A ONE-YEAR STUDY OF THE EPIDEMIOLOGY AND OUTCOMES OF VARIOUS BIRTH DEFECTS IN PEDIATRIC PATIENTS AT GEORGETOWN PUBLIC HOSPITAL COOPERATION

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ABSTRACT

BACKGROUND

Although, birth defects are one of the leading causes of infant deaths and long term disabilities and have contributed significantly to the global burden of diseases, extensive researches have not been carried out in Guyana.

METHODS

A retrospective study, of 138 patients, diagnosed with Congenital Malformations at Georgetown Public Hospital Cooperation, between January 2007- December 2007was carried out. These patients' medical records; inclusive of infant, neonatal intensive care and postnatal; were located and information was recorded in the form of a questionnaire which had structured and detailed parameters. Exclusion criteria were records for all stillborns, pregnanciesterminated at or after 20 weeks of gestation, out- patients and or patients in specialized clinics / institutions. Analysis on various variables (demographic distribution, clinical outcomes, clinical presentation, Apgar score, birth weight, maternal age, sex, ethnicity, previous infant with a birth defect, family history of a birth defect, known teratogenic exposure, maternal medical history, lack of folic acid supplementation and average length of hospital stay) was done using Microsoft Office Excel version 2003 for information on the epidemiology, management and clinical outcomes of the condition in the Guyanese population.

RESULTS

I found an estimate incidence 2240 cases of birth defects occurring annually in Guyana. The majority of cases were from Regions 4 (46.8%) and 3 (10.9%). The majority (73.9 %) of cases was seen in the age group birth-5 months, followed by (9.4%) > 50 months (>12 years old), 6-10 month (5 %) and 21-25 month (4.4 %). There was a male to female ratio of 1.3: 1 of having a birth defect. Afro-Guyanese accounted for almost one half (48%) of the cases followed by Indo-Guyanese, Mixed and Amerindians. The most common types of birth defects were congenital

heart disease, Hirshsprung disease, hypospadia, cryptorchidism, accessory breast, club feet and syndactyl. The average length of stay was 6.5 days. One mother used alcohol and another used an abortificient during the current pregnancy. 82% of patients underwent surgery while 18% had medical interventions. Few patients had laboratory testing done. Patients generally had excellent clinical outcomes given a mortality rate of 0 %.

CONCLUSION

My findings highlight the clinical and public health importance that should be placed on Congenital Malformations in Guyana and to re-evaluate our approach to the condition and to introduce nation-wide screening practices.

INTRODUCTION

Congenital anomalies or **birth defects** have contributed significantly to the global burden of diseases. They account for 15–20% of all stillbirths and 2-3% of all live births, with approximately 60% identified in the first month and 80% by the end of 3 months of life. A major defect is visible at birth in 3 to 4 % of newborns (1% have a monogenetic disease, 0.5% a chromosomal disorder, 1-3% a multifactorial disease) [1] while 7.5% of children display a congenital defect by age 5[1].

According to a World Health Organization (WHO) report, nearly 3 million fetuses and infants are born annually with major congenital malformations, with the most common occurring in the brain (10:1000), heart (8:1000), kidneys (4:1000), limbs (2:1000), and other anatomical locations 6:1000). In 2006, a report by the March of Dimes shows that 8 million babies worldwide are born with gene-related birth defects, which accounts for 6% of all global births in a given year. This same report also published the five most common defects that also account for a quarter of the world's cases. They include heart defects (>million births worldwide yearly, neural tube defects (324,000 births worldwide yearly), hematological disorders such as sickle cell disease and thalassemia (>307,000 births worldwide yearly), Down syndrome (>217,000 births worldwide yearly) and G6PD deficiency (>177,000 births worldwide yearly.

They show no predilection to race, culture, or socioeconomic level. They can be isolated or part of a syndrome and are a leading cause of neonatal and infant morbidity (mental retardation, cerebral palsy, epilepsy, autism, permanent bilateral hearing loss, legal blindness) and mortality with an estimated 495,000 deaths world, of which 20% occurs in developed countries. Approximately 40% of childhood deaths are as a result of birth defects and genetic disorders[2],whereby they are responsible for almost half of all deaths in term newborns.

