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TWO DISEASES (TB/HIV) AND TWO MEDICINES (ATT/ART): ONE PATIENT AND ONE SERVICE!

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SOURCE

Salim S. Abdool Karim et al, 'Integration of Antiretroviral Therapy with Tuberculosis Treatment',.*The New England Journal of Medicine*, N Engl J Med 2011;365:1492-501.Also available at www.nejm.org October 20, 2011, viewed and accessed on 8th Sept 2013 at http://www.nejm.org/doi/pdf/10.1056/NEJMoa1014181

INTRODUCTION

This review will evaluate the article titled 'Integration of Antiretroviral Therapy with Tuberculosis Treatment' by *Salim S. Abdool Karim* et al published in 'The New England Journal of Medicine'. In the process of summarization -- its purpose will be defined, the structure of the article be examined in terms of ease with which any reader can have access to this piece of information. The article will be anatomized based upon its authority, accuracy, currency, relevance, objectivity and stability in that order. The review will also judge the article's accessibility and credibility. Upon overall assessment the article has been found to be well written, clear and relevant.

LITERATURE REVIEW

Most probably the first study to assess time until ART initiation in patients before vs. after TB/HIV service integration is done by Bernhard Kerschberger, et al (Kerschberger B, Hilderbrand K, Boulle AM, Coetzee D, Goemaere E, et al. (2012) The Effect of Complete Integration of HIV and TB Services on Time to Initiation of Antiretroviral Therapy: A Before-After Study. PLoS ONE 7(10): e46988. doi:10.1371/journal.pone.0046988)

The highlight of the study by Kerschberger, that TB/HIV integration is feasible in the setting discussed here and shows that positive outcomes for co-infected patients can be realized immediately: Bernhard Kerschberger, et al found that patients who received care through this

integrated model were 60% more likely to initiate ART. These findings have been found to be robust enough to multiple sensitivity analyses.

One more study in the same setting demonstrated that assessment at an ART clinic during TB treatment reduces loss to follow-up by 80%. Hermans et al. reported a decrease of TB treatment default after integration of HIV and TB services in a large urban HIV clinic in Uganda. The approach "*The two diseases, one patient, one service, one appointment, one health care worker*" also enhances clinic staff's expertise and experience in managing co-infected patients and thus can address better –the patients' considerable clinical challenges—that of drug interactions and toxicity, IRIS, TB deterioration and optimal timing of ART initiation. The advantages of initiation will include, adherence and social support interventions within integrated programs which can mutually reinforce each other. Further integration can avoid the duplication of logistic and administrative services thereby improving the efficiency of service delivery.

Recent data from SAPIT trial (the Starting Antiretroviral Therapy at Three Points in Tuberculosis) has shown that initiation of ART during TB treatment enhances the survival for PLHAs (people living with HIV/AIDS) who have $CD4^+$ T cell counts <500 cells/mm3, compared with starting ART after TB treatment is completed.

An innovative strategy has been developed where TB/HIV Co-infected persons receive comprehensive HIV and AIDS services and TB care at the TB clinic for the duration of their TB treatment, with sending them to an HIV program after completion of their TB treatment

A systematic review by LSHTM (The London School of Hygiene & Tropical Medicine) originally a background paper for the WHO- organizing First Global Symposium on Health Systems Research, has been conducted as to how TB and HIV services could be integrated in practice. They have suggested various models of integration of HIV and TB services, the model where the TB and HIV services both are provided as a single, integrated service within a health facility provides benefits to PLHAs in most settings, relative to referral to the other service even for screening. Single, integrated service models can decrease the transportation costs and patient time required to have the both services, and can save the staff time.

In Malawi, Africa, the Martin Preuss Centre have been following the fully-integrated TB-HIV model upon which Lighthouse and LSHTM have jointly conducted a case study of the integration of TB and HIV services. It has proved to be very beneficial for the TB/HIV co-infected patients. At this centre96% of TB patients who has shown HIV positive status in 2009. And has demonstrated good TB treatment outcomes among both -- HIV-positive and HIV-negative patients, to the tune of more than 85% cured or completed treatment. The results at Martin Preuss Centre has proved that high-quality, integrated HIV and TB services can be provided in resource-constrained settings too. So in Malawi the National ART and National TB Programs have integrated their services in all TB/ART management sites across the country.

IHAA (International HIV/AIDS Alliance) too had conducted a survey of Alliance linking organizations to get a view and record the degree and models of integration of HIV and TB services within community organizations. Various models of integration of TB into HIV programs have been defined, and a range of levels of integration were found. After the survey, the IHAA drafted a TB strategy which aims to enhance the integration of TB/HIV activities.

In India a cross-sectional study to evolve the criteria for HIV testing policy for TB patients has also been conducted by NARI (National AIDS Research Institute) It has been come to the notice that many care providers in India are still not advising TB patients to test for HIV, thereby letting go many opportunities for patients to make use of the HIV services they require. NARI, together with LSHTM, has worked on a qualitative study to look for the challenges and opportunities for integrating TB and HIV services for TB/HIV co-infected patients.

In South Africa LSHTM and the Aurum Institute have collaborated to conduct 'Evidence for Action-related retrospective and prospective studies' to assess the practices in screening for active TB in HIV+persons

The retrospective studies have found that TB symptoms were common among the HIV-infected adults taking ART but very few symptomatic people were appropriately referred vice versa for TB investigation. The prospective studies have shown that a very high percentage of undiagnosed TB existed among PLHAs presenting for ART. Isoniazid Preventive Therapy (IPT) has been demonstrated to be effective in preventing TB among people living with HIV. LSHTM and the Aurum Institute (in South Africa) are working now on, an Evidence for Action-related qualitative study into the barriers and constraints in the implementation of IPT (Isoniazid Preventive Therapy), where TB/HIV co-infection is rampant. The IPT study has identified major provider -related barriers in implementing Isoniazid Preventive Therapy in form of lack of knowledge and experience, benefits of IPT not known, and uncertainty about the availability of guidelines.

In Asia and sub-Saharan Africa many RCTs are being conducted to know the optimal time to initiate ART in PLHAs (people living with HIV/AIDS) who are newly diagnosed with active TB and are eligible to startantiretroviral therapy. These studies are to compare patients starting antiretroviral therapy within thefirst 4 weeks versus 8–12 weeks of initiation of TB treatment. A trial in South Africa has confirmed the current WHO recommendations which advise the patients to start ART and not to wait until completion of TB treatment. Mortality rates have been found to be significantly higher among PLHAs who initiated antiretroviral therapy after completion of TB treatment, compared to those who start within the first two months of intensive phase TB treatment (under RNTCP –Revised National TB Control Program in India) or after completing intensive phase TB therapy In Cambodia among 661 patients were found to have a reduction of mortality of 34%if antiretroviral therapy was initiated in the first two weeks of TB treatment compared to eight weeks A cohort of 313 Spanish patients have demonstrated that initiating ART

in the first two months of TB treatment, was an independent predictor of survival compared to starting antiretroviral treatment after three months of TB treatment

ARTICLE SUMMARY

The objective of this article is to consider if the integration of Anti Retroviral Therapy (ART) with Tuberculosis Treatment could reduce the mortality and to determine the optimal timing of initiation of ART during tuberculosis treatment. To implement earlier ART initiation could be done through integration of TB and HIV services, which could be a more efficient model of care than a separate, vertical program. TB is the commonest Opportunistic Infection (OIs) and a leading cause of morbidity and mortality among PLHAs in almost all parts of the world. The importance and requirement for collaboration between TB and HIV services is being recognized internationally as patients with TB/HIV co-infected often have to navigate two separate health care programs, which can considerably increase the time and transportation costs associated with acquiring the health care. It is utmost that both TB and HIV services are effectively coordinated to ensure the TB/HIV co-infected persons have the access to the care they require from both services to ensure the best results

According to this article, the early initiation of ART in patients with CD4+ T-cell counts of < 50/mm3 increased AIDS-free survival. Deferral of the initiation of ART to the first 4 weeks of the continuation phase of tuberculosis therapy in those with higher CD4+ T-cell counts reduced the risks of IRIS(Immune Reconstitution Inflammatory Syndrome) and other adverse events related to ART without increasing the risk of AIDS or death The current WHO recommendations to initiate ART as soon as possible after the start of tuberculosis treatment, regardless of the CD4+ T-cell count, may need to be revisited in view of the findings of this study.

