangladesh
³Dr. Ferdousi Begum, MBBS, DGO, MCPS, Consultant Gynecologist, Ibrahim General Hospital-Mirpur, Dhaka, Bangladesh

Email:- suman79_bd@yahoo.com

ABSTRACT

BACKGROUND: Globally, the oral health care for pregnant women is inadequate relating to education and health promotion sectors along with disparities in socio-economy and ethnicity. Neglected oral care often has long-term effects on our overall health, including the health of the baby during pregnancy. Serious problems like gingivitis and periodontal disease may also occur during this period as a result of neglected oral hygiene.

OBJECTIVE: This descriptive type of cross-sectional study was carried out to assess the pattern of common oral and dental diseases among pregnant women.

MATERIALS AND METHODS: A total 147 pregnant women attended at the selected hospital and healthcare centre of Dhaka city for routine checkup over a period of five months from September 2013 to January 2014 fulfilled the eligibility criteria were selected consecutively. Pre-tested semi structured interviewer administrated questionnaires were used to collect the information.

RESULTS: The study shows that most of the pregnant women (72%) age ranged from 20-24 years. Also, majority (88%) of them were housewives while only 11% were service holders with monthly family income of BDT≤10000 of more than half of the respondents (52%). Oral complaints found from the study were bleeding gums (78%), sensitive tooth (52%) and cavities (35%) respectively. In addition, 63% never access to their dentists throughout their whole life and only 6% visited their dentists at the time of pregnancy. Lastly, the frequency of oral diseases
revealed in this study was gingivitis (100%), dental caries (54%), dental erosion (52%), periodontitis (27%) and apthous ulcer (16%) respectively.

CONCLUSION: It can be said from the study that educational and occupational statuses of pregnant women in Bangladesh were not satisfactory. An extensive number of pregnant women did not seek oral health care during pregnancy. There is a need for further study on oral health status of the pregnant women to formulate appropriate oral health guidelines for better oral and dental health outcome.

KEY WORDS
Dental diseases, Oral Diseases, Pregnant Women

INTRODUCTION
Pregnancy is a major event in any woman’s life and is associated with physiological changes affecting especially the endocrine, cardiovascular and hematological systems, and often attitude, mood or behavior. The mouth serves as a mirror to general health and also as a portal for disease to the rest of the body. Since the old wives’ tale of “the loss of a tooth for every pregnancy”, oral health during pregnancy has long been a focus of interest.

Oral changes due to the complex physiologic alterations occurring in pregnancy are believed to be related to fluctuations in levels of estrogen and progesterone, leading to an increase in oral vasculature permeability and a decrease in host immune competence, thereby increasing susceptibility to oral infections. These changes include pregnancy gingivitis, benign oral gingival lesions, tooth mobility, tooth erosion, dental caries, and periodontitis.

Gingivitis is the most common oral disease in pregnancy in such situations. It is inflammation of the superficial gum tissue. During pregnancy, gingivitis is aggravated due to increase in hormone (estrogen and progesterone) levels, alteration in oral flora and a decreased immune response, thus reducing the body's ability to repair and maintain healthy gingival tissue. Many studies have reported an increase in subgingival growth of *Prevotella intermedia* during the 2nd trimester of pregnancy, which may be responsible for increased inflammation.

However, other studies have reported a gradual increase in severity until the 36th week of gestation with gingival condition recovering spontaneously after delivery. Based on clinical observations, the prevalence of periodontal diseases during pregnancy varies from 35% in some studies to 100% in others. Pregnancy increases the risk of dental caries. A study reported that 61.5% of pregnant women had caries, and 52.6% had gingivitis.

The pregnant women were 1.97 times more likely to suffer from dental caries and 1.81 times more from gingivitis compared to non-pregnant women. It is believed that increased
consumption of carbohydrates, increased acid in the mouth from vomiting, and reduced salivary production and/or increased acidity of saliva combine to raise the risk of dental caries in pregnant women.\textsuperscript{11}

The increase in progesterone levels during pregnancy causes a decrease in lower esophageal tone and gastric and intestinal motility. The combined effects of hormonal and mechanical changes in the gastrointestinal system and greater sensitivity of the gag reflex also increases the risk of gastric acid reflux.\textsuperscript{12} Gag reflux that make women vulnerable to nausea and vomiting, this condition if persist may lead to enamel erosion. The acid erosion of teeth may occur if pregnancy sickness (morning sickness) or esophageal reflux is severe and involve repeated vomiting of the gastric contents.\textsuperscript{13,14} The pyognic granuloma calling as epulis or pregnancy tumor is the benign inflammatory lesion composing proliferating capillaries mostly observed in 5\% of gestating women during 2\textsuperscript{nd} trimester of pregnancy.\textsuperscript{15} Apthae monitoring, through no type of treatment, salivary changes with variation in pH and composition, an increased frequency of temporomandibular joint disorders seems to be more related to dental losses and malocclusions or poorly executed fillings during this period. The melasma or skin alteration in pregnant women improves after delivery.\textsuperscript{16}

During pregnancy, certain systemic conditions need to be considered. Oral health care provider should be careful in dealing patients of hypertensive disorders because of increased risk of bleeding during procedures and needs to discuss with prenatal care providers prior to initiating any procedures in women with uncontrolled severe hypertension. Hypertensive disorder including chronic hypertension occurs at 12 to 22\% of pregnancies and the tendency of chronic hypertension may be up to 5\%.\textsuperscript{17}

Hypertensive disorder causes adverse outcomes like premature birth, intrauterine growth restriction, fetal demise, placental abruption and cesarean delivery.\textsuperscript{18} Gestational or type III diabetes commonly diagnosed after 24 weeks of gestation occurs in 2 to 5\% women of the United States.\textsuperscript{19} An increased risk of periodontal breakdown is observed in diabetic patients in whom the condition has not been properly controlled. The periodontal infection adversely affects the blood glucose level in diabetic patients.\textsuperscript{20,21}

The pregnancy associating gingivitis and gingival inflammation can be found in diabetic patients carrying the same amount of bacterial plaque than non-diabetic control patients and hence, the diabetes control is important during 1\textsuperscript{st} trimester as the congenital anomalies increases with uncontrolled diabetes.\textsuperscript{22,23}

Oral and dental diseases are the most prevalent and preventable health conditions. Attainment of oral health issues and dental care within the current system of health care accessed by pregnant women throughout their life course provides greater opportunity for reducing known risk factors and providing early treatment, potentially resulting in reduced health care costs and improved oral and dental as well as general health outcomes.
MATERIALS & METHODS

This descriptive type of cross sectional study was conducted to assess the pattern of common oral and dental diseases among pregnant women attended at the out-patient department of Ibrahim General Hospital-Mirpur and National Healthcare Network (NHN) Mirpur Centre both are the Enterprises of Diabetic Association of Bangladesh. The study was carried out from September 2013 to January 2014 among 147 married women who were suffering from different oral and dental diseases.

To get the target sample quickly non randomized purposive sampling technique was followed by using a pre tested semi-structured questionnaires and a check list. Only pregnant women of reproductive age (15-49 years) were included in this study. On the other hand, those who refused to provide informed consent and who were below 15 or above 49 years were excluded from the study.

The severity of oral and dental diseases was assessed at the dental units of same hospital and centre. Instruments used for the clinical examination were periodontal probe, dental mirror, caries probe or explorer and excavator. Data were checked, cleaned and edited properly before analysis.

The data were sorted and analyzed by using the software SPSS version 16. Descriptive statistics were used for interpretation of the findings. Cross tabulations and associations were determined by using the Pearson Chi-square Test where applicable. The analyzed data were presented in the form of frequency distribution tables.

RESULTS

The frequency of patients’ socio-demographic characteristics in relation to oral diseases is provided in Table 1. Maximum 72% were in the age group of 20 to 24 years and only 1.4% of pregnant women correspond to the age group of above 35 years. Among them, 57% of had completed SSC and only 4.8% were illiterate whereas 53% husbands of pregnant women had SSC level and only 5% husbands had no education respectively. Moreover, majority of (88%) them were housewives and only 1% of them were day-laborers while 63% husbands of pregnant women belonged to service holders and only 8% husbands were day-laborers. More than half (52%) of the patients whose monthly family income were less than or equal to 10 thousand BDT and only 1% showing lowest were above 40 thousand BDT. In addition, 41% respondents had only one child and 7% had two or more children.
Table 1: distribution of the pregnant women according to socio-demographic characteristics, in relation to oral and dental diseases (n=147)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>20-24</td>
<td>106</td>
<td>72</td>
</tr>
<tr>
<td>30-34</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>above 35</td>
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<td>1</td>
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<tr>
<td>Educational Status</td>
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<tr>
<td>No Education</td>
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<td>5</td>
</tr>
<tr>
<td>Primary</td>
<td>33</td>
<td>22</td>
</tr>
<tr>
<td>SSC</td>
<td>83</td>
<td>57</td>
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<tr>
<td>HSC</td>
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<td>8</td>
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<tr>
<td>Graduate or Above</td>
<td>12</td>
<td>8</td>
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<tr>
<td>Occupation</td>
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<td></td>
</tr>
<tr>
<td>House Wife</td>
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<td>Day-laborer</td>
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<td>1</td>
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<tr>
<td>Service holder</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Husband's Education</td>
<td></td>
<td></td>
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<tr>
<td>No Education</td>
<td>7</td>
<td>5</td>
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<tr>
<td>Primary</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>SSC</td>
<td>77</td>
<td>53</td>
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<tr>
<td>HSC</td>
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<tr>
<td>Graduated or Above</td>
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<td>16</td>
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<tr>
<td>Husband's Occupation</td>
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<td></td>
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<td>Business</td>
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<tr>
<td>Service-holder</td>
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<td>63</td>
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<tr>
<td>Monthly Family Income (BDT)</td>
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<td>&lt;10000</td>
<td>76</td>
<td>52</td>
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<td>31</td>
</tr>
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<td>None</td>
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<td>52</td>
</tr>
<tr>
<td>One</td>
<td>60</td>
<td>41</td>
</tr>
<tr>
<td>Two or more</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>
Distribution of the patients according to pregnancy related variables, in relation to oral and dental diseases is provided in Table 2. Majority of the (69%) patients had dental problem in 2nd trimester stage, 27% reported at the stage of 3rd trimester and only 4% respondents were at the stage of 1st trimester. More than half (54%) of respondents were expectant for the 1st time and only 9% respondents were pregnant for the third time or more.

Moreover, 68% respondents liked to take sweetened food or drink as light meal, 18% respondents had preference for fruits or milk or egg as snacks and 14% respondents inclined to take fast food or snacks as extra meal in between meals. Prenatal care providers advised only 3% of respondents for dental check-up at pregnancy and majorities (67%) of the participants were recommended by no one.

Table 2: Distribution of the patients according to pregnancy related variables, in relation to oral and dental diseases (n=147)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage of Pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st trimester</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>2nd trimester</td>
<td>101</td>
<td>69</td>
</tr>
<tr>
<td>3rd trimester</td>
<td>40</td>
<td>27</td>
</tr>
<tr>
<td><strong>Number of pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st pregnancy</td>
<td>79</td>
<td>54</td>
</tr>
<tr>
<td>2nd pregnancy</td>
<td>55</td>
<td>37</td>
</tr>
<tr>
<td>3rd pregnancy or more</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td><strong>Type of extra meal taken during pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweetened food/drink</td>
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<td>68</td>
</tr>
<tr>
<td>Fast food/Snacks</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Fruits/Milk/Egg</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td><strong>Dental check up during pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self</td>
<td>99</td>
<td>67</td>
</tr>
<tr>
<td>Prenatal care provider</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Parents or Husbands</td>
<td>29</td>
<td>20</td>
</tr>
<tr>
<td>Others</td>
<td>15</td>
<td>10</td>
</tr>
</tbody>
</table>

Distribution of the pregnant women according to record of visiting dentists, in relation to oral and dental diseases is provided in Table 3. Majority of the respondents (63%) had never visited their dentists, 18% of respondents accessed to their dentists before 2 years or more, 12%
respondents were found to visit their dentists 1 year ago and only 6% respondents appeared at pregnancy.

Table 3: Distribution of the pregnant women according to record of visiting dentists, in relation to oral and dental diseases (n=147)

<table>
<thead>
<tr>
<th>Record of visiting dentists</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>92</td>
<td>63</td>
</tr>
<tr>
<td>1 year ago</td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td>2 years or more</td>
<td>28</td>
<td>19</td>
</tr>
<tr>
<td>prior/ at pregnancy</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>147</td>
<td>100</td>
</tr>
</tbody>
</table>

Distribution of the pregnant women in relation to pattern of oral and dental diseases is provided in Table 5. Here we found 100% respondents experienced of gingivitis, 54% of respondents had dental caries, 52% of respondents were found to have dental erosion, 27% respondents suffered from periodontitis and 16% respondents complained of apthous ulcer.