They also impact on that country’s resources, particularly in the health care sector and create financial, social and psychological burdens on the families’ of children born with defects. These defects can demand frequent multiple hospitalizations andcostlycorrective surgical procedures and even after such corrections, patients will continue to experience shortcomings (whether physical, social or psychological) as a result of their condition. Multiple studies have led

credence to this statement by documenting in infants with congenital heart diseases, difficulty feeding postoperatively; a higher risk of infection;longer hospitalizations and poor postoperative catch-up growth[3].

The etiology of most birth defects is *unknown* but a complex interaction between multiple *environmental* exposures (radiation, infection, ACE inhibitors, phenytoin, valproic acid, retinoids, warfarin, tobacco, androgens, rubella, varicella zoster, diabetes, phenylketonuria, alcohol, maternal thyroid disease, maternal obesity[4], common cold in the first trimesterof pregnancy[5]), *genetic* susceptibilities and cultural practices (consanguinity) are probably involved. This complex interaction of factors operates at crucial periods of organogenesis to produce the defect, either in the form of a single anomaly or in syndromes. The genetic susceptibility is usually enhanced by an environmental trigger and the end result is a phenotypic expression (defect) with various degrees of penetrance and manifestation as either sporadic, single or multiple, visible or hidden, gross or microscopic. This complex interaction of factors also affects the incidence of the defect in various populations.

Classification of these defects is confusing but recently a new hierarchical system came into use (see appendix 2). Like any disease, the diagnosis of a birth defect lies within the history, physical examination and any special tests performed. There may be a positive family history of a particular defect; physical findings in the mother carrying a fetus with a birth defect may include a breech presentation, polyhydramnios or oligohydramnios. Special tests, mainly, ultrasonography; amniocentesis; fetoscopy and fetal blood sampling or chiorionic villus sampling are useful in the prenatal diagnostic stage, as a screening tool or to confirm a suspecting defect based on the positive history and obstetrical findings in the mother. In Guyana, we are limited by our history taking, physical examination and ultrasonography.

The approach to the patient should always be multidisciplinary and should include areas for prenatal genetic counseling, specialist care, patient follow up, referral systems and recurrence risk assessment. There are various treatment options and these depend on various factors such as the type of defect, infant characteristics (prematurity, birth weight), socioeconomics and ethical issues such as early selective termination of pregnancy. Hope for a productive life, lies in the fact that certain defects are correctable by surgical approaches, for example, Club foot; Cleft lip/palate; certain Congenital Heart Defects. There is also a role for diet intervention in defects of metabolic/enzyme pathways such as phenylketonuria. Prenatal therapy for obstructive defects such as hydrocephalus and uropathy, is theoretically possible but in its experimental stages. Last but not least, prevention (screening) is always better than a cure and in this lies the concept of genetic engineering and other interesting approaches (cytogenic / chromosomal with or without skin fibroblast studies, enzyme assays) to birth defects that promise hope for the future.

OBJECTIVES

The objectives of this study will be fourfold: (1) To determine what types of Birth Defects were documented at GPHC in 2007. (2) To determine the epidemiology of these various Birth Defects. (3) To correlate established risk factors (genetic: previous infant with a birth defect, family history of a birth defect, maternal age; environmental: known teratogenic exposure,

obesity, diabetes, lack of folic acid supplementation, maternal infection) with these birth defects. (4) To determine the clinical outcome of the patients.

METHODOLOGY

Profile of the study population

The study population comprised of infants with birth defects who were born from January1, 2007, through December31, 2007, to women at Georgetown Public Hospital Corporation,Guyana.

Guyana, an English-speaking country of 83,000 square miles (215,000 sq.km.), is found in the northern part of the Amazon Basin of South America, just north of the Equatorwith Venezuela to the west, Brazil to the south and Suriname to the east. The population of 751,000[5]is made up of 6 ethnic groups, namely African (40%), East Indian (51%), Chinese, Portuguese, European, Amerindian and Mixed. The Epidemiology Division of the Ministry of Health in Guyana has overall responsibility for disease surveillance.