ARTICLE STRUCTURE

The article starts with an abstract that presents an effective overview of the article by establishing the background to the issue of TB/HIV integration and related points. The article itself is very qualitative in nature and is ten pages long. It is accessible online as a PDF documented the contact details for the authors are adequately provided. There is a logical ordering of points and both the paragraphs and the sentences are just informative making the availability of the information, its reading and understanding all the easier. The conclusion is a straightforward summary of the points made. There are adequate references are provided in a reference section. (16-sixteen references in total). Overall the abstract is effective and, the structure of the article makes it simple and smooth to interpret and understand.

ARTICLE CRITIQUE

AUTHORITY

The article has been featured in an extremely reputable *source 'The New England Journal of Medicine'* (*NEJM*) which is an English-language peer-reviewed medical journal published by the Massachusetts Medical Society and it is among one of the most prestigious and the oldest published medical journal in the world, which publishes editorials, papers on original research, review articles, correspondence, and case reports, This journal aims to inform and educate, the medical community –its main audience. In addition the fact that the article was found in Cochrane Library with Access Number PUBMED 22010915, which is known to be a reliable database, adds to its credibility. Furthermore it is to be noted that the Cochrane Collaboration organizes medical research information in a systematic way in the interests of evidence-based medicine and conducts systematic reviews of randomized controlled trials of health-care interventions, which it publishes in the Cochrane Library. The main author Dr. Salim S. Abdool Karim, MD, PhD, is a world known personality in the HIV fraternity and a clinical infectious diseases epidemiologist whose research interests have been in microbicides and vaccines to prevent HIV infection, and implementation of ART in resource poor settings. In addition to his faculty position as professor of Clinical Epidemiology at the Mailman School, he is pro vice-chancellor (Research), University of KwaZulu-Natal and Director of CAPRISA - Centre for the AIDS Program of Research in South Africa. Dr. Abdool Karim pioneered the NIH-funded HPTN 035 microbicide trial which revealed the potential of anionic polymer, PRO2000, in preventing HIV infection in women. His research on TB-HIV treatment has influenced and continues to shape the clinical management of co-infected patients. He has published widely on infectious diseases, including HIV/AIDS, and co-edited the textbook that is used extensively to teach epidemiology in South Africa. Dr. Abdool Karim is chairperson of the WHO Scientific Advisory Group for Reproductive Health and is a member of the WHO Expert Advisory Panel on Sexually Transmitted Infections and HIV. The contact details of the author are adequately displayed on the article. The reviewer (myself) has heard him and his wife, the co-author of this article, Dr. Quarraisha Abdool Karim, and had the opportunity to meet them at a HIV Conference in Mumbai All of this information indicates that the article is highly plausible

ACCURACY

Being published as an 'original article' in a renowned medical journal of the stature of 'the New England Journal of Medicine' proves its precision. The article has 16 references of articles written by some of world famous HIV Experts like Dr. Cohen and Dr. Meyer implies greatly enhances accuracy and credibility.

CURRENCY

The Journal (NJEM) with this article was published in October 2011, its references date from 1998 to 2010. These dates indicate that the article is very current, as does the content of the article which deals with the latest developments in TB –HIV co-infection treatment.

RELEVANCE

It has been written to provide information for an educated sector (medical doctors) and published in a reputable journal (NEJM) and it is relevant to its main intended audience –the HIV health care providers. The topic covered is also a significant one in the context of HIV Care Support and Treatment (CST). TB is the most common Opportunistic Infection (OIs) in a HIV patient In patients with TB/HIV Co-infection, antiretroviral therapy (ART) may be initiated at the same time as or soon after the initiation of anti- tubercular treatment(ATT). Generally antiretrovirals (ARVs) are often deferred until after the intensive phase of tuberculosis treatment (RNTCP – Revised National TB Control Program in India) because of concerns about the Immune Reconstitution Inflammatory Syndrome (IRIS), a high pill burden, and overlapping side effects when 3 antiretroviral agents are added to the standard 4 anti tubercular drugs (totaling 7 drugs). These challenges may result in interruption or discontinuation of treatment for the acquired immunodeficiency syndrome (AIDS) or tuberculosis (TB), which can lead to drug resistance and potentially limit future therapeutic options. The disadvantages must be weighed against the risk of increased mortality early in the treatment of tuberculosis. The conclusions of the article shows that early initiation of ART in patients with CD4+ T-cell counts of less than 50 cells/mm^3 increased AIDS-free survival. Deferral of the initiation of ART to the first 4 weeks of the continuation phase of tuberculosis therapy in those with higher CD4+ T-cell counts reduced the risks of IRIS and other adverse events related to ART without increasing the risk of AIDS or death. The article touches almost all aspects of TB/HIV and it relates to the global community as HIV and TB both are global issues.

OBJECTIVITY

The information in the article was derived from team of authors' extensive experience working at higher centers of excellence in HIV arena -- Centre for the AIDS Program of Research in South Africa (CAPRISA) South Africa, associated with the Department of Epidemiology and the International Center for AIDS Care and Treatment Programs, Mailman School of Public Health, Columbia University, New York; and Yale University, New Haven USA, The article shows research decisions, and contains both facts and evidences. Opinions have been presented on both sides of the argument (early and late initiation of ART (Anti Retroviral Therapy) at different CD 4+ T cell counts; levels less & more than 50/mm3) are exemplified. The article acknowledges the limitations of the study adequately (3-4 in number). The majority of the claims and arguments made have been supported in the articles and references. The article serves its purpose as an objective presentation of the early vs late initiation of ART in TB-HIV Co-infected patient at

different CD4+ T levels to the medical community in general and HIV Care providers in particular.

STABILITY

Published in a reputed medical journal and available in both print and electronic forms, it can be found on an established and highly credible academic database: The Cochrane Library. For these reasons, the article is stable as a resource and being accessible through a credible and reliable academic database.

ANALYSIS OF GRAPH

Not applicable

RECENT ADVANCES RELATED TO THE TOPIC

There are few studies clarifying the timing of ART initiation in relation to TB treatment start such as -- SAPIT (Starting ART at 3 Points in TB), CAMELIA(Cambodian Early versus Late Introduction of Antiretroviral Drugs), and ACTG 5221 STRIDE studies (Stimulant Reduction Intervention using Dosed Exercise)

All these studies show reduction of mortality and AIDS progression. As we find in patients with CD4 counts of <50 cells/μL, initiation of ART within 2-4 weeks of TB treatment start was associated with a reduction of the combined endpoint of mortality and AIDS progression by 68% in SAPIT and 42% in STRIDE. The CAMELIA study, which enrolled patients with CD4 counts of <200 cells/μL, found a reduction in mortality of 34% with initiation of ART within 2 weeks of TB treatment start in all enrolled patients, regardless of CD4 cell count; however, the median CD4 count was quite low at 25 cells/μL). Collectively, these data indicate that ART should be started very shortly after TB treatment initiation in TB patients with advanced HIV disease. In those with higher CD4 cell counts, it may be safe to defer ART for 2-8 weeks after ATT (Anti Tubercular Therapy) start, but ART should not be delayed until after completion of TB treatment. Importantly, early initiation did not impair HIV RNA suppression in these studies.

The need for early initiation of ART will require coordination between TB care and HIV care, along with increased vigilance for drug toxicities, education about adherence to multiple drugs, and anticipation of increased rates of immune reconstitution syndrome (IRIS)

On the other hand timing of ART in patients with CNS TB disease remains grey. A Vietnamese study of HIV-infected patients with TB meningitis did not find a mortality benefit at 9 months with early (at time of study entry) vs after (2 months after study entry) ART initiation. Mortality in both groups was too high: 55% and 60%, respectively, 9 months after randomization, with the majority of deaths occurring within the first month. As TB meningitis itself can be particularly challenging to diagnose, HIV care providers must retain a high index of suspicion for it and

monitor patients with CNS disease closely, given the poor outcomes associated with this disease. The potential for problems to occur when anti-TB medications and ARV agents are administered concurrently exists. In addition to the drug-drug interactions, the medications may have overlapping toxicities and ascertaining which medication is the offending agent can itself be very be challenging.