Table 5: Distribution of the pregnant women in relation to pattern of oral and dental diseases (multiple responses).

<table>
<thead>
<tr>
<th>Dental diseases</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental Caries</td>
<td>80</td>
<td>54</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>147</td>
<td>100</td>
</tr>
<tr>
<td>Periodontitis</td>
<td>39</td>
<td>27</td>
</tr>
<tr>
<td>Apthous Ulcer</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>Dental erosion</td>
<td>77</td>
<td>52</td>
</tr>
</tbody>
</table>

DISCUSSION

In the United States a study was done to determine national and state-specific estimates of dental care use and found that 27.37% pregnant women were in between 25-29 age group, 26.29% were between the ages of 20-24 years, 8.49% were in between 18-19 age, 23.40% were in between 30-34 years and the rest 14.44% were above 35 years of age.24
Present study revealed that larger proportion of respondents (72%) had fallen within the age group of 20-24 years. 19% of the respondents represented the age group of 15-19 years, 8% respondents were within the range of 30-34 years and only 1% of respondents correspond to the age group of above 35 years (Table 1). According to demographic characteristics among Carolina Oral Health Literacy study participants who were pregnant for the first time, 25% did not finish high school, 30% received a high school or general educational development diploma and 45% completed some college or higher education.

Almost similar result found in the present study where more than half of the respondents (57%) completed SSC level, 23% of the respondents had primary education, 8% of the respondents finished HSC level and participants with graduation and above and no education were 8% and 4.8% respectively (Table 1).

A study was conducted to document oral health practices of pregnant women in two tertiary institutions in North-eastern Nigeria and found that majorities (48.3%) were housewife, 29% were civil servant, 11.6% were student and the rest 10.2% had business. Present study also showed that 88% of respondents were housewives, 11% were service holders and only 1% of the respondents were day-laborers (Table 1). Among 388 participants, 28% pregnant women lived in a low and low-mid socio-economic index, 17% lived in mid-high socio-economic index and the rest 27% were in high socio-economic index.

In this study, more than half of the respondents (52%) had monthly income of BDT ≤10000, 31% participants were within the income group of BDT 11000 to 20000, the salary of 16% respondents was ranged from BDT 21000 to 30000 and only 1% respondents got the salary of BDT above 40000 (Table 1). A study is done to assess the knowledge, attitude and practices of pregnant women and mothers about feeding habits and infant oral health and found that 57.6% were primigravidae, 31.1% had one child and the rest 1.7% had more than two children. Present study showed that 52% respondents had no issues, 41% respondents had only one child and 7% pregnant women had two or more children (Table 1).

A study was conducted to examine the relationships between risk factors amenable to intervention and the likelihood of dental care use during pregnancy and found that most of the respondents (70%) reported that they had dental problem at the stage of 1st trimester, 23% reported at the stage of 2nd or 3rd trimester, 2% had dental problem but no care and the rest 5% are unknown. This study also presents that 69% respondents had dental problem in 2nd trimester stage, 27% reported at the stage of 3rd trimester and only 4% respondents were at the stage of 1st trimester (Table 2).

The relationship between nutrition and dental health is often overlooked during pregnancy as most dieticians and pediatricians lack in training to make preventive or therapeutic oral health
recommendations and due to lack of dietary counseling skills of dentists to assess and provide appropriate nutrition interventions. The main dietary aspect of dental health education is based on two key messages—reduce sugar consumption and drink of fluoridated water. It is extremely difficult to test the importance of just single dietary item on dental caries because its effect likely to go undetected amongst other sugar containing foods and drinks which may be consumed.

Regarding food habit of respondents, present study showed that 94% took their main meals three times in a day and 6% of respondents took their meals twice daily. In addition to this, 35% respondents took snacks in between main meals three times or more daily followed by 33% twice daily, 28% once daily and 4% respondents did not take any extra meal. 68% respondents have chosen sweetened food or drink as snacks in between main meals, 18% consumed fruits or milk or egg as light meal and 14% respondents ate fast food or snacks in between main meals (Table 2).

In 2004-2005 in Ohio surveyed women regarding their perceptions of dental care and dental care practices. More than half (54%) of the respondents reported that dental care was important during pregnancy, yet only 44% actually received care during pregnancy. Fewer than half (40%) stated they were advised by their obstetric provider to seek dental care during pregnancy, and 10% reported a dentist refused to provide them care because they were pregnant. The present study showed that only 3% women were advised for dental check-up during pregnancy by prenatal care providers, 20% by their parents or husbands and 67% did not get any information or advice from dentists or gynecologists (Table 2).

In 2011 a study was carried out to describe the self-reported oral hygiene habits and self-care in the oral health in a sample of Iranian women aged 21-35 years during pregnancy and found that 41% women had dental visit more than 2 years ago, 12% had visit less than 2 but more than 1 year ago, 29% visited dentist 6-12 months ago and 18% visited less than 6 months ago. Almost similar result was observed in the present that majority of the respondents (63%) had never visited their dentists, 18% of respondents accessed to their dentists before 2 years or more, 12% respondents were found to visit their dentists 1 year ago and only 6% respondents appeared at pregnancy (Table 3).

A Danish study in 2003 looked at the self assessment of gingival conditions and found that about 30% have one or more gingival symptoms during pregnancy, bleeding gums at brushing, spontaneous bleeding from gums, gum pain or change in color of gums or swollen gums. In contrast, present study showed that respondents complained of bleeding gums, sensitive tooth, cavities, toothache and gingival swelling were 78%, 52%, 35%, 11% and 10% respectively. Larger section of participants had problems of gum bleeding and tooth sensitivity (Table 4).
Periodontal disease is a common oral infection with prevalence ranging from 10-60%, and refers to gingivitis and periodontitis. Based on clinical observations, the prevalence of periodontal disease during pregnancy varies from 35% in some studies to 100% in others. Pregnant women were more likely to have dental caries and gingivitis compared to non-pregnant women.

Three-quarter of pregnant women (74.5%) had dental caries, while in the non-pregnant group the percentage of caries was around 50.0%. Moreover, it was found that 86.2% of pregnant women had gingivitis in comparison to 72.8% among non-pregnant women. Results in another study also revealed the increased rates of caries in which the prevalence of dental caries was found to be 74% and higher percentage of dental erosion (24.0%) were located in the third trimester of pregnant women.

Furthermore, only 1% pregnant woman had an aphthous ulcer in another study. On the contrary, present study exposed that 100% respondents had gingivitis, 54% had dental caries, 52% were found to have dental erosion, 27% suffered from periodontitis and 16% had problems of aphthous ulcer (Table 5). Finally, no statistical significant associations were found between socio-demographic variables and proportion of oral and dental diseases.

**CONCLUSION**

It has been observed that majority of the respondents are young pregnant mothers of lower income group with lower educational and occupational status. It can be said from the study that educational and occupational statuses of pregnant women in Bangladesh were not satisfactory. Larger portion of the respondents gave priority of sweetened food or drinks as their extra meal which may predispose them to get more oral diseases.

It is also mentionable that an extensive number of pregnant women did not seek oral health care during pregnancy. In addition to this, very few respondents were advised for visiting dentists by their prenatal care providers during pregnancy period. It is also revealed from the study that all the participants suffered from gingivitis and half of them had dental caries and erosion while a small number of respondents got periodontitis and aphthous ulcer.

So, this study provided some directions to future research in this area regarding the impact of oral health knowledge, attitude, behavior and food habit on the pattern of oral diseases with a larger sample size and expanded volume of queries in questionnaire to evaluate the actual proportion of oral diseases and to find out the important predisposing factors in Bangladesh for better oral health outcomes.
REFERENCES


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PHARMACOVIGILANCE-AN EMERGENCE

A Case Study By Dr Deven V Parmar¹ and Dr. Dharani Munirathinam², USA

¹Faculty at Fellow American College Of Clinical Pharmacology
²Pharmacovigilance consultant, ACCP Member

Email:- gokul.dharani@gmail.com

INTRODUCTION

Pharmacovigilance (PV), defined by the world health organization (WHO) as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Emergence of PV activities and the awareness would play a vital role in ensuring that doctors, healthcare professional, together with the patient, have enough information to make an educated decision when it comes to choosing a drug for treatment and eventually achieving the patient safety in large.

HISTORY OF PHARMACOVIGILANCE

In the early days of drug development there were no regulations monitoring the quality, efficacy and safety of drugs. In the late 1950 and early 1960 it became evident that drugs were not only treating diseases but had a negative impact. Adverse drug reactions (ADRs) were acknowledged as a problem related to drug use, following the thalidomide disaster, authorities all over the world began to set up systems in order to monitor the safety of drugs. These spontaneous reporting systems were based on the collection of reports of ADRs from healthcare professionals. The WHO recognized the need for global drug monitoring, and in 1968 the WHO Pilot Research Project for International Drug Monitoring started its operation with 10 participating countries, to develop a system for the detection adverse effects of drugs.[1-4]

PHARMACOVIGILANCE PROCESSES

The PV activities can be roughly divided into three groups: regulatory, industry, and academia. The PV process includes an ongoing continuous reporting process called as the Individual case safety reporting (ICSR) and Aggregate reporting.

In the ICSR process cases are reported from sources that include spontaneous, clinical trials and literature. However, spontaneous reporting of ADRs by physicians and pharmacists has been the backbone of data collection in PV and has proven its value in detecting relatively rare and serious ADRs. Within the new legislation, spontaneous reporting will continue to play an
important role and the range of possible reporters will be expanded by including patients. Spontaneous reporting systems focus on detecting signals of new ADRs and it has proven its strength in detecting previously unknown harm. It has also met criticism; under-reporting and its inability to quantify adverse drug reactions are most often mentioned. The field of drug safety has been receiving a great deal of attention lately.

Now with the new regulations the aggregate reporting structure is evolving from reactive mode to the pro active mode of ADRs reporting and analysis. The cases reported through the ICSR are further analyzed in depth and reported through many reports that include Periodic Safety Update Reports, Periodic Benefit Risk Evaluation Report, Safety Summary Report, and Clinical Overview for the initiation of any changes to the labels for the EU. PADER is the report predominantly submitted for the US FDA. A Developmental Safety Update Report is required to be submitted for the drugs in the late clinical trials and early post marketing phase. In the Aggregate reporting the newer regulation insists on Risk Management Plan by the EU and Risk Evaluation and Mitigation Strategy Report by the US FDA. [6-10]

**PHARMACOVIGILANCE EVOLUTION**

The withdrawal of rofecoxib directed renewed attention to drug safety. The decision to withdraw rofecoxib was made after the safety monitoring board of the APPROVE trial found an increased risk of cardiovascular (CV) events in patients treated with rofecoxib compared to placebo. [5]

The events leading to the withdrawal of rofecoxib, and what have happened since the withdrawal, have been discussed in numerous papers. In the recent years after the withdrawal of rofecoxib in 2004, followed by the debate about the cardiovascular safety of rosiglitazone, which ultimately lead to the suspension of the marketing authorization of the drug in the European Union (EU). In the EU the evaluation of the PV system started in 2006, and lead to legislative changes, which were endorsed in September 2010 and has come into force in July 2012. To support the implementation of the new EU Pharmacovigilance legislation, the European Medicines Agency (EMA) is developing a new set of guidelines for the conduct of PV.

This new guidance on good pharmacovigilance practices (GVP) is organized in 16 different modules. With the new legislation a strengthening of post-authorisation regulation of medicines will be implemented, which has 2 key elements: one related to the process, where it is important that there are clear roles, responsibilities and obligations for the key responsible parties and the other related to the collection of high-quality data relevant to the safety of medicines and patient safety, which is a requirement for the prompt identification of potential risks. [6-9]

The FDA and the current system of post marketing surveillance were criticized. Firstly, the FDA uses only a limited number of data sources (clinical trials and spontaneous reporting) when it comes to assembling information on the safety of a drug. Secondly, the FDA has no control over the performance of post-marketing safety studies. The majority of post-marketing study commitments is never initiated, and the proportion of post-marketing safety studies (phase 4
studies) that were completed declined from 62% between 1970 and 1984 to 24% between 1998 and 2003.