Georgetown Public Hospitalwas established in 1838 mainly for the benefit of seamen and later in April 22, 1999 became a Corporation. As of today it is managed by a board of ten members and a management team spearheaded by a Chief Executive Officer. This tertiary health care institution has 550 beds and offers both in-patient and out-patient services in excess of twelve specialties. There is a Central Medical Laboratory, 24-hour

Pharmacy services, 24-hour Accident & Emergency services, Library, Sewing room, Laundry room, Neonatal Care Unit, Malaria Clinic, Chest Clinic, GUM Clinic, Intensive Care Unit / High Dependency Unit,

Burns Care Unit and a recently established Caribbean Heart Institute, just to name a few.

Study design:

The researcher undertook a retrospective study using patient records on birth defectsfrom GeorgetownPublicHospital for the year 2007.

Inclusion Criteria:

Pediatric patients who were selected are those with a birth defect in utero (diagnosed by ultrasonography), at birth or diagnosed within 72 hours of birth and up to 12 years of age.

Records (maternal, infant, neonatal intensive care and postnatal) from January 2007- December 2007were collected and analyzed.

All types of birth defects were included. Patients who died before any complete medical evaluation (this included, physical examination, laboratory investigations and other special tests) was preformed, he or she was included in the study population. Those with multiple birth defects were also selected. Mothers, who had multiple births with birth defects, were again included in the study.

Exclusion Criteria:

If the patient satisfied the inclusion criterion multiple times within the study period, only the data relating to the first time that patient presented to hospital was recorded. Patients who were managed as out-patients and at the Pediatric Clinics were excluded from the study. Patients who were also referred to specialized institutions (for example, Ptolemy Reid) for care were excluded. Data for stillborn infants, and for pregnanciesterminated at or after 20 weeks of gestation was excluded since there was be no definite and scientific means (no postmortem, no chromosomal studies done in Guyana) to confirm that these infants and fetuses had a coexisting birth defect(s).

Birth defects were grouped according to body systems affected and as either major or minor defects. The latter classification was determined based on the severity of the defect, that is, is the defect correctable by surgical approaches (for example, Club foot, Cleft lip/palate, Polycystic Kidneys, Spina bifida, Congenital Heart Defects) or by diet intervention (defects in metabolic/enzyme pathways) or will the defect lead to significant biological, physical and psychological disabilities; for example, Cerebral Palsy.

Assumptions:

Firstly, the researcher assumed that all patient information was accurately entered in the charts and secondly, there was no missing patient information. Thirdly, the attending physicians would have used established scientific criteria and testing to determine what type of birth defect was present.

Data collection:

This study was approved by the Head of Pediatrics Department, Georgetown Public Hospital. A retrospective review of all notified cases of birth defects from the said hospital within the year 2007 was conducted in the form of a questionnaire (see appendix 1).

All available clinical (maternal, infant, postnatal charts and those from the neonatal intensive care unit) and laboratory (inclusive of enzyme assays, hematology reports, biochemistry results, radiological findings, genetic studies) data entries for these cases had determined the final classification for all the cases of Birth Defects. The database system at Georgetown Public

Hospital was used to identify the pediatric patients with the various Birth Defects. These charts were then found manually.

Independent variables that were studied were*maternal age, sex, ethnicity,previous infant with a birth defect, family history of a birth defect, known teratogenic exposure, maternal medical history (diabetes, hypertension, thyroid diseases, infection), maternal obesity, lack of folic acid supplementation*, and *demographic distribution* of the cases. There was no bias in terms of sex and ethnicity. Age was entered as a categorical variable (birth -5 mo, 6- 10 mo….). In the "history of preceding maternal infection", the investigator looked for any documented signs and symptoms and laboratory evidence of an infection. The demographic distributionincluded cases from all of the ten natural regions in Guyana. In the category of known teratogenic exposure, the investigator included those substances that have been scientifically established as a direct cause of the birth defect; namely maternal smoking and alcohol use, illicit drug use, ACE inhibitior use during second and third trimesters, skin preparations containing vitamin A (Accutane™).