As per one article published in BMC Infectious Disesase. 2012 Jul 31;12:168. titled '*Early versus delayed initiation of antiretroviral therapy for Indian HIV-Infected individuals with tuberculosis on anti tuberculosis treatment*.' by Sinha S*, et al.* of Department of Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi has arrived at conclusion 'Early initiation of HAART' for patients with HIV and TB significantly decreases incidence of HIV disease progression and has good tolerability.

This year (June 2013) WHO has issued the most latest recommendations on the initiation of ART in a TB –HIV co-infected persons.As per WHO, among PLHAs, TB is the most frequent life-threatening opportunistic infection and a leading cause of death. ART should be provided to all people with HIV with active TB disease. HIV care settings should implement the WHO Three I's strategy: *Intensified TB case-finding, Isoniazid preventive therapy (IPT) and Infection control at all clinical encounters.*

With only 40% of the people with active TB being tested for HIV, Multidrug-resistant TB (MDR-TB) is an added menace for patients with HIV. MDR-TB/HIV patients face most complicated clinical management, fewer treatment options and poorer treatment outcomes. With limited information being available about the association between HIV and MDR-TB at the population level, MDR-TB/HIV have been found in hospital and other settings, especially in Eastern Europe and in Southern African countries with a high HIV prevalence.

The burden of MDR-TB should be reduced by strengthening HIV prevention, improving infection control and improving collaboration between HIV and TB control activities, with special attention to the groups at the highest risk of MDR-TB and HIV infection, such as people who inject drugs and those exposed in congregate settings.

Key selected existing recommendations of WHO: Timing of ART for adults and children with TB (from http://www.who.int/hiv/pub/guidelines/arv2013/en/index.html*)*

- ART should be started in all TB patients, including those with drug-resistant TB, irrespective of the CD4 count (strong recommendation, low-quality evidence)
- Anti- tuberculosis treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment (strong recommendation, moderate quality evidence).

- The HIV-positive TB patients with profound immune-suppression (such as CD4 counts less than 50 cells/mm^3) should receive ART immediately within the first two weeks of initiating TB treatment. ART should be started in any child with active TB disease as soon as possible and within eight weeks following the initiation of anti- tuberculosis treatment irrespective of the CD4 count and clinical stage (strong recommendation, low-quality evidence).

- Efavirenz should be used as the preferred NNRTI in patients starting ART while on anti - tuberculosis treatment (strong recommendation, high-quality evidence).

- WHO recommends ART for all patients with HIV and drug-resistant TB, requiring second-line anti-tuberculosis drugs irrespective of CD4 cell count, as early as possible (within the first eight weeks) following initiation of anti-tuberculosis treatment (strong recommendation, very-low-quality evidence).

CONCLUSION

The review epitomizes and critically reviews S.S Abdool Karim'sand *et al* article '*Integration of Antiretroviral Therapy with Tuberculosis Treatment*'.The content, structure, strengths and limitations of the article were construed and dissected. The article has shared to a better understanding amongst the HIV fraternity, of the pros and cons of early and late initiation of ART in a TB–HIV Co-infected patient at different CD 4 levels. It is an accessible, easier to read, well researched and highly credible. It truly contemplates that integrating antiretroviral therapy (ART) with tuberculosis treatment reduces mortality though the timing for the initiation of ART during tuberculosis treatment remains uncertain. This article is being recommended for medical experts especially, the HIV care providers.

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REASONS FOR DELAY IN INPATIENT ADMISSION AT AN EMERGENCY DEPARTMENT

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SOURCE

Published by Journal Ayub Medical Coll Abbottabed in 2008 and I found it at http://www.ayubmed.edu.pk/JAMCP/PAST/20-1/Tashkandi.pdf

REVIEW OF LITERATURE

There has been quite a number of works on the reason for patient delay in the Emergency Department. Many of these studies have ascribed the delay in Emergency Department to overcrowding as rightly referenced by the authors, as in Derlet R, et al (1) Andrulis DP et al (2).

However many of the literatures showed that factors responsible for overcrowding was indirectly responsible for delay in Emergency Department. Such include insufficient emergency department or inpatient beds, delays while waiting for the laboratory tests (3). Previous studies did not separate the delay into before and after admission to inpatient ward was advised. This attempts to clearly depict the stage at which the delay sets in and hence would be easier to design a solution for the specific factor.

None of the articles cited is less than 10years old. However by 2004 when the study was done and 2008 when it was published most of the articles were current under 3 years old. As a matter of fact, there has been a number of newer studies on overcrowding and other sources of delay to impatient admissions (4, 5).

The review used the Vancouver referencing and the references were quite authoritative.

INTRODUCTION

In this article I shall examine the author's perception about the burden of Emergency Department patient delay and the possible effects of this situation on the patient's satisfaction. We want to see if the author's analysis agrees with the existing literature especially as there are newer articles than this. Has the author indicated the advantage of determining the stage at which the

delay occurs most? I would also want to determine if the study brought out possible solutions to the identified causes of delay in Emergency Department.

I will look at how other researchers see the issue of delay in Emergency Department and the solutions they have proffered, comparing it with what obtains here. I will like to agree with the write up where it is possible otherwise I will disagree with reasons, where I am not convinced. I will try to bring fresh reflections.

SUMMARY

This study titled- Reasons for delay in inpatients admission at an emergency department was conducted by Mohammed A. Tashkandy and his colleagues at Al-Noor specialist Hospital, Makkah, Saudi Arabia.

This retrospective study done in 2004 reviewed the time of arrival at the emergency department, time of advise for inpatient admission and time of admission into the inpatient ward for 4876 patients who visited the emergency department during the study period. The demographic data was taken from the emergency department cards while the timing was in addition collected from the medical and nursing personnel notes.

The study focused to elicit the reasons as to why patients stayed more than 2 hours in the emergency department, a period beyond which this study defines as delay.

Since the various services to the patient consumed various times, the services that took maximum time was considered as the main reason for the delay for that patient.

Using students t-test to measure the difference in duration between both groups, chi-square test and 95% confidence interval (P-<0.05), it was found that out of 4876 who visited the Emergency Department, only 355 (7.3%) were admitted.

Out of the ones admitted 238 (67%) were delayed (P<.001) while males 135 (56.7%) were more than female. 58% of group A spent at least 2-3 hours in the emergency department while only 25% of group B spent at least 2-3 hours in the Emergency Department. This means that more people are delayed 2-3 hours and more in group A than in group B.

The most common reason for delay in group A (before admission was advised) is multiple consultations with further investigation. 70 (45%) followed by critical care management 30 (20.5%) on the other hand, the greatest cause of delay in group B (after the advise for admission has been given) is file making process 40 (43.5%) followed by investigations, done on the way to the wards 25 (27.2%) ($p<0.001$).

The data analysis confirms that most of the admitted patients were delayed in the emergency department before the advice for admission was given. The main reasons for the delay were multiple consultations followed by file making process, critical care management and

investigation done on the way to the ward. Diseases of the circulatory system caused more delay at the emergency department than other groups.

In order to decrease delay in the emergency department these prominent factors of delay must be addressed.

ARTICLE STRUCTURE

Over all, this entire article is well articulated and very concise in presentations. The author tried to avoid ambiguous statements. The abstract was so detailed and clear that it was quite easy to understand the main body of the study. At every stage of the write up, the author defines every new term she introduces, such as what period constitutes delay.

The authors used tables to more clearly present their findings.

The discussion captured objectively what the results showed while the confounding factors and limitations of the study were adequately mentioned.

However the paper presented too many information such as comparing the number of hours stayed in the emergency department and the group and comparing the hours delayed and the admitting diagnosis. These tend to confuse the reader and one almost lost focus as to reason why there is delay in emergency department. The references were well displayed using the Vancouver system.