Thirdly, the FDA has no authority to take direct legal action against companies that do not fulfill their post-marketing commitments. In response to the criticism, the Centre for Drug Administration (CDER) at the FDA asked the Institute of Medicine (IOM) to assess the US drug safety system. In September 2006, the IOM released the committee’s findings and recommendations in a report ‘The future of drug safety: promoting and protecting the health of the public’. The main message in this report is that the FDA needs to follow the safety of a drug during its whole life cycle. This life-cycle approach includes identifying safety signals, designing studies to confirm them, evaluating benefits as well as risks, using risk-benefit assessments to integrate study results and communicating key findings to patients and physicians.[6-10]

DEVELOPMENTS

Pharmacovigilance and the methods used need to continue to develop in order to keep up with the demands of society. The Erice Declaration on transparency, which was published in 1997. In this declaration, PV experts from all over the world, representing different sectors, emphasize the role of communication in drug safety with the following statements:

• Drug safety information must serve the health of the public

• Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for health care providers

• All the evidence needed to assess and understand risks and benefits must be openly available

• Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated and made accessible to all

• Innovation in drug safety monitoring needs to ensure that emerging problems are promptly recognized and efficiently dealt with, and that information and solutions are effectively communicated.

It is believed that these factors will help risks and benefits to be assessed, explained and acted upon openly and in a spirit that promotes general confidence and trust. This declaration was followed in 2007 by the Erice Manifesto for global reform of the safety of medicines in patient care. The Erice Manifesto specifies the challenges which must be addressed to ensure the continuing development and usefulness of the science, in particular:

• The active involvement of patients and the public in the core debate about the risks and benefits of medicines, and in decisions about their own treatment and health
• The development of new ways of collecting, analyzing and communicating information about the safety and effectiveness of medicines; open discussion about it and the decisions which arise from it

• The pursuit of learning from other disciplines about how PV methods can be improved, alongside wide-ranging professional, official and public collaboration

• The creation of purposeful, coordinated, worldwide support amongst politicians, officials, scientists, clinicians, patients and the general public, based on the demonstrable benefits of PV to public.[10,11]

In the past, PV has been most concerned with finding new ADRs, but Waller and Evans suggest that PV should be less focused on finding harm and more focused on extending knowledge of safety. In recent years, regulatory agencies have been reforming their systems in order to keep pace with the developments in PV, with the focus on being more pro-active. [17]

**EUROPE**

In 2005, a document was drafted by the Heads of the Medicines Agencies called ‘Implementation of the Action Plan to Further Progress the European Risk Management Strategy’. In July 2007, the EMEA published a document in which they discussed the achievements booked to date. These achievements included the implementation of legal tools for monitoring the safety of medicines and for regulatory actions. Particular emphasis was placed on:

• Systematic implementation of risk management plans

• Strengthening the spontaneous reporting scheme through improvements of the Eudra-Vigilance database

• Launching the European Network of Centre’s for Pharmacoepidemiology and Pharmacovigilance(ENCePP) project to strengthen the monitoring of medicinal products

• The conduct of multi-center post authorization safety studies

• Strengthening the organization and the operation of the EU PV system

In the course of the next 2 years, two main areas will be covered by the European Risk Management Strategy: further improving of the operation of the EU PV system and strengthening the science that underpins the safety monitoring for medicines for human use.
METHODOLOGICAL DEVELOPMENTS

TRANSPARENCY

The Erice Declaration, as well as Waller and Evans, stated that transparency is important for the future of pharmacovigilance. In the last few years transparency around ADRS has increased. The registration of clinical trials will allow the necessary tracking of trials to ensure full and unbiased reporting for public benefit. A number of countries, including Canada (http://www.hc-sc.gc.ca), the Netherlands (http://www.lareb.nl) and the UK (http://www.mhra.gov.uk), have made their databases containing the data from the spontaneous reporting system freely available to the public. [10]

CONDITIONAL APPROVAL

Both the FDA report and the report from the EU described earlier emphasize that compliance by marketing authorization holders needs to be improved when it comes to additional post-marketing studies. A possible solution to this problem would be a time-limited conditional approval, which would place pressure on the manufacturers to conduct and report additional safety studies. Within the EU, the EMEA has introduced a conditional marketing authorization. The Committee for Medicinal Products for Human Use (CHMP) delivers a conditional marketing authorization for products where there is a specific patient need. Examples include products for seriously debilitating or life-threatening diseases, medicinal products to be used in emergency situations in response to public threats and products designated as orphan medicinal products. A conditional marketing authorization is granted in the absence of comprehensive clinical data referring to the safety and efficacy of the medicinal product. However, a number of criteria have to be met including:

1. A positive risk-benefit balance of the product
2. Likelihood that the applicant will be in a position to provide the comprehensive clinical data
3. Unmet medical needs being fulfilled
4. The benefit of the immediate availability of the medicinal product to public health outweighing the risk inherent in the absence of additional data.

Conditional marketing authorizations are valid for 1 year, on a renewable basis. The holder is required to complete ongoing studies or to conduct new studies with the objective of confirming that the risk-benefit balance is positive. In addition, specific obligations may be imposed in relation to the collection of PV data.
The authorization is not intended to remain conditional indefinitely. Rather, once the missing data are provided, it should be possible to replace it with a formal marketing authorization. The granting of a conditional marketing authorization will allow medicines to reach patients with unmet medical needs earlier than might otherwise be the case and will ensure that additional data on a product are generated, submitted, assessed and acted upon. [13-16]

**RISK MANAGEMENT PLANS**

Another step in a more pro-active post-marketing surveillance is the introduction of risk management plans (RMPs). Such RMPs are being set up in order to identify, characterize, prevent or minimize risk relating to medicinal products, including the assessment of the effectiveness of those interventions. A RMP may need to be submitted at any time in a product’s life cycle, for example, during both the pre-authorization and post-authorization phases. A RMP is required for all new active substances, significant changes in established products (e.g. new form/route of administration), established products introduced to new populations, significant new indications or when an unexpected hazard is identified.

The EU RMP consists of 2 parts: the first part contains a ‘safety specification and a PV plan’ and the second part contains an evaluation of the need for risk minimization activities and, if necessary, a risk minimization plan. The safety specification contains a summary of what is known and what is not known about the safety of the product. This specification encompasses the important identified risk and any information and outstanding safety questions which warrant further investigation in order to refine the understanding of benefit-risk during the post-authorization period.

A risk minimization plan is only required in circumstances where the standard information provision, by means of a medicine’s summary of product characteristics, is considered inadequate. Insufficient patient information leaflets or inadequate labeling of the medicine are additional reasons for drawing up a risk minimization plan. Where a risk minimization plan is considered necessary, both routine and additional activities are to be included. Some safety concerns may have more than one risk minimization activity, each of which should be evaluated for effectiveness.

Many RMPs have already been established; however, to date, no quantitative or qualitative reports have been released by the EMEA. Information to the public about RMPs has also been scarce. If RMPs are to take an important place in PV, they need to be made public and easily accessible to scientists, professionals and patients. [17-19]
UPDATE: CHANGES TO RMPS

In August 2013, there were two important changes to RMPs in the EU.

UPDATES TO RMPS

There is no longer an automatic requirement to update RMPs on a fixed-time basis. The Agency and the NCAs are now adopting a risk-based approach to RMP updates.

An updated RMP should now be submitted:

- at the request of the Agency or an NCA;
- whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important PV or risk-minimization milestone being reached.

When justified by risk, the competent authority may still specify a date for submission of the next RMP as a condition of the marketing authorization in exceptional cases.

If the date for the submission of a periodic safety update report (PSUR) and the need to update a RMP coincide, both can be submitted at the same time.

CHANGES TO 'IMPORTANT MISSING INFORMATION'

The word 'important' has been removed from the phrase 'important missing information' within risk-management documents defining what constitutes a safety concern in an RMP.

Safety concerns are now classified as:

- important identified risks;
- important potential risks;
- missing information.

Previously, International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use E2E and all EU risk-management documents
used the terms 'important identified risks', 'important potential risks' and 'important missing information' to define safety concerns in RMPs. [17-19]

**RISK EVALUATION AND MITIGATION STRATEGY**

The US FDA requests for a report similar to the EU RMP called the Risk Evaluation and Mitigation Strategy (REMS). In 2007, a new law that gave FDA many new authorities and responsibilities to enhance drug safety was enacted. It's called the Food and Drug Administration Amendments Act- sometimes called "FDAAA"- and one of its provisions gave FDA the authority to require a Risk Evaluation and Mitigation Strategy-(REMS) from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks.

A REMs may be required by the FDA as part of the approval of a new product, or for an approved product when new safety information arises. Essentially, a REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use.

Since medicines are very different from each other, each REMS for each medicine is also different.

This presentation discussed REMS and how they are used to help ensure that the benefits of certain medicines continue to outweigh their risks. [20]

**FUTURE PERSPECTIVES**

On a regulatory level, progress has been made during the past few years. However, the results of these changes have yet to become apparent and, therefore, it has not yet been proven if these developments have contributed to better PV conduct. In order to further prove PV as a science, it is essential that academia develops new methods which can strengthen the current system.

Pharmacovigilance as we know it today has been about detecting new ADRs and, if necessary, taking regulatory actions needed to protect public health, for example, by changing the summary of product characteristics (SPCs) or withdrawing the drug from the market. Little emphasis has been put into generating information that can assist a healthcare professional or a patient in the decision-making process of whether of not to use a drug. The gathering and communication of this information is an important goal of PV. [21]
PHARMACOVIGILANCE AWARENESS

Involvement of patients

Another important development is the recognition of the patient as an important player in PV. Patients are the users of drugs, and it is their use of a drug in a safe manner that is the ultimate goal of PV activities. In an increasing number of countries patients are now allowed to report ADRs to the spontaneous reporting system. The EU and US FDA acknowledge the role of the patient in spontaneous reporting. [21]

PHARMACOVIGILANCE IN INDIA

In India there was never a compulsion to have a strong PV system to detect adverse reactions of the marketed drugs. However, the increased interest of Indian regulatory authority in PV is clearly reflected by several instances including the amendment of Schedule Y, organizing several seminars, and training programs with WHO and several press releases from DCGI from time to time stressing the importance of a strong PV system in India, including the recent press release announcing the setting up of an independent PV team to review the safety of the anti-diabetic drug rosiglitazone.

Thus, the pharmaceutical companies who have been marketing generic drugs in India are now faced with greater regulatory reinforcement and increased accountability demands for ensuring a favorable benefit-risk balance of their products are required to take a more active approach to PV. This includes monitoring and reporting of spontaneous adverse reactions, submission of PSURs, conducting the risk-benefit analysis of new drugs, and relevant communications. For the companies conducting clinical trials in India, the regulatory timelines for reporting and the conditions for expedited reporting have been clearly defined.

SCHEDULE Y

The legislative requirements of PV in India are guided by specifications of Schedule Y of the Drugs and Cosmetics Act 1945. The Schedule Y also deals with regulations relating to pre-clinical and clinical studies for development of a new drug as well as clinical trial requirements for import, manufacture, and obtaining marketing approval for a new drug in India.

Schedule Y was thoroughly reviewed and its latest amendment, dated 20th January 2005, indicates the continued commitment of DCGI to ensure adequate compliance of PV obligations of the pharmaceutical companies. In the amended Schedule Y, an attempt has been made to
better define the responsibilities of pharmaceutical companies for their marketed products as well as relating to the reporting of adverse events from clinical trials. The section entitled post-marketing surveillance includes the requirement for submission of periodic safety update reports (PSURs), PSUR cycle, template for PSUR, and the timelines and conditions for expedited reporting.

NATIONAL PHARMACOVIGILANCE PROGRAM

This is a nation-wide program, sponsored and coordinated by the country's Central Drugs Standards Control Organization (CDSCO) to established and manage a database of adverse drug reactions (ADRs) for making informed regulatory decisions regarding marketing authorization of drugs in India for ensuring safety of drugs. NPP sponsored by WHO and funded by World Bank became operational since January 2005.

The details of this program are beyond the scope of this article. Some of the major functions of this program include the monitoring of spontaneous ADRs, review of the PSURs submitted by the pharmaceutical companies and assessing the safety information so as to make appropriate recommendations on product label amendments, product withdrawals and suspension. NPP has its own form for spontaneous ADR reporting. The data elements of this form are almost similar to that of CIOMS form or MedWatch Form 3500A. The protocol of NPP provides guidance to healthcare professionals on completion of the spontaneous adverse event reporting form and describes the activities at various centers of PV.

As there is limited guidance available in Schedule Y as well as the protocol published by the NPP, it becomes imperative for the Indian pharmaceutical companies to consult the guidance documents available from International Conference of Harmonization, US FDA, and European Agency for the Evaluation of Medicinal Products (EMEA) so as to develop well laid down procedures for optimally meeting their PV obligations for NCEs as well as for the generic drugs [22-26].