Dependent variables that were studied included the *clinical outcome*s. Another dependent variable that was tested was the *clinical presentation* in the reported Birth Defect cases. Other dependent variables that were investigated were *average length of hospital stay* after birth, *Apgar score, birth weight.*

Statistical Analysis:

Specific data was entered into Microsoft Office Excel version 2003 and univariate and or multivariate analysis was carried out. Inferential statistics, in particular the *Chi-square (χ^2) test – The One-tailed Test* was applied to analyse the data in order to provide answers for my specific objectives. In these tests, a p-value of 0.05 was used. Analyses included correlations between independent and dependent variables. The additional bio-data collected such as patients' initials and addresses, was collected for the sole purpose of avoiding duplication of cases.
The findings of all of the data analyses was discussed, conclusions drawn, and recommendations made. Written and electronic copies of this report were presented to the supervisor for assessment and to Dr.MadanRambarran. The investigator will then present her findings using Microsoft Power-point to an audience of her colleagues, supervisor and to other special invitees in November, 2008.

RESULTS

A. Epidemiology

- Incidence.

According to WHO, 3 million fetuses and infants are born annually with a birth defect. The world's population as of September 2008 is 6.721 billion. Guyana has an estimated population of 751,000[6] and this translates to an estimated 2240 cases of birth defects annually in Guyana.

- Demographic distribution of cases.

Region 4, Demerara/Mahaica, had the majority (68.8%) of documented congenital malformation cases in Guyana. Regions 3 (EssequiboIslands/ West Demerara) followed closely behind with a percentage of 10.9. Regions 7 (Cuyuni/ Mazaruni), 8 (Potaro-Siparuni) and 9 (Upper Takatu/ Upper Essequibo) had the least documented cases (1.56 %).

- Age.

The majority (73.9 %) of cases documented for birth defects was seen in the age group birth-5 months, followed by (9.4%) > 50 months (>12 years old), 6-10 month (5 %) and 21-25 month (4.4 %). No cases were detected in the age groups 26-30 month, 31-35 month and 41-45 months of age.

- Sex.

There was a male to female ratio of 1.3: 1 of having a birth defect.

- Ethnicity.

Afro-Guyanese accounted for almost one half (48%), with the Indo-Guyanese contributing to more than one third of the cases. More cases were observed in the Mixed population than the Amerindians populations. In one documented case, no ethnicity was charted.

B. Clinical Manifestations.

- Clinical and Work-up findings based on the most common type of birth defects found

Patients with CHD mainly complained of shortness of breath, fever, easy fatigability, chest pains, and few had cyanosis. Physical examination findings in this subset of patients were varied and included cyanosis, febrile, tachypnea, systolic murmurs, hepatomegaly and digital clubbing. Few had documented laboratory findings (hematological, urinalysis) and radiographic findings (cardiomegaly, lung infiltrations/edema) in the charts and only data for two patients were found to have had echocardiography, of which one was abnormal.

Those diagnosed with hypospadias complained of an abnormal passage of urine from the penis. The majority of these patients only had hemoglobin testing done. None had abdominal ultrasonography, urinalysis or uretocystographic studies done to rule out any other coexisting defects. Cryptoorchid patients had the universal complaint of ‘testes not palpable.’ It was not known, if the surgeon(s) for these crytoorchid patients had any suspicions of testicular cancer in those presenting late for surgical correction.

The parents of patients with club feet knew what the diagnosis was and hence, the chief complaint was that of club feet. These patients had minimal work-up done, in that only a preoperative hemoglobin count was ordered.

Those with syndactyl had various complaints ranging from limb abnormality to webbed fingers. These patients had no laboratory investigations done. Those with aganglionic colon, or Hirshsprung disease complained of chronic constipation. One of these patientshad documented findings of aganglionosis on rectal biopsy.Lastly, those with accessory breast tissue, like those with club feet, knew their diagnosis prior to admission. Twenty-two patients had no documented chief complaint(s).

- Duration of hospitalization.