AUTHORITY

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ACCURACY

I would comment that the accuracy of the article is high. It sets out to find the reason for over stay of patients in the emergency department, even when they have been given inpatient admission. This it achieved effectively and went further to determine at what point the delay occurred. The large sample size of 4,576 who visited emergency department and 355 who were admitted is more likely to give good result than a small sample size.

However the study outcome may not be exhaustive as many other conditions that cause overcrowding in the emergency department indirectly cause delay and such were not included.

This included shortage of hospital beds, aging population with concomitant ailments and insufficient emergency department staff (1). While this study relied on the actual events that happened and extracted from the emergency department cards and doctor/nurses notes, most other studies used the opinions of the interviewed emergency department staff who filled questionnaire. This is highly subjective. Hence a more accurate result is likely with this study.

Again most of the factors responsible for the delay in this study were same in Miro's and Rehmani's studies. (6, 7)

PERIOD

The study was conducted in August 2004 but was published in 2008. This is about 6yrs old project. Since the publication many other many other similar studies have been conducted (9, 10).

However this has formed the basis for many other studies such as the effect of the emergency department delay on patients out come.

RELEVANCY

The authors were well focused in determining the reasons for delay in patient admission. Their introduction explained the need to determine these factors in order to address them. The author went straight to design the study that will not only determine there is delay but will also indicate the stage at which the delay occurred, the service that caused the delay the medical condition that is associated with the longest delay and the gender that is more implicated. The detailed breakdown of these causes makes it easy to address.

Though the study did not determine the effect of the delay on patient's outcome, it incorporated all relevant information that agreed with the literature review to determine the most important factors contributing to emergency department delay.

OBJECTIVITY

This study is highly objective. The patient's Emergency Department card was used. This captured the exact time as recorded by the attendant healthcare who was blinded as to the use of the card for the study. Doctors and nurses wrote without any bias or knowledge of the aims of the study. The exact time when patient was advised for admission was also honestly recorded by the attendant physician.

To avoid any subjectivity, the admitting diagnosis was sorted out with the standard ICD-10 codes. The data was subjected to the standard analysis with 95% confidence interval using the student's t-test and chi-square test. The results were compatible with similar jobs by other authors.

STABILITY

This article is stable considering that articles of later dates have confirmed the findings of this study and have gone further to determine the impact of the delay on the patients outcome and the various steps to improve emergency department visit in order to eliminate delay. For example, some studies have suggested using higher level medical staff at the emergency department who have the capacity to diagnose and admit the patient. This will reduce the multiple consultations that occurs when junior medical staff man the emergency department and must contact the consultant for further decision to admit.

ANALYSIS OF GRAPH/TABLE

There are 4 tables. Table one is a demographic one which shows the age group, gender and nationality that are delayed most (beyond 2 hours) in the emergency department.

This table therefore shows that age group 13-30, males and Saudis are delayed most (beyond 2 hours) in the emergency department.

Table two shows the group A or B and the number of hours they are delayed. In group A (where greatest delay occurs before advice for admission), greatest number of patients in this group are delayed between 2-3 hours where as in group B (where greatest delay is after they have been advised for admission) most of the patients are delayed 3-4 hours.

In table three, the reason for delay and the number of patients affected are shown; multiple consultation with further investigation was the highest cause of delay in group A at the emergency department (48%), where as in group B file making process caused the highest delay 43.5%.

Table four shows the ailment that had the greatest delay in the emergency department using 1CD-10 codes. It showed that diseases of the circulatory system followed by external causes of morbidity and mortality had the greatest delay (35% and 33% respectively).

RECENT ADVANCES RELATED TO THE TOPIC

Since the last 6 years there have been many studies on overcrowding and patient delay in the emergency department. These include the work done by Huang Q et al 2010 in which they redefined delay as, time from emergency department arrival to decision to admit of more than 12 hours (9) as opposed to the present study which used > 2 hours to define delay. In this same study 11.6% of admitted patients experienced delay as opposed to the 67% of the admitted in this review study. The team using the 12 hrs as delay concluded that delays to admission from the emergency department are associated with increased inpatient lost and inpatient cost. (9). Therefore improving the patient delay in the emergency department will reduce hospital cost and improve quality of care.

Current research has placed more emphasis on the emergency department external factors such as hospital bed availability, laboratory investigations, specialist availability and even elective surgeon schedules to be the major determinant of emergency department delay than emergency department internal bottle necks such as insufficient emergency department staff, emergency department bed shortages etc.

CONCLUSION

This article has clearly shown that there are different factors that cause delay when a patient arrives at the emergency department. Group A which most of the times are intra emergency department factors, and the delay after the patient has been advised for admission. Group B, which are largely external to emergency department. Hence, where as the multiple consultation/laboratory investigation is the major cause in Group A, file arrangement is the major cause of delay in Group B. The study further drew attention to the relationship between gender and nature of the ailment with the delay in the emergency department.

REFERENCING

The references were relevant to the hypothesis and given in Vancouver format and were from the authorities in the subject field.

It would be appropriate to have more researches focus on the outcome of the admitted victims of emergency department delay. Since some of the factors for the delay are external to emergency department while some are within the emergency department, there should be a wholistic approach to address both intra emergency department and extra emergency department factors in order to bring about improved inpatient care at less cost. It will also remove the frustration which patients and relation go through in the emergency department.

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CHARACTERISTICS AND CAPABILITIES OF EMERGENCY DEPARTMENTS IN ABUJA NIGERIA, 2011

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SOURCE

Emerg. Med. J. Vol.10.1136/emermed-2011-200695

REVIEW OF LITERATURE

This study aimed at assessing the emergency department of the Nigerian capital Abuja which mirrors the state of emergency in Nigeria. The study aimed to use the state of emergency in the emergency developed areas as a yardstick to be able to determine the situation in Nigeria. If possible the literature should show what it is in other resource limited environment.

The literature should indicate the emergency department standard code employed for assessment.

The authors indicated that there is no study that addressed how emergency medicine is delivered in Nigeria.

However going by the literature as referenced, the author looked at the similar study of emergency infrastructure in a resource limited country as Nigeria (1).

The survey instrument was said to have been used in four other countries to profile their emergency department but it was not referenced properly.

There were not sufficient references especially similar studies done in Nigeria (2, 3).

INTRODUCTION

In this article review we will look at the various aspect of this article in terms of its relevance, structure, accuracy, objectivity and stability. We shall also look at how it relates to the existing literature. We shall look at the data analysis and see if the results agree with what the author has inferred or set out to achieve. We shall also see if there are some significant results which the

author did not infer from the data. We shall summarize the article bringing out the main points which the article has determined.

We shall also look at the background of the authors, the setting in which the study was carried out and whether the suggestions of the authors were relevant to the study population and background, we will suggest how to improve on the outcome and further studies which may be necessary as a result of the present findings.

We point out our areas of agreement with the authors and our areas of disagreement, stating reasons why we disagree. We shall look at similar studies by other authors and see how it agrees or differs from this study. We will finally conclude the review by stating the benefits of the study and the grey areas that need further studies.

ARTICLE SUMMARY

This article looked at the present state of the emergency departments of a resource limited society of Abuja, capital of Nigeria. The authors looked at 24 emergency departments in the area via questionnaire administered to the emergency department staff and authorities as to the emergency department characteristics with reference to 2008. They found that majority 92% of the emergency departments had their emergency department in same area with their medical and surgical care. All the emergency departments were attending to both adult and pediatric cases and all accepted that their emergency departments were underutilized. The emergency departments lacked basic and essential technologies such as CT scanners, cardiac monitor, ventilators. The authors also found that the level of emergency care depended on the level of doctors that manned the emergency department. The higher the doctor the greater complex emergency cases they could handle.

The authors concluded that most patients are not using the emergency departments during emergencies and suggested that it may be necessary to determine the type of emergency equipment that can be relevant and affordable in the resource limited settings and the need to train emergency physicians to contain the brain drain suffered in some areas.