REFERENCES


7) European Medicine Agency Updates on RMP: EMA website


CLINICAL UNDERSTANDING OF A LIFE-THREATENING ASTHMA HELP TO IMPROVE PEDIATRIC PATIENT’S OUTCOMES

An Article Review by Dr. Alain Kabongo, South Africa
MBBS, MMSc (Ped. Emergency) Student of Texila American University
Email:- alainkabongo2001@yahoo.fr

SOURCE

KEYWORDS
Asthma, Breathing, Pediatric, Intensive Care, Clinical Data, Children

REVIEW OF LITERATURE
This part of the article should give a state of research on the topic. It should demonstrate opinions on previous studies, current research, and should describe the outstanding lines related to the topic. I did not see any organization around the research question developed in this study. Areas of controversies are well identified and formulated, and there is not suggestion for further studies while acute asthma in children remains a challenging health problem that need more investigations for appropriate management in terms of reducing hospital admission, mortality rate and improve the quality of life.

Clinical data regarding patterns of children suffering from life-threatening asthma (LTA) warranting pediatric intensive care is important for understanding disease severity patterns and its impacts. The literature cited in the study shows some signs of excessive referencing. For example, the study by (Hon & Nelson, 2006) is mentioned unnecessarily as the context does not warrant this. The argument, for which study by (Stein, Canny, Bohn, Reisman, &Levison, 1989)
is mentioned, is adequately presented in other references given for that particular argument. Therefore, this reference could have been skipped. These two aforementioned citations do not contribute to the theoretical or methodological concept of the topic. Some of the references are interesting; hence, they support the discussion of findings and other theories as well.

Literature regarding similar studies on life-threatening asthma in pediatric patients has not been cited adequately and the literature review is short. The clinical data, especially in table 1, warrants a comparison with the previous findings in similar studies, but this comparison has not been provided in sufficient details. The findings that can have serious consequences to future decision making regarding life threatening asthma are not highlighted satisfactorily. Despite these factors, this article adds critical and more information to the existing literature regarding pediatric patients who have particular type of acute worsening of asthma, called status asthmatics’, which does not respond to initial treatments.

INTRODUCTION

In this article review, I will outline and discuss in different paragraphs, significance of the article, whether this fit to the existing literature; its accuracy, article structure, its objectivity, and we will briefly analyzed different figures and tabulations by reporting types of analysis performed, and I will assess whether the author’s analysis support reasoning and claims. I will examine whether the analysis support the main findings in this study. I will suggest new information, methodology and other approaches that might bring contributions to the scope or the principal idea of this work. I will compare ideas in this study with other’s opinions, of course related to the topic.

I will discuss how the same topic is assessed by others. I will point out effects of the author’s reflexion that has not been addressed in the present paper. I will examine the journal for reliability or connection between ideas. I will suggest how to improve the scope of this study with further investigations. I will discuss what need to be examined on the topic. I will extend the writer’s attempts to connect ideas with my own reflexion.

I will show my agreement with the author’s ideas and explain why they comply with my knowledge. I will support aspects of the journal’ claims, analysis, and I will withdraw my support in relation to other opinions, by revealing lack of convincing lines. I will add more analytical terms to analysis of topics not considered and I will finally suggest new way of reasoning.
ARTICLE SUMMARY

Since severe asthma in children is a frequent reason for admission to pediatric intensive care unit (PICU), this retrospective study was aimed at reporting the clinical pattern of children being admitted to PICU in a tertiary care hospital, due to LTA and severe bronchospasm. The medical records were analyzed for children admitted to PICU with LTA over a period of 7 years and 8 months. It was found that there were only 30 admissions with LTA. This number accounted for only 3 per cent of total PICU admissions.

Many of the admitted children were toddlers, representing an average age of 3.1 years. 50% have had previous history of admission due to asthma, 25% had history of poor compliance to chronic medication of asthma as usually prescribed. Some of the patients had a background of prematurity, lung and neurodevelopmental diseases, parainfluenza, and rhinovirus infections. So, by comparison with non-ventilated patients, those who were mechanically ventilated had a significant PIM2 score (Pediatric index of mortality 2 score) representing these values: 1.65 vs 0.4, p < 0.001, however increased pCO2 levels (9.3 vs 5.1, p = 0.01).

The majority of patients receive conventional treatment, including steroids and bronchodilators according to available guidelines and the outcome was good. Regardless of the ventilation status, all patients had brief PICU stays; they improved significantly and were discharge from the PCU after an average of 2.5 days.

ARTICLE STRUCTURE

The article, we have reviewed has a particular structure’s map. Otherwise, it has made sufficient knowledge, and adding other new findings. The conceptual framework has a lack of more information. This article is structured with the following subheadings: abstract, introduction, methods, results, discussion, and conclusion. A sample size is not given in methodology, but a number of 30 admissions are recorded in the findings, this is confusing, meaning that we can consider the admission to be called sample size. In my opinion and according to the international research methods, methodology chapter should state the design used in the paper, population, sampling procedures and sample size, data collection and analysis procedures. However, in the article entitled “Outcome of Children with Life-Threatening Asthma Necessitating Pediatric Intensive Care, we do not know which software was used to store, i.e. helped for data analysis and that generated different tables, So the author has only stated that Mann Whitney U test and χ2 or Fisher exact test were performed to compare the data.

The Contents are not presented in an engaging manner and the reader has to sift through the manuscript to get the relevant and useful information. The significant findings are not properly
highlighted. Table 1 shows a good summary of the clinical data, but the percentage of male children is mentioned as zero in the table 1. This appears to be a typographical mistake, which should have been corrected while formatting of the paper. The correct total percentage of male is 43 or 44 per cent. Overall, this article has a poor structure, which needs further improvement. In text, citing of sources is well done using Vancouver style.

ARTICLE CRITIQUE

AUTHORITY

Kam-Lun Hon is the principal author, who collaborated with Wing-Sum Winnie Tang, Ting-Fan Leung, Kam-Lau Cheung, and Pak-Cheung Ng. He is a physician holding numerous postgraduate degrees include MD and he is a professor with good academic credentials at the Chinese university of Hong Kong. Dr Kam-Lun Hon is more involved in different field of research related to children diseases. He has published more than 30 scientific articles and his last publication was in 2013. The journal where this article was published is the official journal of the Italian society for pediatrics, existing since 1975; it is accounted among the prestigious scientific journal for reliable publications.

ACCURACY

Analysis of the clinical data is presented accurately and objectively. Relevant risk factors were presented along with treatments given at pediatric intensive care unit (PCU). The outcomes described and presented in the article are precise, and highlight all the necessary aspects of the study. There is a small sample size of patients, and the likelihood of type II error in different parameters limits the effectiveness of this study. It must be noted, however, that the objective of this paper is to report the clinical data and infer any patterns therein, so the information provided appears accurate and specific to the topic.

PERIOD

It is challenging to confirm that whether an article is new or old. In science, particularly in medicine, a new article is a progression of previous studies; this could be a response to scientific suggestions or just an implementation of recommendations. The research was retrospective based on the patient’s records registered between the period of October 2002 and May 2010, the month is not specified. The article was published in 2010, probably in the next months after the completion of the research. Therefore, we can confirm that the article is four years old and still useful for academics and medical practitioner as a reference tool.
RELEVANCY

Since the aim of the study was to observe the clinical pattern (not just the outcome), so the contents are relevant to the topic to certain extent. The title itself is, however, incomplete in representing the study. The word “outcome” mentioned in the title represents a part of the whole study or the whole clinical pattern. If the contents of the article are seen critically, it is observed that necessary reference to previous literature is missing in the background of the paper. The results and the discussion section, however, provide relevant and sufficient information regarding the data analysed and presented in this paper.

OBJECTIVITY

This paper reports the clinical pattern of certain LTA pediatric patients. The discussion on the findings is appropriate. Overall, information in this article is developed objectively, but since the paper does not indicate any blinding of the data collector, so there may be some biasness involved. One might argue that this is a clinical report and since there is no prior hypothesis described, so blinding was not needed. Another positive point that indicates the objectivity of the information is the fact that decision for PICU admissions was made based on multiple factors including parameters like blood gas and pulse oximetry.

STABILITY

This article entitled “Outcome of children with life-threatening asthma necessitating pediatric intensive care” is still the only new to be displayed among the other, this, on scientific website; MEDLINE, COCHRANE. For now, I can conclude that this article may be stable at this moment regarding its publication year, unfortunately could not find reviews on this specific topic.

ANALYSIS OF GRAPH/IMAGE/TABLE

The first table (1) describe “Clinical data of children with status asthmaticus admitted to PICU”. This table presenting numerical data is well illustrated. Its interpretation is reported in the results’ section, in my opinion to make reading easier and comprehensible, a clear and short interpretation should be under the table. I do agree that findings displayed in tables may be assessed in the discussion section.
In the first section of table 1, there is not subheading, however, hence three variables are not well defined, it is unclear to understand whether they represent the demographic profile of participants such as “Male %; Median age (IQR), yr and Median (IQR) PIM2, %.” In the section of treatment at PCU, Systemic CS (%) does not have a p Value recorded and the reason is not given, the only note is “not applicable (N/A)”. The second table presenting “The incidence of PICU admissions for LTA during the study period” is well done, representing year in ascending order, its interpretation is short and clear.

**RECENT ADVANCES RELATED TO THE TOPIC**

Acute asthma, i.e. status asthmaticus is pediatric an emergency that needs urgent medical attention, good assessment, and guided management. Admission to pediatric intensive care unit should comply with certain criteria, such as history of respiratory support, stridor, decreased level of consciousness, respiratory failure, and failure of routine management to wean bronchospasm.

In a review of literature entitled “Management of status asthmaticus in children” conducted by Koninckx M and colleagues (2013), the suggestion is that the initial treatment for PSA (pediatric status epilepticus) should be oxygen therapy, rapid 2 agonist, given repetitively, aerolised anticholinergic in combination with steroids and magnesium sulfate intravenously. Additional therapy can be useful as well, such as epinephrine, heliox, inhalational anaesthetics, non-invasive respiratory support, ketamine, and mechanical ventilation. In another retrospective study, conducted in PCU at tertiary hospital in India, data collected from 2006 to 2010, including 33 children admitted children showed a minimal morbidity and mortality rate in children with severe asthma who are given an optimal treatment consisting of aerolised bronchodilator and intravenous steroids.

In recent studies, severe asthma in children had notorious attention from researches; all of them suggest the same conclusion that children should be assessed objectively and the management plan should follow guidelines. In a trial conducted by Bigham MT (2008), aimed to compare the effectiveness Helium/oxygen-driven albuterol aerolised in the management of children with status asthmatics, demonstrated that some of the kits of management have poor outcome, however, they do not reduce the hospital’s length of stay. McDowell KM and colleagues (1998) suggest that intensive care and the management following good guidelines improve the outcome of children with status asthmaticus and reduce length of stay. There have been numerous researches conducted in terms of overcoming the challenges of acute asthma, reducing the length of hospital stay and PCU admission and decrease mortality rate.
CONCLUSION

This article, titled “Outcome of Children with Life-Threatening Asthma Necessitating Pediatric Intensive Care” has presented the outcomes and clinical patterns of pediatric patients with status asthmaticus necessitating pediatric intensive care in adequate length. Despite the sample size (number of 30 patients) which is small, and the mixing of results, the appearance is that the outcome of children with acute asthma, admitted to pediatric intensive care unit is good. However the results are not limited, but converge to the same conclusion reported by other studies and previous. The structural process of the article should be organized and clear. This article has shown some indication of excessive referencing.

It is suggested that unnecessary citations should be skipped and repetition of arguments should be avoided. The typographical error in table 1 also reduces its overall quality of the paper. Attention should also be made on the interpretation. Important findings should be highlighted in a way that it is easier for the reader to find what information is more important and relevant to the topic than the other. Sufficient referencing to the previous findings of similar studies has not been made. It should be noted that despite different caveats, this study is important in increasing clinical understanding of a life-threatening condition.