The average length of stay was 6.5 days. One patient (myelomengocele) spent 38 days while one with hypospadia stayed 23 days. Length of hospital stay varied with several factors mainly age, severity of defect, clinical condition, and complexity of surgery. It could not be determined if post-op complications influenced the length of hospitalization.

- Relationship amongst prenatal, natal and postnatal histories

By exclusion, 136 charts had no information on the prenatal status while two had documented findings of an 'unremarkable' prenatal status .Only three mothers had documented normal obstetrical and gynecological histories.

One mother used alchohol and another used an abortificient during the current pregnancy while one had a urinary tract infection in pregnancy. Two mothers had previous medical histories of asthma and diabetes mellitus while 5 were hypertensive.

One hundred and ten charts had no data on perinatal history and of the remainder: 2 babies were preterm, three were born by spontaneous vaginal delivery, 18 were breastfed (partially or exclusively could not be determined), 2 never breastfed, all were vaccinated for age and 3 had documented delayed milestones development.

- Biological Systems Affected.

The majority of cases were from the Musculoskeletal System (22%), followed by the Genitourinary (20%), Cardiovascular (16%) and Gastrointestinal (14%) systems. The orofacial system had 14 documented cases (10%) while the Reproductive and Central Nervous System had equal number of reported cases (4%). The least number of cases were from the ear (3%) and respiratory system (<1%).

- Relationship between birth weight and Apgar scores.

Of the 22 patients (n=138) with documented birth weight, only one had a low-birth weight of 1 kg. Nine patients had documented Apgar scores, and of these all had a 9, 10, 10 score.

D. Management.

Patients with birth defects were either treated medically or surgically or both. An alarming 78 (56%) patients had no documented treatment option. This information was missing from the charts and or failed to be documented by the attending physician.

Of those who were treated, 49 (82%) patients underwent surgery while 11 (18%) had medical interventions in the form of analgesia, antibiotics, diuretics etc. Those who had medical intervention included all CHD (TOF, PDA) and one case of cleft lip and palate.

Of those who had surgery, 20 (41%) had also postoperative antibiotics, 28 (57%) had postop analgesia, 1 post-surgical patient had neither antibiotic nor analgesia. Within the surgical group, 20 (41%) had both postop antibiotics and analgesia.

Those who had surgeries were patients with cleft lip/palate, hypospadia, epispadia, antral polyp, cryptorchidism, ankyloglossia, accessory breasts, club feet, syndactyly, encephalocele, myelomengocele, Hirshsprung disease and those with congenital defects to the toes and femur.

E. Clinical Outcomes & Prognosis.

One of my objectives was to find out what clinical outcomesexisted in these patients with birth defects. Of the whole population, 74 (54%) had no documented outcome. Of the remaining, 91 % were *discharged*, 6% *improved* after intervention, while 1.5% did *not improve*. 1 (1.5%) patient (with cleft lip/palate) was *referred*to another unknown institute for further care and management. No patients *died* while in the hospital, and so no postmortem records were found.

F. Mortality.

I found no reported mortality amongst the study population.

DISCUSSION

The global burden of disease is rising, and congenital malformations or birth defects significantly add to the burden. Guyana had an estimated annual incidence of 2240 cases of birth defects.

All of the four objectives for this research project were met. Concerning the epidemiological profile (see appendix 1) of Congenital Malformations in Guyana, 79.3% of these defects were diagnosed by the time the patient was between 0-5 months of age. There was a male to female ratio of 1.3: 1 of having a birth defect. Defects were most common in Afro-Guyanese followed by the Indo-Guyanese, Mixed and lastly in the Amerindians populations. Region 4 had the majority of cases, followed by Region 3. Regions 7, 8 and 9 had the least documented cases.