ARTICLE STRUCTURE

The article is well structures and followed the standard format which begins with an abstract. The abstract was clearly delineated into headlines of objective, method, results and conclusion. This was followed by non headed introduction which was quite informative, giving the relevant Nigeria background and the emergency burden of a 150 million people and yet with little or no elaborate emergency department. The study population was clearly shown though the sampling method was not adequately stated. The results were shown as figure and tables. Whereas the figure 1 showed the overall emergency department characteristics, table 1 showed the response including patient experiences in the emergency department, length of stay in the emergency department and rate of inpatient admission from the emergency department.

The author drew his conclusions from the results as stated but I would say he over concluded as some of the conclusions were not part of the objective of the study, neither were they inferred from the result.

The author recognized the need to look at some confounding factors that constituted limitation to the study in order to encourage future study that addresses all the issues raised.

The reference was done but very scanty.

AUTHORITY

The authors of the study are:

- Dr. Leana Shoryle Wen, a Harvard trained emergency physician, a Rhodes scholar and writer. She wrote "When Doctors don't listen, how to avoid misdiagnosis and unnecessary test. At an early age she made a name for her numerous studies and books.
- John Oshiomogho – Dr. Oshiomogho is a research assistant, department of medicine, University of Catlgary.
- George Eluwa – A physician, Deputy Director of Operation at Research Population Council in Abuja Nigeria.
- Anne P. Steptoe – She is the Software Development Manager at the Weather Network.
- Ashley F Sullivan – A Dentist.
- Carles A. Camargo – An associate Professor of Medicine and Epidemiology at Harvard Medical School and an Emergency Physician at the Massachusetts General Hospital.

The team used internet based procedure and hence an extent in computer science. It also involved both local (Nigeria based) and international researchers and this gave a lot of the credibility to the study. The study has high volume references and citation as shown in the net.

ACCURACY

While anecdotally and via other authors (2, 3), it is known that there are poor emergency departments in Nigeria. This is expected in a country of over 150 million persons, yet no Emergency Medical Services, no Emergency Medical Residency and Emergency Medicine is not yet recognized as a discipline. Hence, both at national, state and local government level emergency care is unacceptably low.

While the study concludes along this state of affairs in emergency medicine, the study was not elaborate enough to have come out with this result. It looks like an exaggerated state of affair and conclusion.

First the population sample is too small to generalize. Out of over 60 tertiary health institutions in Nigeria, only three are in Abuja hence this cannot mirror the emergency medicine situation in Nigeria. The study depended on the opinion of the staff who may paint a gory picture due to their frustration with their individual management. Nigeria witnesses average of 2 national industrial action involving the doctors each year. Hence a more observational and proactive study would have been more accurate.

The study concluded that there is brain drain and hence emergency physicians should be trained. Did the study confirm brain drain? Can't the brain drain also affect the newly trained emergency medicine physician? Hence that may not be the answer to the issue of brain drain.

However, the researchers admitted that the research is fret with many confounding factors but felt the study should at least spark off further research in addition to drawing attention of the government and health authorities to the deplorable state of our emergency departments.

PERIOD

This study characteristics and capabilities of emergency departments in Abuja Nigeria was accepted in September 2011 and published in November 2011. This is about 5 years. The question is has there been improvement in the emergency department and emergency medicine situation in Nigeria since this last publication. Are their newer studies that will supersede this?

In one of the later publications – (4) Federal Ministry of Health announced it has established a framework for the take off of the first paramedic school in Nigeria as a first step towards re-organizing and updating the nations emergency medicine and hence the emergency department. In a recent newspaper publication, the president of the newly established Society of Emergency Medicine Practitioners of Nigeria announced that the main objective of the society is to collaborate with the governments and ensure that the emergency departments are updated, emergency physician's residency is established and there is a national pre-hospital emergency medical service (EMS). With all these on, the state of the emergency department would have to be re-assessed to enable the system know what exactly needs to be added. Hence a lot would have occurred during the last 5 years.

RELEVANCY

I will consider this article on its relevance to the people of Nigeria and to the body of science. I will also consider this article as to whether the study objective and outcome was focused on during the discussion or whether the title of the study reflects on the body of the work, and the conclusions.

One major problem in West Africa is the escalating conditions of trauma injuries and other life threatening emergencies. The countries within these regions are fighting to reduce this burden. This study identified the problem of poor emergency departments including that of trained

physicians. Using the empirical data, the nation knows the direction to face and what remedies to apply. This study can also help other resource limited nations experiencing same trauma and emergency burden.

The study aimed at elucidating the nature and capabilities of the emergency department and the study focused on through the abstract, while designing the methodology, collecting the results and the discussions that followed. The analysis of data shows that there was deficient medical equipment, trained staff and high admission rate from the emergency department. These are consistent with the objective and call for immediate solution or further study.

OBJECTIVITY

While the study is quite relevant, I am not too sure it has same level of objectivity.

First there is no evidence that the emergency department staff who were administered with the questionnaire were blinded to the objective of the study.

Secondly they were asked to air their opening which could be highly subjective depending on their relationship with the management. If it is perceived that the information will get to the public, they would want to sound as if all is well but if it will determine assistance from the government and international body, then a picture of poor emergency department need is created.

The emergency department assessment should have started with the basic resuscitation and emergency care equipment and materials, such as oxygen, oxygen delivery mask, AEDs, BVM etc, rather than CT scan which is not up to 10 in the whole country. There is the WHO emergency department evaluation criteria that should have been used.

The conclusion on brain drain, training of emergency physicians are not direct reference from the data/result.

The study did not state the size of the hospitals if they are of same size, then the expectation for their emergency department will not be same. Since there are only 2 tertiary health institutions as I mentioned earlier means some of the emergency departments considered must be small or glorified primary centres. Hence using CT scan is a measure will not give good result. Given it convenient sampling was used, it may still give a questionable conclusion as was done.

STABILITY

Because of the situation in West Africa due to the nations inability to recognise emergency medicine as an important discipline, progress in emergency care will be very slow. Consequently the result of studies like this will be stable and be referenced for a long time before appreciable changes can come on board.

Moreover a study like this will be needed to let the health authorities who have been complacent with emergency health issues to understand that all is not well and that actions has to be taken immediately to address the emergency care issue.

ANALYSIS OF GRAPH/TABLE/FIGURE

It shows that 24 out of 29 emergency departments responded median annual visit is 1500 per emergency department or 54 emergency department visits per 1000 population.

75% of the respondents affirmed that most of their patients do not come by ambulance (20% come by ambulance).

38% of emergency department typically have their patient stay less than 1 hour while 25% report they usually stay over 6 hours in the emergency department.

In 40% of the emergency departments, more than 40% of all emergency department attendants are admitted.

In 21% of the emergency departments (5EDs) doctors were physically present all through 24 hours.

In the remaining 19 emergency departments who did not have 24 hours coverage, doctors were available from within the hospital in 67% hence covering the 24 hours.

In 83% of the emergency departments there was a 24 hours laboratory service available.

Hence the analysis was quite consistent and objective. One would have expected that the authors would discuss the absence of overcrowding and its negative impact on the emergency department performance as it happens in US and other developed countries. Discussion should have touched non patient delay in majority of the emergency departments as patients are treated under 1 hour in the rate of admission from the emergency department is alarming and this is not agreement with those of other countries such as 7.3% in Saudi Arabia (6)

CONCLUSION

This article is quite relevant to the present poor emergency care system in Nigeria. The authorities needed some empirical data to re-enforce the need for their intervention. The authors did some good jobs except that the objectivity was weakened and their final conclusion did not quite agree with the results/data received.

They would have concluded, looking at issues like deficiency of basic emergency department equipment, high admission rate from the emergency department, poor attendance to the emergency department and how to ensure that medical personnel are present 24 hours, though they proffered solution to this (7).

Why I agreed with the author that USA differs from Nigeria by volume of attendance and number of emergency departments (8).

I do not agree that the emergency department location and layout in Nigeria do not differ from that of USA markedly (9).

Going through internet shows very high citation of this article indicating its strategic importance to both the health authorities and researchers.