REFERENCE


MENSTRUAL CHANGES AMONG HIV POSITIVE WOMEN ON ANTI-RETROVIRAL TREATMENT IN SOUTHWESTERN NIGERIA

A Research Article by 1Adebimpe Wasiu Olalekan, 2Adebimpe Mujidat Adebukola, 3Adeoye Oluwatosin Adediran 4Omisore Akinlolu Gabriel, 5Adewole Adefisoye Oluwaseun, Nigeria

1Department of Community Medicine, College of Health Sciences, Osun State University Osogbo, Osun State, Nigeria
2Hospital Management Board, Osogbo, Osun State, Nigeria
3Department of Community Medicine, LAUTECH Teaching Hospital, Ogbomoso, Oyo State, Nigeria

Email: tosinadeoye2002@yahoo.com

ABSTRACT

There are conflicting reports regarding menstrual irregularities and HIV infection in women. Varying degrees of menstrual abnormalities have been reported with prolonged ARV use, and these have implications for drug adherence. The objective of this study was to assess the effect of ARV drugs on menstrual pattern among HIV positive women in South-western Nigeria. It was a descriptive cross-sectional survey among 238 HIV positive women on anti-retroviral therapy randomly selected after excluding for co-morbidities. Research instrument was semi structured interviewer administered questionnaires, and data was analyzed using the SPSS software. Level of significance for statistic test was p ≤ 0.05.

Mean age of respondents was 38.6±2.3 years and 205(86.1%) had commenced ART for a period of 1-5 years mostly 1st line ART, 45(18.9%) have missed their ARVs at one time or the other in the last 1 year. Self reported adherence was good among 227(95.4%), calculated adherence was above 95% among 185(77.7%) with a mean calculated adherence of 93.0±3.6% and a median of 95.0%. About 167(70.2%) of respondents reported a change in their menstrual pattern.

Different patterns of menstrual changes reported were changes in number of days, interval between menstruations and flow of menstrual blood, 52(73.2%) believed that use of ART caused these menstrual changes, only 36(50.7%) reported these changes to the doctor. Predictors of having menstrual disturbances include missing pills, poor adherence and use of ARVs for period longer than 5 years. ARVs were found to be common causes of menstrual irregularities. Thus, clients’ concerns should always be addressed most especially issues that may compromise ARV adherence.
KEYWORDS

Anti-retroviral therapy, Menstrual irregularities, Adherence, ARV

INTRODUCTION

Many women with human immunodeficiency virus (HIV) infection complain of abnormalities or changes in their menstrual cycle. (Chirgwin et al. 1996; Hoytt 1998; Maclean 2000) These changes vary from one woman to another and they include: heavier bleeding that lasts longer than usual, bleeding or spotting between periods, more frequent periods, lighter periods with longer time in between, missed periods and no periods at all. (Maclean 2000)

Clinicians experienced in the care of women with HIV infection also often feel that a higher than expected percentage of women in their care complain of menstrual problems. The absence of menstrual period (amenorrhea), lighter than normal menstrual bleeding (oligomenorrhea) and other menstrual changes from HIV-related cause is however still speculative. (Hoytt 1998) Factors such as severe weight loss, chronic diseases, drug abuse, use of contraception, uterine fibroids, genital tract infections or peri-menopausal symptoms can also cause such changes. (The Well Project 2011)

The objective of this study was to study the effect of HIV infection and treatment on self-reported menstrual changes among HIV positive women

REVIEW OF LITERATURE

Some menstrual changes are directly related to HIV disease and associated immune suppression. Others are associated epidemiologically with HIV because of common risk factors, such as sexual behavior or substance abuse. (Abularach and Anderson 2005) Severe weight loss or wasting syndrome may present with amenorrhoea; chronic illnesses, low levels of platelets may contribute to heavier bleeding, long-term constant stress can affect any woman’s menstrual cycle, significant use of illegal drugs especially heroin and marijuana may also alter menstrual flow and cycle, herbal preparations may contain herbs that affect menstruation such as black cohosh, raspberry root, and some anti-retroviral drugs may also affect menstruation. (Abularach and Anderson 2005; Nielsen 1999; Treat Yourself Right 2009) Protease inhibitors have been linked to increased bleeding in some individuals, but this association has only been well established for hemophiliacs. (New York State Department of Health AIDS Institute 2011)

There are conflicting reports regarding menstrual irregularities and HIV infection in women. Studies have shown that women receiving anti-retroviral therapies (ART) have fewer menstrual abnormalities than immune-compromised HIV-infected women who are not receiving ART; higher viral loads and lower CD4+ counts have been associated with increased cycle variability.
and polymenorrhea. (Harlow SD, Schuman P, Cohen et al. 2000; New York State Department of Health AIDS Institute 2011) However, menstrual irregularities have been reported despite the use of ART among some subjects. (Ogundahunsi et al. 2011) Another study among HIV-positive women found that, overall, being HIV-positive only slightly increased a woman’s chances of having either a very short menstrual cycle (less than 18 days) or a very long cycle (more than 90 days). (Chirgwin et al. 1996)

Often, menstrual problems are caused by hormonal changes that occur naturally in most women over time. They may also be due to conditions not related to HIV. However, HIV and anti-retroviral drugs have been said to have some effects on menstrual cycle. (Treat Yourself Right 2009) There have been a few anecdotal reports but no clinical studies suggesting that the protease inhibitor ritonavir may cause heavier and longer periods. (New York State Department of Health AIDS Institute 2011; Nielsen 1999; Treat Yourself Right 2009) A study done on the characteristics of menstruation in women infected with HIV observed no association between HIV status and menstrual changes. (Ellerbrock et al. 1996).

Whether these menstrual changes are related to HIV, clinical staging, CD4 count and most especially pattern of adherence to ART are important factors not yet given prominence among available studies. This is coming at a time when the HIV epidemic is gradually becoming a feminine issue, when second line drugs are gradually taking over from first line and adherence strategy discussed and managed holistically with clients.

In HIV-infected women, little is known about menstruation and abnormal vaginal bleeding. (Hoytt 1998) despite the importance of the menstrual history in evaluating ovarian function and detecting gynaecologic disorders among these group of women Clinicians prescribing anti-retroviral drug for HIV positive women may also benefit from the outcome of this study. The objective of this study was to study the effect of HIV infection and treatment on self-reported menstrual changes among HIV positive women.

Methodology

The study was a descriptive cross sectional survey carried out in Osogbo, the capital of Osun State in South-western Nigeria. HIV treatment, care and support in the capital city takes place in the secondary (State government hospital) and tertiary (State government University teaching hospital) health care levels. Primary health care centres were mainly for HIV counselling and testing services and were excluded from this study. HIV prevalence in the city was 2.5%, a bit lower than the national average put at 4.1%. Target population constitutes HIV positive women of reproductive age group.

Eligible women would have been on ART for at least one year. In addition, women on treatments or medications or drugs that could influence menstruation (such as contraceptives) were totally excluded from this study. Women with history of genital tract infections and fibroids were also excluded from the study through clinical history taking and abdominal palpation or examination as well as other relevant investigations (where necessary). Using Leslie Fischer’s formula for calculation of sample size for population less than 10,000, a sample size of 218 was estimated,
and this was increased to 240 to account for attrition and non-response. A total of 250 questionnaires were taken to the field.

There were 2 eligible facilities in Osogbo, Asubiaro general Hospital which is secondary, and LAUTECH teaching hospitals which is tertiary in nature, and both have about 2000 registered clients of ART. Questionnaires were equally shared among the 2 facilities. On a bi-weekly clinic day per facility, a list or sampling frame of all eligible women of reproductive age group was obtained from the triage nurse. A systematic sampling of one in three eligible women on the list was done, and this continued until the questionnaires allocated for that day got exhausted. Data collection took place between January 2013 and June 2013.

Data were collected by trained research assistants using pre tested interviewer administered semi structured questionnaires. Interviews were conducted under strict confidentiality and privacy in the post test counseling rooms of the clinics. Details of the study and its objectives were explained to all respondents and participation voluntary, informed consent was obtained from each participant. Ethical clearance was obtained from Osun State University, Osogbo ethical review committee. Permission was also obtained from the Project Coordinators of the respective HIV/ART program as well as the Medical Director of the health facilities used. A limitations: of this study was our inability to screen for other organic causes such as fibroids, though clinical history were taken in order to exclude them.

Questionnaires were manually sorted out and data obtained were entered into the computer. Statistical Package for social Sciences (SPSS) version 17 was used to analyse the double entered data that was also checked for outlier values to ensure its validity. Frequency tables were generated and relevant summary measures calculated. The chi square test was used to demonstrate association between categorical variables while level of significance for the statistical tests was considered at p < 0.05.

RESULTS

Mean age of respondents was 38.6+ 2.3 years with about 46.2% of them being in the 30-39 years age group. 205(86.1%) had commenced ART for a period of 1-5 years mostly 1st line ART, 184(77.3%) are married, 158(66.4%) had more than primary level education, while about half 129(54.2%) of them were traders by occupation (Table 1). Table 2 showed that 45(18.9%) have missed their ARVs at one time or the other in the last one year. Self-reported adherence was good among 227(95.4%), calculated adherence was above 95% among 185(77.7%) with a mean calculated adherence of 93.0+3.6% (How is it calculated) and a median of 95.0%.

Figure I showed that 167(70.2%) of respondents reported a change in their menstrual pattern. Different patterns of menstrual change were reported including changes in number of days, interval between menstruations and flow of menstrual blood, 52(73.2%) believed that use of ART caused these menstrual changes, and 22(31.0%) of them said they can identify their drugs
combination associated with menstrual changes, 36(50.7%) reported these changes to the doctor while 27(38.0%) did nothing.

Table 5 showed association between menstrual changes and some selected variables. Women who have missed pills in the last one year are two and a half time more likely to have experienced menstrual disturbances than those adhering well to ARVs. Women who scored a calculated adherence rate of >95% are about 7 times more likely to have experienced menstrual disturbances than those adhering well to ARVs. Women who had been on ART for prolonged period of >5 years are twice more likely to have experienced menstrual disturbances than those using ARVs for <5 years. Thus menstrual changes were more of adherence with ARVs in this study, especially when taken for more than 5 years.

DISCUSSION

About two-third of the respondents in this study were in the age range 20 – 39 years, age range considered to be very sexually active and those usually involved in high risk sexual practices; (Okochi, Oladepo, and Ajuwon 2000; Olugbenga-Bello, Adeoye, and Osagbemi 2013) it is thus not surprising that HIV infection is more among this age group.

A recent national estimate of HIV prevalence show that HIV prevalence rate for youths (age 20-24 years) peaked at 4.6%. (O moyeni, Akinyemi, and Fatusi 2012) Over seventy percent were however found to be married; an observation which differs from a previous study where sero-prevalence of HIV was higher among the singles than the married. (Okonko, Okerentuga, and Akinpelu A O 2012) In another study that assesses the determinants of antiretroviral treatment adherence among HIV/AIDS patients, majority of the respondents were found to be married and this characteristic was found to positively influence adherence. (Bach et al. 2013)

Only about 2 out of every 10 respondents reported missing their anti-retroviral drug between the last one week and one year prior to the study, this is in congruent with the calculated adherence where about 7 out of respondents had adherence to be optimal (greater than ninety five percent). This level of adherence is also reflected in the ART regimen found among respondents as more than ninety percent of them were using the first line ART regimen.

Complete adherence to ART drugs are associated with low probabilities of resistance, (Sethi et al. 2003) while poor adherence can lead to the virological failure of cheap first-line treatment regimens and the spread of multi-drug resistant forms of the virus, resulting in a public health calamity. (Paterson et al. 2000; S. P. Wasti et al. 2012) Majority of the respondents in this study were on the first-line treatment regimen probably due to their optimal adherence to ART.

Almost a third of the respondents in this study reported change in their pattern of menstruation since commencement of ART. The change in pattern varies and they include irregular menstruation, ceased menses (amenorrhoea), lighter than normal menstrual bleeding (oligomenorrhea) and menorrhagia. Previous studies have reported similar findings of varying
menstrual problems among females infected with HIV.(Harlow SD, Schuman P, Cohen et al. 2000; Hoytt 1998; New York State Department of Health AIDS Institute 2011; Treat Yourself Right 2009) Causes of menstrual problems among HIV-seropositive women include higher viral loads and lower CD4+ counts usually associated with increased cycle variability and polymenorrhea,(Harlow SD, Schuman P, Cohen et al. 2000) heavy bleeding (menorrhagia) or painful periods (dysmenorrhea) could be due to low platelets (thrombocytopenia) associated with HIV infection, or a complication of severe pelvic inflammatory disease,(Hoytt 1998) weight loss, chronic diseases, drug abuse, use of birth control medications, ART drugs, uterine fibroids, itching, genital tract infections, or peri-menopause have all been implicated in menstrual problems.(The Well Project 2011)

Among respondents that reported change in their menstruation pattern in this study, about two-thirds of them thought it was due to their ART drugs. The protease inhibitor Ritonavir has been implicated in a previous study and there have also been reports of the ARV drugs such as Zidovudine (AZT), Stavudine (d4T) and Didanosine (ddI) changing menstrual patterns(Treat Yourself Right 2009). Actions taken by the women who thought ART drugs were responsible for their change in menstruation pattern ranged from stopping all their medications to stopping only suspected drugs.