The most common types of birth defects encountered were congenital heart defects, hypospadias, cryptoorchidism, club feet, syndactyly, Hirshsprung disease and accessory breasts (see appendix 2, table 1). Hypospadias occurs in 1:300 boys and is defined when the urethra opens on the ventral aspect of the penis[7]. Its pathogenesis involves the complex interaction of both genetic and environmental factors. Recent genetic sequencing has located a novel hypospadias locus at chromosome 7q32.2-q36.1, which houses genes like AKR1D1 (aldo-keto reductase family 1, member D1) and the PTN gene; involved in the androgen pathway and the coding for pleiotrophin (an embryonic differentiation and growth factor), respectively[7]. Other genomic risk factors include the mutation of the genes of penile development (HOX, FGF, Shh) and testicular determination (WT1, SRY) and those regulating the synthesis and action of androgen. Also, chromosomal abnormalities such as CXorf6 and ATF3 have been found, with the former associated with isolated hypospadias of varying severity [8, 9] .Environmental risk factors include a diet lacking in fish and meat (4-fold increased risk), male infants born to obese women (more than 2-fold increased risk), PIH (2.0-fold risk), absence of maternal nausea (1.8 fold risk) and nausea in late pregnancy[10], pregnancy-related intakeof progestins [11].Many effective techniques are used in the surgical repair of hypospadias with a recent finding that transdermal dihydrotestosterone (DHT) makes an important adjunct to preoperative surgery[12].

One of the most commonurogenital abnormalities in newborn boys is Cryptorchidism or undescended testis. Many risk factors have been identified throughepidemiological studies, namely lowbirth weight, small for gestational age (SGA),prematurity and exposure to estrogens; anti-androgens; diethylstilbestrol.

Cryptorchidism can occur in syndromes, suchas the persistent Müllerian duct syndrome, Down's Syndrome, prune belly, and Prader-Willi (Virtanen et al., 2007). The cause of cryptorchidism remains unknown in most cases but severalpathogenetic mechanisms have been expressed. Many theories have been proposed as to the cause, such as placental malfunction and alteredhCG secretion, with the former supported by findings of increased incidenceof other genital abnormalities such as hypospadias in cryptorchid patients.

Mutations in the genes of androgen receptor, 5-alpha-reductase and insulin-like hormone 3 (INSL3) with its receptor (LGR8) has been found in some cryptorchid patients[12]. Cryptorchidism has also been linked with an increased GGNand CAG repeats[12]. Furthermore, a tendency of familial aggregationof cryptorchidism exists (Elert *et al.*, 2003) and in 2005, Yoshida*et al.*, discovered an association with a specific haplotype of the estrogen receptor alpha gene and cryptorchidism. Patients who are homozygous for the gene have increased susceptibility to the effects of estrogenicenvironmental endocrine disrupters such as pesticides.

Cryptorchidism may also be associated with pre-eclampsia, maternaldiabetes, hypogonadotropic hypogonadism and genital under masculinization as a result of impaired gonadotropin action or function,inborn errorof cholesterol biosynthesis, or impaired androgen biosynthesisand metabolism (Forest, 2006).

Changes in the activity of the genitofemoral nerve (GFN) and itsneurotransmitter CGRP (calcitonin gene related peptide) may also be liked to increased cases of cryptorchidism [12]. Syndactyly is characterized by two or more fused fingers and toes which is inherited as an

autosomal dominant trait (except type VIII in which autosomal recessive) with incomplete penetrance and variable expression[13]. It is one of the most common congenital anomalies of hands and feet and can occur as either an isolated abnormality or as part of a malformation syndrome. The overall prevalence of syndactyly is reported to be 3–5 per 10,000 births [13] and the rate of isolated syndactyly is 1.3–2.2 per 10,000 births.

Familial syndactyly is reported to constitute about 10–40% of the total number of syndactyly cases. Implicated in the etiologies are mutations of fibroblast growth factor (FGF) receptors and alterations of transcription factor Msx-2 [13].Types I, II, III and V have been mapped to chromosomal regions 2q34-q36, 2q31-q32, 6q21-q23.2 and 2q31-q32, respectively, whereas type IV has not been mapped as yet and manifesting as a complete syndactyly of all fingers with polydactyl and flexion of the fingers[13].Right and left sides as well as both upper and lower limbs are affected equally and is frequently bilateral. A recent large population-based study reported an increased risk of congenital digital anomalies, including syndactyly after maternal cigarette smoking during pregnancy. The goals of management are improved function, appearance, and social acceptance. Surgery is rarely necessary.