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EXPLORATORY STUDY OF POLICY PROCESS AND EARLY IMPLEMENTATION OF FREE NHIS COVERAGE OF PREGNANT WOMEN IN GHANA

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SOURCE

Sophie witter, Bertha Garshang, Valery Ridde International journal for equity in health 2013, 12:16: doi: 10-11-86/1475-9276-12-16. Electronic version can be found at www.equityhealth.com/content/12/1/16.

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INTRODUCTION

Review is a critical analysis of the article "An exploration study of the policy process and early implementation of the free NHIS coverage for pregnant women in Ghana published in international Journal for equity in health 2013.

In this review of this article following steps were taken. It was summarized, then was analysed for print structure by out. Lastly review did the critical analysis of the article evaluating its authority currency, accuracy, objectivity and coverage Tables & figures were also analysis.

ARTICLE SUMMARY

The purpose of this article is to do exploratory analysis of the policy of free maternal memberships in Glama 2008 by NHIS. The method of analysis was a review of existing literature based on key informal interviews N-13 There key informants were stakeholders in health system, public administration at national level and 2 districts. The revolts of the study highlights that new policy with limited state holder consultation was mainly political initiative. No costing was done prior. Through guidelines were issued, awareness of 18 pregnant mothers was very poor. The healthcare providers were concerned about work load or services and claims management. Users still face the informed changes in antenatal care.

The study concluded that providing free healthcare does not solve weakness in systems. Long term commitment & financial support is required to make this policy effective.

ARTICLE STRUCTURE

The article is available on pubmed & PDF (248 KB). It was introduced with abstract, background, methods, results, discussion conclusion & references. The online links included biomed central PMC full texts. The full text version is free to readers including PDF version PM'o 23446355, indexed for Medline, PMCID: PMC 3599129. The which has been cited by biomed central citation, google scholar ISI web of science and promed central.

ARTICLE CRITIQUE

AUTHORITY

The international journal of health is an open access, pees reviewed, online journal presenting evidence relevant to the search for and attainment of equity is health across and within countries. If aims to improve the understanding of issues that influence the health of population. This includes discussion of political policy related, economic, social and health related influences.

Editors in chief: Efrat shadmi, University of Haifa, Leiya sui, John Hopkins University.

Founding editor- Barbara starfield John Hopkin University society affiliations- Affiliated to WONCA health special interest group.

ACCURACY

The exploratory study was based on six main research question which were adopted from check list. Which distilled good practice for implementation of policies there good practices centered on six area of policy design. A document review was conducted of relevant MOH & Ghana health services. The documents of relevance were analyzed systematically using 6 main research questions. 13 key informant semi structured interviews were conducted.

CURRENCY

The electronic version in complete and can be found on equity healthy: can/content/12/1/16. The study was conducted between March and June 2012 using two research methods literature review and key informant interview.

REFERENCE

This is a scientific journal with scientific data bare. It was written to inform preventive social medicine health worker and will be of interest to policy makers, administrators involved in development and implementations of policy.

OBJECTIVITY

The article is based on exploring the implementation of good practices in health policy making Centered around six areas of policy design such as process, cost, implementation monitoring, evaluation perception & recommendation.

STABILITY

This is internationally acclaimed scientific journal or academic data or resource. The article is being cited in further research papers such as biomed central, googlescholar, pubmed central. The results were endorsed by govt. sector.

Analysis of Figure-I- Framework for results of exploratory interview under headings such as policy, financing, implementation. If precisely explains the process of evaluation of policy.

RECENT ADVANCES RELATED TO TOPIC

Holders, Adjais, Armar Klemesu M, Gtaham W: providing free maternal healthcare: Ten lesson from evaluation of national delivery exemption policy is Ghana.

Global health action 2009.

EXCLUSIONS

The article analyzed following points to arrive at conclusion such as background, process, communication reimbursement, sustainability, to implementation, management. Monitoring, evaluation, perception of effects on cost, access, staff and facilities. Many themes from previous evaluation have recorded such as timely reimbursement & reaching the poorest. This study have concludes that free care has not solved systemic weakness wider concerns about supply demand element, quality of care are important to make policy effective.

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DRINKING WATER COMPOSITION AND INCIDENCE OF URINARY CALCULUS

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SOURCE

Iranian journal of Kidney Diseases /volume 5/ Number/ January 2011. PMID: 21189428 [pubmed- indexed for medline]

This article was received in January 2014, revised in June 2010 and accepted in September 2010.

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INTRODUCTION

This is the review of the article “Drinking water composition and Incidence of Urinars calculus.’ It is study for pathophysiology of urinary calculus due to electrolytes in water and whether these electrolytes contribute to water quality besides hardness causing the calculus formation.

ARTICLES SUMMARY

This study was conducted in Iran in its 787 radiology centers bet 2007 & 2008 by equal probability selection method for collecting samples for study the regional drinking water composition was obtained. Water hardness was measured by EDTR test and classified in 5 groups. The incidence of calculus was then estimated.

The relation between regional drinking water and urolithiasis was calculated for each mineral for which stone risk index was used. (SRI= Calcium/mg×Co^3) in mgl.

The study showed o significant correlation between hardness of tap water. Inverse relation was shown with magnesium level of tap water & urolithiasis. Stone risk index that is ratio of calcium to magnesium bicarbonate product had positive correlation with calculus incidence potential therapeutic application of SRI.

ARTICLE STRUCTURE

The article is available on pubmed & PDF It was introduced with material, methods, results, discussion conclusion references. The online links included biomed central, PMC, Full text version is free in PDF, version printout PMID: 211 89428. The article has been cited by pubmed ebesco, proquest.

ARTICLE CRITIQUE

AUTHORITY

The Iranian journal of Kidney Diseases is a poor reviewed journal and official publication of Iraniam society of Nephrology. It has been published quarterly since 2007 and every 2 months near 2001. The journals objective is to serve as focal point for debates & exchange of knowledge through original papers, case reports, on all aspects of kidney diseases Impact factor: 0.94

Chairman: Ezzatollah Abdi, President, Iranian Society of Nephrology, Tehran, Iran

Editor in Chief: Mohsen Nafar, Secretary General, Iranian society of Nephrology.

Editorial Manager: Behrang Alipour, Iranian Society, of Nephrology.

ACCURACY

Utilizing a multistage stratified sampling 2310 patients were diagnosed in the imaging centers of Iran between 2007 & 2008. These were composed of 1755 patients settled in 24 provinces. The data and their relationship with incidence of calculus was evaluated by met regression models. Stone risk index was used to assess the risk of calculus formation. This brought accuracy in prediction of calculus.

CURRENCY

The paper was accepted by journal in September 2010 and cited in pubmbed in Jan. 2011. The data was collected from incidence bet 2007 & 2008 by epsem sampling.

REFERENCE

This study was useful to medical & emergences physicians besides urologists & nephrologists. It will be immense value to preventive medicine healthcare workers, public health workers, sanitation depts. & policy makers.

OBJECTIVITY

The article explores correlation between hardness of tap water and incidence of calculus in there areas but found lack of correlation. Studies did not show extra tendency of stone formation in people living in hardest water areas. The study showed inhibitions effect of Mg & HCO3 on stone formation. Their study merely suggests a nonlinear correlation & fit model.

STABILITY

The article with its source in internationally acclaimed scientific journal on academic data base. The article was cited in further research papers. The study was endorsed by govt. sector Iranian National water and water waste Engineering company.

ANALYSIS OF GRAPHS

Table I- incidence of calculi in provincial capital of Iran & tap water data.

Figure-1- A nonlinear curve demonstration relationship between incidence of urolithiasis and drinking water Mg

Table 2- Incidence with drinking water Mg composition & stone risk index in the region.

Figure 2- relationship between urolithiasis & stone risk factor

RECENT ADVANCES RELATED TO TOPIC

1. Seirakowski- evaluated 2302 pbs admitted for urolithiasis in USA and found inverse relationship between water hardness and urolithiasis.
2. Churchitt- Discharge diagnosis of 1000 general hospitals in USA from 1940 to 52 and found positive relation between water hardness & urinary calculus.
3. Shuster- Similar study of 2295 pts of USA. Inverse Relationship.