About half of women with reported menstrual changes reported this observation to their doctor. This finding is very important as such actions of stopping ARV medications without the care givers knowledge could lead to drug resistance. Previous studies have also revealed that patients who had side-effects were more likely to be non-adherent.(S. P. Wasti et al. 2012; S. Wasti et al. 2011) The significant association between respondents that have been on ART drugs for more than one year and change in menstruation pattern may be supporting previous findings that have implicated ARV drugs, especially the protease inhibitors.(Treat Yourself Right 2009)

It is important to however note that HIV-infected women with abnormal or dramatically changed menstrual bleeding should have the full investigation accorded HIV-negative women to determine the cause of the abnormality. Heavy bleeding can cause anaemia, a problem already prominent among women with advanced HIV infection, and can be a symptom of an underlying problem such as a fibroid tumor, blood clotting problems, or infection. Amenorrhea can be a symptom of pregnancy, ovarian cyst, ovarian failure, or menopause.(Hoytt 1998)

When evaluating amenorrhea and other menstrual irregularities in HIV-infected women, clinicians should review the patient’s disease status, including the presence of opportunistic infections, and inquire about substance use and use of medications, such as psychotropics, that contribute to abnormal menses.

Clinicians should obtain a pregnancy test for all HIV-infected women of childbearing potential who give a current history of amenorrhea or irregular vaginal bleeding, regardless of history of sexual activity or contraception use. Patients who are pregnant should be referred to an obstetrical HIV-experienced clinician for evaluation and management as soon as possible.(New York State Department of Health AIDS Institute 2011) In the course of identifying the cause of
menstrual irregularities, women should report to their providers any side effects observed and all related symptoms.

CONCLUSION

ARVs are common causes of menstrual irregularities among women. Women may be tempted to miss drugs or seek alternative care elsewhere when these menstrual abnormalities get unbearable. Stakeholders in ART care should always strive to address concerns of clients, most especially issues that may compromise ARV adherence.

REFERENCES


18) Treat Yourself Right. 2009. Menstrual Irregularities - Living with HIV.


**TABLE 1: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (n = 238)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>60</td>
<td>25.2</td>
</tr>
<tr>
<td>30-39</td>
<td>110</td>
<td>46.2</td>
</tr>
<tr>
<td>40-49</td>
<td>68</td>
<td>28.6</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
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<td></td>
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<tr>
<td>Single</td>
<td>29</td>
<td>12.2</td>
</tr>
<tr>
<td>Married</td>
<td>184</td>
<td>77.3</td>
</tr>
<tr>
<td>Separated/Divorced</td>
<td>25</td>
<td>10.5</td>
</tr>
<tr>
<td><strong>Educational status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>29</td>
<td>12.2</td>
</tr>
<tr>
<td>Primary</td>
<td>51</td>
<td>21.4</td>
</tr>
<tr>
<td>Secondary</td>
<td>78</td>
<td>32.8</td>
</tr>
<tr>
<td>Tertiary</td>
<td>80</td>
<td>33.6</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
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<td></td>
</tr>
<tr>
<td>Student</td>
<td>15</td>
<td>6.3</td>
</tr>
<tr>
<td>Petty Trader</td>
<td>129</td>
<td>54.2</td>
</tr>
<tr>
<td>Farmer</td>
<td>13</td>
<td>5.5</td>
</tr>
<tr>
<td>Artisan</td>
<td>13</td>
<td>5.5</td>
</tr>
<tr>
<td>Civil servants</td>
<td>48</td>
<td>20.2</td>
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<tr>
<td>Unemployed</td>
<td>20</td>
<td>8.3</td>
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<tr>
<td><strong>Religion</strong></td>
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<tr>
<td>Christian</td>
<td>150</td>
<td>63.0</td>
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<tr>
<td>Islam</td>
<td>78</td>
<td>32.8</td>
</tr>
<tr>
<td>Traditional;</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>Others</td>
<td>7</td>
<td>3.0</td>
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### TABLE 2: ART USE AND ADHERENCE

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (n=238)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Missed medications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>193</td>
<td>81.1</td>
</tr>
<tr>
<td>In the last one week</td>
<td>6</td>
<td>2.5</td>
</tr>
<tr>
<td>In the last one month</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>In the last six months</td>
<td>8</td>
<td>3.4</td>
</tr>
<tr>
<td>In the last one year</td>
<td>26</td>
<td>10.9</td>
</tr>
<tr>
<td><strong>Self reported adherence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>227</td>
<td>95.4</td>
</tr>
<tr>
<td>Bad</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Can’t say</td>
<td>6</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Calculated adherence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;90</td>
<td>11</td>
<td>4.6</td>
</tr>
<tr>
<td>90-94</td>
<td>42</td>
<td>17.7</td>
</tr>
<tr>
<td>&gt;95</td>
<td>185</td>
<td>77.7</td>
</tr>
<tr>
<td><strong>ART commencement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5 years</td>
<td>205</td>
<td>86.1</td>
</tr>
<tr>
<td>&gt;5 year</td>
<td>33</td>
<td>13.9</td>
</tr>
<tr>
<td><strong>ART regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; line</td>
<td>230</td>
<td>96.6</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; line</td>
<td>8</td>
<td>3.4</td>
</tr>
</tbody>
</table>
FIGURE 1: RESPONDENTS EXPERIENCING A CHANGE IN MENSTRUAL PATTERN
TABLE 3: TYPES OF CHANGE IN MENSTRUAL PATTERN OF RESPONDENTS SINCE COMMENCEMENT OF ART

<table>
<thead>
<tr>
<th>Types of change in menstrual pattern (n=71 with multiple responses)</th>
<th>Frequency (n=71)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menstruation has been irregular</td>
<td>39</td>
<td>54.9</td>
</tr>
<tr>
<td>Menstruation disappeared for some months, then comes again</td>
<td>15</td>
<td>21.1</td>
</tr>
<tr>
<td>Menstruation has disappeared since then and never come back</td>
<td>16</td>
<td>22.5</td>
</tr>
<tr>
<td>Menstrual flow has reduced in number of days</td>
<td>20</td>
<td>28.2</td>
</tr>
<tr>
<td>Menstrual flow has increased in number of days</td>
<td>12</td>
<td>16.9</td>
</tr>
<tr>
<td>Menstrual flow heavier than before</td>
<td>6</td>
<td>8.5</td>
</tr>
<tr>
<td>Interval between 2 consecutive months menstruation is now prolonged</td>
<td>9</td>
<td>12.7</td>
</tr>
<tr>
<td>Interval between 2 months menstruation is now reduced</td>
<td>23</td>
<td>32.4</td>
</tr>
</tbody>
</table>
### TABLE 4 - ASSOCIATED GYNAECOLOGICAL PROBLEMS EXPERIENCED AND RESPONDENTS’ REACTIONS CONCERNING THE CHANGES IN MENSTRUAL PATTERNS

<table>
<thead>
<tr>
<th>Variables (n=71 with multiple responses)</th>
<th>Frequency (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated painful sexual intercourse</td>
<td>16</td>
<td>22.5</td>
</tr>
<tr>
<td>Associated reduced enjoyment during sexual intercourse</td>
<td>10</td>
<td>14.1</td>
</tr>
<tr>
<td>I strongly believe that ARVs caused these menstrual changes</td>
<td>52</td>
<td>73.2</td>
</tr>
<tr>
<td>I can even identify which ARV may be responsible</td>
<td>22</td>
<td>31.0</td>
</tr>
<tr>
<td>Actions respondents have taken</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reported to the doctor</td>
<td>36</td>
<td>50.7</td>
</tr>
<tr>
<td>Had once stopped ARVs</td>
<td>8</td>
<td>11.3</td>
</tr>
<tr>
<td>Did nothing</td>
<td>27</td>
<td>38.0</td>
</tr>
</tbody>
</table>
### TABLE 5: ASSOCIATION BETWEEN MENSTRUAL CHANGES AND SOME SELECTED VARIABLES

<table>
<thead>
<tr>
<th>Variables</th>
<th>My menstrual pattern has changed</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n/%)</td>
<td>No (n/%)</td>
</tr>
<tr>
<td><strong>(a) Bi-variate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24</td>
<td>21(15.7)</td>
<td>22(16.5)</td>
</tr>
<tr>
<td>25-40</td>
<td>26(19.1)</td>
<td>53(39.4)</td>
</tr>
<tr>
<td>&gt;40 years</td>
<td>20(15.0)</td>
<td>19(14.0)</td>
</tr>
<tr>
<td>Missed pills in the last one year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13(6.2)</td>
<td>59(27.2)</td>
</tr>
<tr>
<td>No</td>
<td>52(24.8)</td>
<td>88(41.8)</td>
</tr>
<tr>
<td>Calculated adherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;95%</td>
<td>64(30.5)</td>
<td>23(11.0)</td>
</tr>
<tr>
<td>&gt;95%</td>
<td>35(16.7)</td>
<td>88(41.8)</td>
</tr>
<tr>
<td>Duration of ART</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5 years</td>
<td>58(28.0)</td>
<td>27(12.8)</td>
</tr>
<tr>
<td>&gt;5 years</td>
<td>102(49.2)</td>
<td>21(10.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>(b) Bi-variate analysis</strong></td>
<td>OR</td>
<td>p value</td>
</tr>
<tr>
<td>Missed pills in the last one year</td>
<td>0.4</td>
<td>0.002</td>
</tr>
<tr>
<td>(constant=No)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calculated adherence</td>
<td>7.0</td>
<td>0.001</td>
</tr>
<tr>
<td>(constant = &lt;95%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of ART</td>
<td>0.4</td>
<td>0.007</td>
</tr>
<tr>
<td>(constant=&gt;5 years)</td>
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</table>
CARDIAC MONITORING IN HER-2 POSITIVE ELDERLY PATIENTS TREATED WITH TRANSTUZUMAB

An Article Review By Dr. Rajani Sinha, India
(MBBS, MMSc in Oncology Student of Texila American University)
Email: - dr.rajanisinha@yahoo.com

SOURCE


KEYWORDS

Cardiotoxicity, Transtuzumab, HER -2 over expression, Breast Cancer, Elderly

INTRODUCTION

Human epidermal growth factor receptor -2 (HER-2) is a member of EGFR (epidermal growth factor receptor) family, plays a very significant role in cell growth and proliferation [1] HER – 2 protein is over expressed in 20% of breast cancer and is associated within aggressive course, poor prognosis and response to treatment [2-3]. The introduction of transtuzumab, a monoclonal antibody directed against, the extra cellular domain of HER - 2 receptor, has revolutionized the treatment of HER – 2 positive early breast cancer and has led to significant improvement in disease free survival and overall survival over chemotherapy alone.

In randomized multicenter trials with HER – 2 over expressing metastatic breast cancer patients, addition of transtuzumab to first line chemotherapy has improved objective response rate, the time to disease progression and overall survival over chemotherapy alone [4,5]. Hence transtuzumab is now considered as the standard of care for all patients who over amplify HER – 2 neu receptors.
These benefits have come with the cost of increased risk of cardiotoxicity. Transtuzumab related cardiotoxicity is mediated by interruption of normal HER – 2 signaling pathway in the heart, which is responsible for maintenance of normal growth, repair and survival of cardiomyocytes. Cardiotoxicity related to transtuzumab is different from that of anthracyclins as it is not dose related and appears to be largely reversible on discontinuation of therapy. There is no alteration is ultra structural abnormalities where as that due to anthracyclins are caused by free radical induced oxidative stress to cardiac muscles cells [12].

REVIEW OF LITERATURE

In the pivotal metastatic Breast Cancer trials cardiac dysfunction was seen in the patient treated with transtuzumab and chemothera. The incidence was greatest among the patients who received concurrent anthracyclins. The findings led to design the subsequent transtuzumab trials which included prospective monitoring of cardiac effects and protocols for its management. The risk of cardio toxicity also driven efforts to develop non- anthracyclin based regimens for HER – 2 positive breast cancer patients.

Four major adjuvant trials: HERA ( herceptin adjuvant trial), NSABP-B31 trial, the national surgical adjuvant breast and bowel project,(N CCTG) N 9831 trial, the North Central Cancer Treatment Group and (BCIRG) 006 trial, the Breast Cancer International Research Group – investigated various adjuvant approaches with transtuzumab. More than 13000 women enrolled were HER-2 positive. Results indicated that adjuvant transtuzumab reduces recurrence by nearly 50% and increases overall survival by 33% therefore; transtuzumab is adopted as the standard for care in early breast cancer.