Congenital cardiovascular malformations are the most commonform of birth defects, occurring in 6.6 - 8.1 per 1000live births[14]. They are categorized as either cyanotic (tetralogy of Fallot, pulmonary atresia, truncusarteriosus,transposition of the great vessels, total anomalous pulmonaryvenous return, and tricuspid atresia, coarctation of the aorta, criticalaortic stenosis, interrupted aortic arch, and hypoplastic left heart syndrome) and noncyanotic lesions with the former accounting for 25% and contribute to significant morbidityand mortality. Diagnosis is mainly done byantenatal ultrasonography but many are identified by the physicians' physical examination. Treatment is usually medical or surgical. In terms of prevention, many published studies have suggested that routine pulseoximetry on all newborns 4 hours after isan effective screening tool for detectionof CCHD, but, The American Academy of Pediatrics has not stated a formal opinion on its useas a screening tool[14].

Accessory breast tissue, occurs in 0.4-6% of the general population, usually develop along the embryonic milk line with the most common in the axillary region[15].Many are asymptomatic with the minority causing pain and restriction of arm movement[16]. They can undergo hormonal changes and are subjected to pathologies like those of normally positioned breasts, including neoplastic and fibrocystic changes. Surgery is usually the option in cases of malignancy, in symptomatic cases and for cosmesis purposes.

Acetylcholinesterase staining of rectal suction biopsy specimens is widely performed in the diagnosis of Hirschsprung's disease, but results are sometimes incorrect or atypical in newborns. In a recent study by Kawahara et al, anorectalmanometry using sleeve microassembly was found useful in the diagnosis of neonatal Hirschsprung's[17].

The majority of cases were from the Musculoskeletal System (22%), followed by the Genitourinary (20%), Cardiovascular (16%) and Gastrointestinal (14%) Systems. The orofacial system had 14 documented cases (10%) while the Reproductive and Central Nervous System had equal number of reported cases (4%). The least number of cases were from the ear (3%) and respiratory system (<1%).

Patients with birth defects were either treated medically or surgically or both. An alarming 78 (56%) patients had no documented treatment option. Of the whole population, 74 (54%) had no documented clinical outcomes. Of the remaining, 91 % were *discharged*, 6% *improved* after intervention, while 1.5% did *not improve*. 1 (1.5%) patient (with cleft lip/palate) was *referred* to another unknown institute for further care and management. The mortality rate was zero.

In hopes to establish an etiology, it was discovered that one mother used alcohol, one an abortificient during the current pregnancy and one had a urinary tract infection in pregnancy. Two mothers had previous medical histories of asthma and diabetes mellitus while 5 were hypertensive. Only two mothers had documented findings of an 'unremarkable' prenatal status and three had documented normal obstetrical and gynecological histories3 patients had documented delayed milestones development, one a low-birth weight of 1 kg, two were preterm and of the nine patients with documented Apgar scores; all had a 9, 10, 10 score.

Cleft lip and palate, was found to be relatively common major malformation. Notwithstanding, neural tube defects, mainly myelomengocele; meningocele; encephalocele and spina bifida occur with a significant frequency. Common minor malformations found in my study included club foot, accessory breast,

ANKYLOGLOSSIA AND SYNDACTYL IN DESCENDING FREQUENCY

Ankyloglossia**,** a short or tightlingual frenulum also referred to as tongue-tied, represents a significant proportionof the identified barriers to successful breastfeeding. It has a prevalence of 4-5%, is more common in males and with an unknown pathogenesis which may involve a genetic etiology manifesting as an autosomal dominant trait[18]. It is associated with feeding (poor infant latch, maternalnipple pain.); speech; social and mechanical (dental) problems[18]. Its severity, accessed by the HazelbakerLingual

Assessment Tool by scoring the function andappearance of the tongue, may indicate the need for future frenuloplasty which has been shown to improve milk transfer; infantgrowth; maternal nipple pain and breast pathology[19].