4. Barkers Desinam- United kingdom, positive correlation will hardness and upper urinary calculus.

5. Koshri Et al- 85 cities in Japan Mg/Ca ratio or tap water was Negatively correlated with urinary calculus

CONCLUSION

- No significant relationship found between water minerals & urinary calculus.
- Mg content had marginally inverse relation
- Ratio of calcium to Mg,HCO3 product was found to have strong Positive correlation

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HIGHLIGHTING THE EPIDEMIOLOGY OF HIV VIRAL TROPISM IN HIGH BURDEN POPULATIONS

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SOURCE

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REVIEW OF LITERATURE

Human immunodeficiency virus type-1 (HIV-1) is one of the most complex microorganisms as it is known for its genetic heterogeneity. Currently knowledge based on molecular epidemiologic studies have clearly shown that the most prevalent forms of HIV 1 are subtypes (clades) C, B and A. In sub Saharan Africa and India, Subtype C accounts for about 50% of all infections thus making it the most common clade worldwide. However clade B is common in western countries.

HIV-1 subtypes differ by as much as 20-25% at the genetic level, and have varying biological characteristics, including differences in disease progression, pathogenicity, transmissibility and co-receptor usage.

HIV infection is dependent on the coreception present on the surface of the CD4 cell. And available studies have clearly established a relationship between HIV 1 coreceptor use and the disease stage. However most of these studies were conducted on HIV 1 subtype B.

In general, in the early stages of HIV infection and disease, it is associated with greater prevalence of only chemokine type 5 (CCR5)-tropic (R5) HIV-1, which is characterized with slower progression to AIDS while the emergence of C-X-C chemokine receptor type 4 (CXCR4)-using virus (X4) has been associated with greater treatment experience and higher risk of death, and coincides with more rapid CD4+ T-cell depletion and disease progression.

HIV 1 subtype B is most prevalent in high income countries of the west and consequently is the most studied in terms of receptor usage and its relationship to disease state. This relationship is not well understood for other subtypes especially A, C, and D which are common in Africa and South East Asia.

The introduction of the CCR5 antagonist; Maraviroc, has generated more interest in the study of tropism of this virus in sub Saharan Africa and Asia where most of the burden of the disease exist.

INTRODUCTION

The introduction of Maraviroc which is a CCR5 antagonists as an antiretroviral drug necessitates the need to study HIV tropism for other HIV 1 subtypes especially those present in other countries in South East Asia and Sub Saharan Africa which accounts for a majority of the burden of the infection. The study under review was undertaken to evaluate HIV-1 co-receptor tropism in the developing world where non-B subtypes predominate, in order to assess the therapeutic and prophylactic potential of CCR5 antagonists in these regions.

In this vain, this review aims to highlight the prevalence of R5 and X4-tropic HIV-1 among samples obtained from patients with HIV-1 subtype C infection from India and South Africa, and with subtype A/A1 and D infection from Uganda, and to explore the demographic and clinical characteristics associated with R5 infection. In addition, the review will also highlight the ability of the Trofile® assay to determine tropism of non-B subtypes of HIV-1, which previously had not been explored in a large study.

ARTICLE SUMMARY

In this study, HIV 1 infected patients were recruited into a prospective cross sectional observational study from Uganda, India and South Africa. The subtype infection was also established for each country as Indian and South Africa patients were infected with subtype C while Ugandan patients are infected with subtype D. Study protocols that were used were reviewed by the eithics board of each institution. However sites (institutions) were selected based on their experience with HIV management and research.

In all countries most of the respondents reported heterosexual contact as means of transmission however blood transfusion was reported as a means of transmission in 3 patients. The Indian patients had lower CD4 count than patients from other countries however viral load was consistent across all three countries. A total of 307 samples from India, 678 from Uganda, and 297 from South Africa were collected. All samples has HIV 1 RNA higher than 500 copies/mL.

R5 tropism were detected in 96% of treatment naïve and treatment experienced patients in India; 71% of treatment experience patients in South Africa, 71% of treatment naïve and treatment experience patients in Uganda. Dual/Mixed tropic HIV 1 was found in 4% of Indians, 25% of South Africans and 29% of Ugandans. Presence of R5 type virus correlates with high CD4 count.

ARTICLE STRUCTURE

The article was presented in a standard format with an abstract which gave an overview of the article. The abstract structured into various segments containing introduction, methodology, results and conclusion. The article was well elaborated with charts and statistical analysis summarized in tables. It gave correlates between R5 tropism and CD4 count across of the countries. The background gave a concise overview of tropism. The methodology was presented in a structured format under the following subheadings: Study design, Study methodology, Sample size and statistical analysis.

The results were also presented using a structured format which has tropism as a subheading as such making it much easier to access specific data.

ARTICLE CRITIQUE

AUTHORITY

The article is published in the Journal of the International AIDS Society which is a highly respectable journal with a good impact factor. It is a great source for scientific peer reviewed information about HIV. The article is an authentic one as it is backed with robust references.

ACCURACY

Information contained in the article is accurate and all of them are well referenced.

PERIOD

The article was published in 2012 however data was collected between 2007 and 2008.

RELEVANCY

The article was conducted alongside a team of expert all with very sound academic background. It is a very relevant article as information about viral tropism in South East Asia and Sub Saharan Africa is very essential giving that Maraviroc has been introduced as an antiretroviral drug. This drug requires tropism testing before commencement.

OBJECTIVITY

The information contained in the article is evidence based.

STABILITY

The article is published in a journal with international reputation and has been cited in several other articles.

ANALYSIS OF GRAPH/IMAGE/TABLE

Not applicable.

RECENT ADVANCES RELATED TO THE TOPIC

Not applicable at the moment.

CONCLUSION

This is a well written article in a reputable peer review journal that examined HIV 1 coreceptors in samples collected from India, Uganda and South Africa. This is important because treatment options are being developed that depends on Coreceptors being used by the viruses at time of initiation of treatment.

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THE DOUBLE BURDEN OF TB AND HIV CO-INFECTION IN SUB SAHARAN AFRICA

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SOURCE

Cantwell MF, Mckenna MT, McCray E, Onorato IM. Tuberculosis and race/ethnicity in United States: impact of socioeconomic status. Am J Respir Crit Care Med. 1998;157:1016–20.[PubMed]

REVIEW OF LITERATURE

Those infected with *M. tuberculosis* carry live tubercle bacilli, however, the number of this bacilli and its latency state affect infectivity. Disease usually occurs when the bacteria multiply, overcome immune defenses, and become numerous enough to cause obvious clinical symptoms. Patients with pulmonary tuberculosis (PTB) are the most important source of infection. They transmit the disease in aerosolized droplets. These droplet nuclei contain the infectious particles from respiratory secretions and are usually less than 5 micrometers. When people with active pulmonary tuberculosis cough, sneeze or spit, they expel these droplets and when inhaled, transmission occur. They can remain suspended in the air for long periods of time. A single cough can produce 3,000 infectious droplet nuclei. [1]

Patients with sputum smear-positive tuberculosis are much more infectious than those with smear-negative sputum [2].The risk of infection is determined by the infectiousness of the source; that is, how many tubercle bacilli are being released into the air, the closeness of contact, light and humidity, and the immune status of the host[3,4]. Following infection, the tubercle bacilli multiply in the lungs, spread to the local lymph nodes, and other body tissues but after about six weeks after this primary infection, the body develops an immune response to the tubercle bacilli called delayed hypersensitivity. In the majority of cases, the immune response stops the further multiplication of the tubercle bacilli, and the only evidence of infection is a positive response to an immunological test, of which the most commonly used is the tuberculin skin test [5,6]

The proportion of any population infected depends on the rate and duration of exposure and this varies from one group of people to another. Although the infection rates in boys and girls are usually the same, adult men show higher infection rates than adult women [7].