Comparisons between studies related to cardiotoxicity are difficult as they used different criteria for assessing cardiac function. The rate of asymptomatic decline by more than 10% in LVEF ranged from a high of 18% in BCIRG 006, to a low of 3% in HERA.

In HERA incidence of cardiototoxicities were higher in transtuzumab group and more in patients who were treated with cumulative doses of doxorubicin ( 287 mg/m² vs 257 mg/m²or epirubicin (480 mg/m² Vs 422 mg/m²) and had lower baseline LVEF (55% - 60% Vs. > _ 60% and 60% - 65% Vs > _ 65%).

No association was found between cardiac end points and older age, previous cardiac disease, hyperlipidemia or hypertension.
The Finland Herceptin trial (Fin HER) ,HER -2positive patients who received 9 weeks of transtuzumab infusion showed better rate of 3 years recurrence free survival that the women who do not. No decrease in LVEF or Cardiac failure was observed.

**BRIEF REVIEW OF ARTICLES**

(1) *Reversibility of Transtuzumab*– Related Cardiotoxicity: New Insights Based on Clinical Course and Response to Medical Treatment. Michael S.Ewer et al [6] studied on the patients who developed cardiotoxicity while receiving transtuzumab and they improved on discontinuation of the drug (suggesting its reversible action on cardiac myocytes). The found that the mechanism underlying transtuzumab related cardiotoxicity are different from anthracyclins, in part due to absence of ultrastructural changes (evident on endomyocardial biopsy). Mean recovery time of LVEF was 1.5 months and most of the patients could resume the treatment.

(2) *Heart Remodeling induced by adjuvant transtuzumab*– Containing chemotherapy for breast cancer over expressing human epidermal growth factor receptor type – 2. Prospective study by Piotrowski G etal.[7]. They investigated the cardiac changes that occurred in patients of HER -2 positive breast cancer who received transtuzumab in adjuvant setting and concluded that transtuzumab induces left ventricular and left atrial cavity dilatation together with LV systolic function impairment.

(3) *Transtuzumab related cardiac events in the treatment of Early Breast Cancer*. Fried G, Regev T, Moskovitz M.. [8].

A retrospective study was performed on the patients of cancer breast HER – 2 positive who received transtuzumab, cardiac events (CE) were observed in 21% patients. There was a significant decrease in LVEF between baseline/ post AC and during transtuzumab treatment (mean LVEF 64.29% vs 61.97%, P < 0.001). Treatment related risk factors were age and interval since last AC. Transtuzumab loading dose did not influence CE rates. Patients who received left chest wall irradiation had significantly increased CE rates vs patients without radiotherapy (p <0.05). Any cardio vascular risk factor caused increased risk though not statistically significant.

Concluded that age and prior Anthracyclins appeared to predict the cardiotoxic event hence cardiac monitoring seems important for all patients during treatment with transtuzumab especially in elderly.

(4) *Adjuvant trastuzumab cardiotoxicity in patients over 60years of age with early breast cancer, a multicentric cohort analysis.* [10]
L. Tarantini et al. analysed 499 HER 2 +ve early breast cancer patients who were treated with adjuvant transtuzumab and chemotherapy at 10 Italian institutions. They evaluated disease prevalence and patient characteristics in patients over 60 years of age and prevalence of transtuzumab and chemotherapy cardio toxicity and risk factors. They concluded that 32% of HER 2 positive EBC patients treated with transtuzumab chemotherapy are ‘over 60’. These patients have increased cardiovascular risk profile and develop a transtuzumab chemotherapy cardiotoxicity commonly.

(5) Early increases in multiple Biomarkers Predict Subsequent cardiotoxicity in Breast Cancer patients treated with Doxorubicin, Taxanes and transtuzumab. by Ky B et al.

They found that early increases in Troponin I and MPO (myelo-peroxidase) offer additive information about cardio toxicity risk in patients undergoing doxorubicin and transtuzumab therapy.

ARTICLE SUMMARY

The article states that they reviewed the records of elderly breast cancer patients >_ 70 years of age who were treated with transtuzumab since 2006. NYHA classification was used to define symptomatic cardiotoxicity.[25] Asymptomatic cardiotoxicity was defined as an absolute drop of LVEF by >_ 20% or a drop of >_ 10% with final LVEF < 50%. They studied 45 patients of median age 75.9 years, of them, 12.5% patients of early breast cancer and 23.8% patients with advanced disease experienced asymptomatic cardiotoxicity. 8.9% patients developed symptomatic congestive heart failure were all with advanced breast cancer. All the patients except one recovered in a median time of 5 weeks. They concluded that elderly breast cancer patients treated with transtuzumab have an increased incidence of cardiotoxicities as they have history of cardiac disease and/or diabetes. They have advised for continuous cardiac monitoring in this group of patients.

ARTICLE STRUCTURE

The article is well written. It has short paragraphs with bold headings. This makes it easy to comprehend.

The article starts with an abstract which tells us in nutshell the subject and the outcome of the study. It also tells us the background behind the study. It has an introduction which sites the brief concept of HER-2 receptor and transtuzumab. The mechanism of action of transtuzumab induced cardiotoxicity is due to blockade of HER – 2 signaling which is responsible for growth, repair.
and survival of cardio myocytes [12]. A large review of advanced breast cancer patients showed increased risk of cardiac events in patients receiving concomitant transtuzumab and anthracyllin derivative plus cyclophosphamide ~ 27% and a substantially lower risk in patients treated with paclitaxel and transtuzumab ~ 13% or with transtuzumab alone ~ 3-7%. Other major risk factors for transtuzumab related cardiotoxicity is age > 60 years, lower baseline LVEF [4, 14] and prior anthracycline exposure.

Next paragraph describes about patients and methods. It says detail about the patients inclusion criteria and exclusion criteria. Definition of cardiotoxicity assessment is clear LVEF assessed either by MUGA scan or by echocardiography [16]. Cardiac events were classified according to NYHA system to document symptomatic CE. [17] Definition of asymptomatic cardiotoxicity is clear.

Results of the retrospective study is described in detail. 26.7% of patients experienced cardiac events. 17.8% developed asymptomatic LVEF decline and 8.9% developed symptomatic congestive heart failure (CHF). All the patients recovered completely after discontinuation of transtuzumab over a median time of 6 weeks. After reversal of LVEF, treatment was restarted with transtuzumab. Only one patient had repeat asymptomatic fall in LVEF which completely recovered without discontinuation of the drug.

All the patients with symptomatic CHF presented with rapidly progressive (< 10 days) dyspnoea and orthopnea. Echocardiography, 2 D ECHO and chest X-ray were used to diagnose CHF. Patients presenting with cardiac events (symptomatic or asymptomatic ) were more often had cardiovascular risk factors. They also were associated with overweight BMI > 30 (P = 0.045), history of previous cardiac event ( P = 0.047) and diabetes mellitus (P = 0.017).

This was followed by discussion and conclusion. In all the breast cancer patients who over express HER – 2 neu receptors, transtuzumab is the standard of care [18,19]. Since incidence of cancer is increasing with age and nearly 70% of newly diagnosed cancer are > 65 years of age [20], elderly cancer patients are expected to increase in the coming years. So, the information of efficacy and safety of anticancer treatment is needed especially in this subgroup of patients who are mostly excluded from pivotal studies. [15, 21] Hence, this study aimed to assess cardiac safety profile and potential cardiac risk factors associated with transtuzumab treatment in patients > 70 years.

The study showed that overall incidence of cardiac events ~26.7% and symptomatic CE in 8.9% cases. Most of the cases(91.7%) are reversible. The results were slightly higher than that reported in transtuzumab pivotal trials [4,5]. This discordance is due to the characteristics of patient population- age and comorbidities. Authors said that their findings were more consistent with that from M D Anderson Cancer Centre than those from pivotal studies.
Authors concluded that there is significant increase in incidence of cardiac events in those patients who had history of cardiac disease &/ or diabetes. Hypertension and smoking history were not demonstrated to increase transtuzumab related cardiotoxicity transtuzumab safety profile among elderly breast cancer patients are similar to already reported in earlier studies [13], high proportion of reversibility and safety on retreatment [14, 6] and lack of association between transtuzumab dose [14] and left sided radiotherapy [22] and cardiotoxicity.

Authors also mentioned that there is need for close surveillance of early symptoms and cardiac function in elderly breast cancer patients treated with transtuzumab and to refer them to cardiologist if one or more cardiovascular risk factors are present before or during the treatment with transtuzumab for careful monitoring by multidisciplinary team.

The style of writing is concise and fluid. It serves the purpose of transferring basic aim of study and suggests that further prospective clinical trial are awaited to have more cardiac safety data in elderly population. It also suggest that troponin I level might help to establish diagnosis and prognosis in such patients [24,25].

The article is supported by well documented and acclaimed references.

**ARTICLE CRITIQUE**

**AUTHORITY**

The authors are from Breast Cancer Centre, Department of Medical Oncology Vall d’ Hebrón University Hospital Barcelona, Spain. The lead author C. Secrano is heading the department. The co-authors are working in the same faculty.

**ACCURACY**

The authors have tried to be accurate. They have referred to relevant articles published in various journals like New England Journal, Journal of Clinical Oncology. These articles throw light on the main side effect of transtuzumab - cardiotoxicity – rate of incidence, mechanism of action and reversibility on discontinuation of the drug, so this article is accurate. It is unique in the sense that it has studied cardiotoxicity related to transtuzumab in elderly population which are usually underrepresented in most of the clinical trials. Moreover it will also stimulate more clinical trials to include such patients based on their conclusions which will prove accuracy of the study in a prospective way.
CURRENCY

The article is current as there has been no similar study in the past. There has been multiple studies in younger patients which highlights the cardiotoxic effects of transtuzumab and its reversible action.

RELEVANCE

The article is relevant because the incidence of cancer is greatly increasing with age and almost 70% of newly diagnosed cancer patients are in age group >65 years [20] so the study is very much relevant as it has focused on the cardiotoxicity related to transtuzumab treatment in the elderly patients who mostly have one or more cardiovascular risk factors.

OBJECTIVITY

The information in this article has been taken with the objective to analyse the risk of cardiac events in relation to treatment with transtuzumab in elderly breast cancer patients who generally are predisposed with one or more cardiovascular risk factors.

STABILITY

The fact that this article is published in the Annals of Oncology speaks by itself the stability of the article.

ANALYSIS OF GRAPH / IMAGE / TABLE

Table 1- gives details of patient demographics- number of patients in various age subgroups, ECOG performance states, stage of the disease, histological type and their baseline LVEF.

Table 2 - shows details of LVEF variation (symptomatic or asymptomatic) cardiac events distributed by stage of the disease per patients.

Table 3 – gives univariate and multivariate analysis of Cardiac Risk Factors (CRF). Comprehensive analysis of CRF and transtuzumab related cardiac toxicity in an elderly breast cancer population suggest a significant increase in incidence of CE among patients with a history of cardiac disease and diabetes. Other factors like hypertension and smoking history do not relate to increase in cardiotoxicity though the data interpreted is by a small sample size.
RECENT ADVANCES RELATED TO THE TOPIC

Data obtained from this study can serve to advise clinicians to be cautious while administering trastuzumab in elderly, Her-2 positive breast cancer patients especially when they have one or more CRF. It is the first kind of its study that may stimulate further prospective studies involving elderly patients to prove more accurate data with respect to trastuzumab related cardiotoxicity.

CONCLUSION

Trastuzumab can be safely administered in elderly patients with strict surveillance and monitoring of LVEF before and during trastuzumab treatment. The fact that mortality rate at 5 years after diagnosis of CHF is ~ 50% in patients > 65 years [23], it is necessary to monitor early symptoms and cardiac function in trastuzumab treated elderly patients. Hence, can be referred to cardiologist for prompt management of early symptoms in such patients.

REFERENCES


RARE OCCURRENCE OF ENTEROCUTANEOUS FISTULAE FOLLOWING ONLAY MESH REPAIR FOR INCISIONAL HERNIA: A CASE SERIES

A Case Study By Shah BC, Degloorkar S, India
(Senior Consultant Surgeons, Department of Surgery, Bhaktivedanta Hospital, Mumbai)
Email: bcs.vsd@gmail.com

ABSTRACT

Enterocutaneous fistula (ECF) is a rare and late complication following mesh repair for incisional hernias. This report is a case series of two patients reporting ECF following 10 and 13 years after open surgery for the incisional hernia. Laparotomy was performed in both and the defect was repaired by anatomical closure without a mesh. This case report emphasizes that although polypropylene mesh has been shown to be relatively safe in many studies, it can at times be associated with long-term ECF.