Clefts of the lip and/or palate occur in 1 of 600 newborns [20] worldwide, making them the most common of all major birth defects. The incidence varies with geographic location, ethnic group, and socioeconomic conditions. They are developmental craniofacial abnormalities that result partly from the failure of neural crest cells to migratecompletely. The etiology is most likely multifactorial. Numerous studies suggest that involvement of the pathways of folate metabolism may play a role in the etiology of orofacial clefts. Some studies have suggested that women with a mutation (C677T) in the methylenetetrahydrofolate reductase

(MTHFR) genehave an increased risk. Establish related teratogens include alcohol, valproic acid, and cigarette smoking. Seventy percent are isolated clefts (nonsyndromic) and 30%occur as part of asyndrome[20]. Syndromic clefting are linked to sever cognitive deficits and oftensevere while those isolated clefts of the lip and/or palate (ICLP) are lesssevere. The pattern of cognitive deficits reporteda lower than average general IQ with specific deficitsin language function. These deficits are due to abnormal brain structure and function since the the development of the brain and face are intimatelyrelated. This abnormality is in the pattern of tissue distribution in

which the frontal andparietal lobes are increased in volume and the temporal and occipital lobes aredecreased in volume with also decrease in cerebellum volume[20].

Nonsyndromic cleft lip with or without cleft palate (NSCLP) requires prolonged multidisciplinary rehabilitation. Researches have shown variation in several genes contributing to NSCLP. Recent research shows that 22q12.2-12.3 and 8q21.3-24.12 may harbor clefting genes[21]. One recent studyreveals that firstly, higher levels of maternal postpartum red cell and serum folate are associated with a lower risk for cleft lip with or without cleft palate and secondly, an increased risk for cleft palate[22]. This same study published that higher level of serum homocysteine were associated with an increased risk for both cleft lip with or without cleft palate and isolated cleft palate.

The clinical management of orofacial clefts requires a multidisciplinary approach. Surgical repair is the mainstay of treatment and is usually performed at 2–3 months of age for cleft lip while repair of Cleft Palate is typically performed at 8–12 months of age. Genetic counseling plays a major role. It is recommended that all women of reproductive age use folic acid to reduce their risk.

Neural-tube defects, which include spina bifida, anencephaly,craniorachischisis, and encephalocele, occur in approximately1 per 1000 births in the United States[23]. It has been found that although periconceptional folic acid supplementationreduces the occurrence and recurrence of neural-tube defectsby 70 percent,most pregnant women with this complication do not have clinical folatedeficiency[23].To explain this phenomenon, **studies confirm**autoantibodies in serum from women with a pregnancy complicated bya neural-tube defect that can block cellular folate uptake by binding to the folatereceptors, namely ED27 and KB cells on placental membranes[9].

Many causes of neural-tube defects exist, includingdrugs (antifolate, antiepilepticagents),chromosomal abnormalities, and environmentaland geneticfactors[23]. Also, the risk of neural-tube defects may increaseafter abortionsor miscarriages and autoimmunity resulting from epitopes of the folate receptors exposed in vivo secondary to injury and proteolysis[23].

The clinical picture was quite compelling in some the cases but the majority had scanty specific and scientific entries by the examining physician. The Musculoskeletal, Cardiovascular, Gastrointestinal, Genitourinary, Reproductive, Orofacial, Integumentary, CNS, auditory and Respiratory systems were the most involved in descending order.In terms of the diagnostic work up of these patients, few had a whole body work-up. The tests were limited to hematological, radiological; sonography and one case had a biopsy (rectal).

The majority had surgical versus medical intervention, in the form of supportive and symptomatic treatment. No patients were screened for a birth defect and no patients died. They were either discharged, improved, unimproved or referred.

Although this study was successful, many limitations were faced, mainly time and electronic malfunctions. In terms of the medical documentation system, I was unable to access all of the records. Many charts were incomplete with scanty clinical documentation by the examining physician.

I conclude that the epidemiology, management practices and outcomes for congenital malformations in Guyana were determined in spite of the alarming proportion of missing data. One disappointment, however, is that comprehensiveness and more details could not be met.

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