KEYWORDS

Complications, Mesh repair, EC fistula

INTRODUCTION

Mesh repair is recommended as the first-line surgical management for abdominal hernias as the recurrence rates are significantly lower. [1] Of the two types of meshes used, polypropylene mesh has been associated with a lower incidence of post-operative complications including infections, ECF and recurrent hernias relative to multifilament polyester mesh and is widely used now-a-days. [2] Mesh repair using onlay technique is found to be safe and effective for incision hernia. [3] Although, recurrences of the hernia and seroma formation were reported to be the most common complications following onlay repair of incision hernia, reports of ECF are contradictory. [4, 5] We describe here two cases of ECF as a long-term complication following onlay mesh repair for incision hernia.

Case 1:

A 40 year old female, who was operated for incision hernia following a caesarian section with onlay mesh repair using polypropylene mesh 10 years ago, presented with the complaints of...
swelling and pain in the infraumbilical region for the past 2 weeks. Contrast enhanced computed tomography (CECT) revealed clumping of bowel loops adhering to the abdominal wall. There was no evidence of contrast leak suggesting ECF but an exploratory laparotomy that was performed after obtaining written informed consent from the patient revealed the discharge of a faeculent material with erosion of the mesh by the bowel loop. Mesh was removed and the abdomen was closed in layers.

Case 2:

A 58 year old female with concurrent diabetes mellitus and systemic hypertension, who had two episodes of open onlay mesh repair (the first 13 years ago and the second 10 years ago) in the past, presented with the complaint of non healing abscess in the abdominal wall (Figure 1) for the past 6 weeks. CECT abdomen showed clumping of bowel loops to the abdominal wall without any contrast leak. Exploratory laparotomy revealed ECF (Figure 2). The mesh was excised along with the bowel loop and the abdomen was closed in layers.

**DISCUSSION**

Incision hernia may be treated by either a simple repair or by using mesh. Although, reports indicate a lesser incidence of recurrence of hernia following the use of mesh, controversy exists in literature about its effectiveness. [6] Different techniques of mesh repair have been advocated, but onlay has been found to be more safe and effective than the others.

ECF following onlay mesh repair for incisional hernia is less common than after subfascial repair. [2, 7] Studies have shown that multifilamented polyester mesh, excision of hernia sac, lack of omental interposition and the presence of fascial gap are associated with a higher incidence of ECF. [2] Although ECF has been reported within few months following repair of the hernia, it is usually a long-term complication being reported after many years. [8-10] Even the present series reports these following 10 and 13 years of surgery. ECF occurs usually due to a chronic erosion of bowel by the mesh placed which is in direct contact with intestinal loops. [11] Although Basoglu [12] has recommended omental coverage to decrease the contact of the mesh with the intestinal loop and thereby the chances of ECF, we are unaware of whether this was performed in our patients.

To conclude, ECF following onlay mesh repair is uncommon and occurs as a late complication. Placing omentum between the mesh and the intestinal loop may aid in preventing ECF.

**Conflict of interest:**

There is no conflict of interest.
REFERENCES


FIGURE 1. NON HEALING ABDOMINAL ABSCESS

FIGURE 2. EXCISED PART OF THE INTESTINE WITH FISTULAE
THE EFFECT OF COMBINED ORAL CONTRACEPTIVE PILLS (COCP) CONTAINING
LEVONORGESTREL AND ETHINYLESTRAadiOL ON KIDNEY FUNCTION

An Article Review by 1Ekhator C.N., 2Omorogiuwa A. and 1Akpamu U., Nigeria

(1 Department of Physiology, Faculty of Basic Medical Sciences, College of Medicine, Ambrose Alli University, Ekpoma, Edo State, Nigeria.
2 Department of Physiology, school of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City, Edo State, Nigeria)

Email:- uwaifoha@yahoo.co.uk

ABSTRACT

BACKGROUND

Despite the modifications on Oral Contraceptive Pills (OCPs) in term of content and dosage to lessen their side effect, paucity of information existed on the effect of COCP on kidney function.

AIM OF STUDY

Hence, this study investigates the effect of COCP containing 0.15mg levonorgestrel (a progestogen) and 0.03mg ethinylestradiol (an estrogen) on kidney biochemical parameters and electrolytes.

METHODS

The study involves 15 female rabbits divided into three groups (A, B and C). Group A served as the control, while B and C served as the test groups and were administered the COCP per body weight human doses for 7 days and 14 days respectively. At the end of the study, blood sample was obtained for the determination of plasma creatinine, urea, Na, Cl and K using standard laboratory procedures.

RESULTS

Results showed significant increase (p<0.05) in plasma creatinine, urea and K+ but a decreases in plasma Na+ and Cl- in the tests compared to the control.

CONCLUSION
Considering the observed changes in the parameters herein studied, COCPs usage is not without impact on kidney function and may cause homeostasis dysfunction and hence the need for further studies.

**KEY WORDS**

Estrogen, Progestogen, Electrolyte, Creatinine, Urea.

**INTRODUCTION**

The World Health Organization in 1998 and other studies estimated that over 100 million women worldwide are on oral contraceptive pills (OCPs) [1]. Hitherto, it is known that many women discontinue it uses primarily because of issues concerning cycle control, weight gain, water retention, perimenstrual symptoms, and hypertension [2,3] venous and arterial cardiovascular complications [4-6] nausea, breast tenderness, irregular menstrual bleeding and thrombosis [7-10]. These side effects are of great clinical importance and have over the years resulted in many important changes in the composition and use of these preparations to reduce the side effects.

Of greater concern, is the fact that despite extensive clinical experience, many metabolic effects of OC treatment remains to be explored. In fact, there are only few studies evaluating body composition and OCP usage. Indeed, the questions about metabolic effects of OCPs and weight gain are of particular relevance to females during OCP treatment. Recently, our findings reported that levonorgestrel and ethinylestradiol containing COCP elicit anti-obesity properties and potentials for weight management in both the obese and non-obese rabbits [11]. In fact, natural and synthetic female sex hormones have been reported to have various effects on water and electrolyte balance; a function of the kidney known to be critical for normal cellular function and maintaining adequate blood and plasma volume (PV) and osmolality [12].

This finding lead to the curiosity of what the consequence of this COCP containing levonorgestrel and ethinylestradiol may have on kidney function considering it physiological role. The goal of this study was to evaluate the effects of levonorgestrel and ethinylestradiol containing COCP on kidney function indicated by some selected parameters and electrolytes.

**METHODS**

**EXPERIMENTAL ANIMALS**: Fifteen adult female rabbits were obtained from Aduwawa market in Benin City, Nigeria, and transported to the experiment site where they were housed in a well-ventilated room under a 12/12 hours light/dark cycle and fed feed (Vital feed (Grower pellets produced by Grand Cereals Ltd, a subsidiary of UAO Nigeria PLC, Jos, Plateau State), grass and water ad libitum.
DRUG OF STUDY: COCP tagged AVA 30ED (containing Levonorgestrel 0.15mg and Ethinylestradiol 0.03mg) was purchased from a Pharmacy store in Ekpoma, Nigeria. AVA 30 ED is a combined oral contraceptive consisting of 21 hormonal tablets and 7 non-hormonal tablets. Because of the small amount of hormone contents, it is considered as a combined low-dose oral contraceptive preparation.

EXPERIMENTAL GROUPING: The rabbits were divided into three groups (A, B and C) of 5 rabbits each; A served as the control, while B and C served as the test groups treated for 7 days and 14 days respectively.

DRUG ADMINISTRATION: Each day a tablet was dissolved in 100ml distilled water and the appropriate dose per kg was measured out for oral administration via an oro-gastric tube using a 2ml syringe. The dose was determined based on comparative dosage per body weight proportion akin to humans.

SAMPLE COLLECTION: At the end of the experiment and 24 hours after the last administration of COCP, blood samples were collected from each rabbits by means of cardiac puncture using 5ml hypodermic syringe and needles under mild chloroform anesthesia. Sample analysis: The collected blood sample was immediately sent to the biochemical laboratory for analysis. Serum urea and creatinine level were analysis as described by Baker et al. [13] serum potassium, sodium and chloride were analyzed using standard method as described by Tsalev and Zaprianov [14].

DATA ANALYSIS: The mean ± standard deviation was determined and one-way analyses of variance was performed using SPSS version 17 soft ware. The significance level was set at p<0.05.

RESULTS

Table 1 shows the variations in selected kidney function parameters of rabbits treated with COCP containing 0.15mg levonorgestrel and 0.03mg ethinylestradiol synthetic hormones. COCP was observed to significantly increase (p<0.05) urea and creatinine in a manner that is dependent on period of ingestions compared to the control (group A). Furthermore, on electrolytes with kidney function significant indicated by K, Cl and Na, COCP was observed to have a significantly (P<0.05) time dependent impact on K, Cl and Na levels. Specifically, the impact on K level was a time dependent increase in the test groups while Cl was a time dependent decrease compared to the control. Although Na was observed to reduce significantly with COCP ingestions when compared to the control (136.00±1.41mmol/L), however, it increases with increased period of ingestion but the difference was statistically not significant (see table 2).

DISCUSSION
The two most influential female sex hormones; estrogen and progesterone, change in concentration across the menstrual cycle and are governed by OCP usage [12]. In the present investigation, it was observed that COCP, containing 0.15mg levonorgestrel (a progestogen) and 0.03mg ethinylestradiol (an estrogen), significantly increases creatinine outputs suggesting an increase in muscle metabolism. This is sequel to the fact that creatinine is produced and excreted at a constant rate which is proportional to the body muscle mass [15]. The mean significant increase in creatinine in this study is in line with the study by Oelker et al. [16] who studied an oral contraceptive containing an antimineralocorticoid progestogen, drospirenone, but contradicts the study by Surasak et al. [17] who reported no significantly changed in mean serum creatinine following 6 cycles of OCPs ingestion containing Drospirenone. Although depressed levels of plasma creatinine are rare and not clinically significant, its plasma elevation is indicative of under excretion, suggesting kidney impairment and as such regarded as the most useful endogenous marker in the diagnosis and treatment of kidney disease and measured primarily to assess kidney function [18,19]. This effect on creatinine may be the progestegen content reason own to a report by Smith and Sizto [20] that high progestogen increases serum creatinine.

Our findings on electrolytes with kidney function significance showed that COCP containing 0.15mg levonorgestrel (a progestogen) and 0.03mg ethinylestradiol (an estrogen), significantly increases plasma Na⁺ and K but decreases plasma Cl⁻. This finding is in accordance with several other previous studies [16,17] where a different oral contraceptive containing drospirenone as progestogen. This effect on electrolytes showed by OCPs suggests that the COCP used in this study may alter the fluid nature of extra cellular fluid. Thus understanding the interactions between OCP and the fluid regulatory system is crucial. In fact, female sex hormones have been reported to influence sodium and water distribution and thus fluid compartment volumes and dynamics [12] and may not be unrelated to the hypertensive effect of OCPs previously reported by several studies. The mechanism behind this effect of the COCP used in this study may be explained by the fluid retention potentials by activating the renin-angiotensin-aldosterone system, enhances vasodilation, capillary permeability and lower operating set point of plasma osmolality by estrogens [21-25]. Progesterone on the other hand has also been noted to antagonizes estrogenic effect [22] by competing directly with the same mineralocorticoid receptor as aldosterone, which may cause a transient natriuresis [26].

Our findings therefore suggest that levonorgestrel and ethinylestradiol containing COCP, may deregulate hemostatic. Similar assertion has been reported in the study of Klipping et al. [27], who studied two combined oral contraceptives containing ethinyl estradiol 20 microg combined with either drospirenone or desogestrel on hemostatic parameter and found changes in hemostatic parameters such as increase in activation markers for thrombin (clotting activation), fibrin (fibrinolytic activation) turnover, in (pro)coagulatory, and in (pro) fibrinolytic parameters as well as a decrease in PAI-1 antigen levels. He then concluded that these suggested that the overall balance between factors influencing hemostasis were maintained on an up-regulated level in both study groups [27].

CONCLUSION
Judging by the results from this study, it is commendable that further animal researches and human studies be investigated on, as levonorgestrel and ethinylestradiol containing COCP may not be without effect on kidney function. There is also a need to access the effect of other OCPs on kidney function and other body organs.

REFERENCES


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