PATHOGENESIS

The amount of the tubercle bacilli and the integrity of the immune system of the host are important determinants of the risk of progression from infection to disease [7] When infection progresses to disease, it is manifest as infiltrates and lesions within the lung tissue, enlarged lymph nodes within the chest, pleural effusion, or disease disseminated in other parts of the body. The immune response of the patient results in a pathological lesion, which is characteristically localized, often with extensive tissue destruction and cavitation. These cavitating lesions occur most commonly in the lungs and contain many actively dividing bacilli. Sputum from patients with these lesions is usually smear positive.

If the primary infection resolves, small numbers of tubercle bacilli can remain dormant in scarred areas of the body for many years. Post-primary TB may then occur by the process of endogenous reactivation, and it may arise in any other organ system to which the tubercle bacilli were seeded during the primary infection. Active disease can also follow from secondary or exogenous re-infection in a person who already has a latent infection. HIV infection is an important factor. The life time risk of developing tuberculosis in individual who are HIV seronegative is about 5 to 10%, and is about 50% or higher with an annual risk of 5 – 15% for individuals who are HIV seropositive. [7,8]

Other factors that can increase an individual's risk of developing TB following infection include malnutrition, tobacco use, alcohol, corticosteroids, immunosuppressive drugs and other diseases like diabetes mellitus, silicosis, leukemia, measles, and whooping cough in children but none is as important as HIV [7,8]

CLINICAL MANIFESTATION

The clinical manifestation of TB can be divided into pulmonary and extra pulmonary. Patients with pulmonary TB present with a chronic productive cough, fever, and weight loss. The common signs or forms of extrapulmonary TB (EPTB) are pleural effusion, lymphadenopathy, pericardial effusion, miliary disease, and meningitis. [9]

HIV/TB

The relationship between HIV and tuberculosis has been established in several researches. The Human Immunodeficiency Virus causes a progressive decline in the number of CD4+ T lymphocytes and these CD4+ cells are vital in the body's defense against tubercle bacilli as such HIV Infection increases an individual's risk of developing disease, re-infection with tuberculosis, and rapid progression to overt disease. [10,11]

GLOBAL BURDEN OF TB

Tuberculosis is a leading cause of morbidity and mortality in developing countries despite all the extensive control efforts. The advent of anti tuberculosis drugs in the 1940s and the later adoption of the short course regime in the 1980s were landmark achievements that were believed will reverse the impact of the disease; although significant achievements was recorded in developed countries, such can't be said for developing countries [12]. In developing countries, about 7% of all deaths are attributed to TB which is the most common cause of death from a single source of infection among adults [13] In fact; it ranks as the second leading cause of death from an infectious disease worldwide. The WHO estimated 9 million new cases in 2011 and 1.4 million TB deaths. It is also estimated that more than 90% of new TB cases and deaths occur in developing countries. It is the first infectious disease declared by the World Health Organization (WHO) as a global health emergency [14] Asia and Africa alone constitute 86% of all cases [15]

TUBERCULOSIS: THE NIGERIAN SITUATION

In 2010, the WHO estimated that 210,000 new cases of TB occurred in Nigeria; thus ranking it 10th amongst the 22 high burden TB countries in the world. Lagos, Kano, and Oyo have the highest TB prevalence rate. The prevalence of TB in Benue State is also high but this might be attributed to the high HIV prevalence. The Nigeria TB Control program is making great effort to fight the scourge of the disease in the country, however, problems of poor health infrastructure, poor referral system, and sub optimal coverage still sets it back.

TB AND POVERTY

Strong associations exists between poverty and tuberculosis, as the highest rates of TB are found in the poorest section of the community [16] Studies have established that the disease frequently occur in low-income people living in overcrowded areas and persons with low level of education. [17] Poverty promotes the development of active tuberculosis because of poor nutrition which may be associated with a weaker immune system. On the other hand, poverty also result in overcrowded living conditions, poor ventilation, and poor hygiene which is likely to increase the risk of transmission of TB [18]

INTRODUCTION

Tuberculosis as a disease have been with human for several thousands of years now and earliest evidence of the disease is said to have been found in a Bison dating back 17,000 years. However, the bacillus causing the disease was identified by Robert Koch in 1882.

Tuberculosis is caused by *Mycobacterium tuberculosis*; an aerobic bacillus [1]. It has very high lipid content in its cell wall and this is responsible for its unique clinical features [1]. The *M. tuberculosis* complex includes five species: *M. tuberculosis, M. bovis* (and bacillus Calmette-Guérin), *M. canetti, M. africanum,* and *M. microti.* Within the species complex, most human

disease is due to *M. tuberculosis* sensu stricto. Important to note is *M. bovis;* it accounts for a small fraction of human TB cases and is naturally resistant to the drug pyrazinamide [1]

ARTICLE SUMMARY

The article started with an introduction which described briefly how Robert Koch discovered tuberculosis. This introduction is then followed by a description of how tuberculosis is transmitted stating clearly that the amount of the tubercle bacilli and the integrity of the immune system of the host are important determinants of the risk of progression from infection to disease.

The pathogenesis and clinical manifestation of tuberculosis was also described stating clearly the cardinal symptoms tuberculosis which include cough lasting more than 2 weeks, drenching night sweats, low grade fever and weight loss. The link between this symptoms and the pathogenesis was also described.

HIV is a main driver of Tuberculosis and this was clearly mentioned in the article. The immunosuppression caused by HIV infection predispose individuals to tuberculosis infection.

The article clearly described the strong associations that exists between poverty and tuberculosis, as the highest rates of TB are found in the poorest section of the community. The study have established that the disease frequently occur in low-income people living in overcrowded areas and persons with low level of education.

ARTICLE STRUCTURE

The article was presented in a standard format with an abstract which gave an overview of the article. The abstract structured into various segments containing introduction, methodology, results and conclusion. The article was well elaborated with charts and statistical analysis summarized in tables. It gave an overview of tuberculosis before proceeding into the main topic which is the impact of socioeconomic status.

ARTICLE CRITIQUE

AUTHORITY

The article is published in the American Journal of Respiratory Medicine and Critical Care which is a highly respectable journal with a good impact factor. The article is an authentic one as it is backed with robust references. The article is authentic and funders are clearly stated.

ACCURACY

Information contained in the article is accurate and all of them are well referenced.

PERIOD

The article was published in 1998. Data was collected over a 20 weeks period within same year.

RELEVANCY

The article was conducted alongside a team of expert all with very sound academic background. It is a relevant article as it aimed to link tuberculosis, HIV and poverty while considering various variables like race.

OBJECTIVITY

The information contained in the article is evidence based.

STABILITY

The article is published in a journal with international reputation and has been cited in several other articles.

RECENT ADVANCES RELATED TO THE TOPIC

A recent study published in 2012 reiterated the significant of cigarette smoking as an established cause of pulmonary impairment and was significantly more prevalent among non-Hispanic Whites compared to other racial/ethnic groups. The proportion of non-Hispanic Whites impaired among never-smokers was 70% compared to 78% among ever-smokers. This alongside poverty, HIV infections among others are now established risk factors for tuberculosis.

CONCLUSION

This age old disease that traces back to 17,000 years ago is still one of the biggest killer infectious diseases till date. Its association with poverty has since been established and still exists till today especially in sub Saharan Africa, however, the biggest driver of this disease is the HIV pandemic.

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OPTIMISM FOR ACHIEVING A CURE FOR HIV INFECTION

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SOURCE

Valentin Le Douce, Andrea Janossy Houda Hallay, Sultan Ali, Raphael Riclet1, Olivier Rohrand Christian Schwartz 'Achieving a cure for HIV infection: do we have reasons to be optimistic' The Journal of Antimicrobial Chemotherapy, Volume 67 Issue 5 May 20121063–1074. Published online 2012 January 31. doi: 10.1093/jac/dkr599 also available at http://jac.oxfordjournals.org/content/67/5/1063.full.pdf+html

INTRODUCTION

This review will assess the article titled 'Achieving a cure for HIV infection: do we have reasons to be optimistic' written by *Valentin Le Douce,* et al published in 'The Journal of Antimicrobial Chemotherapy'.

In the process of portrayal -- its purpose will be defined, the structure of the article be examined in terms of serenity with which any reader can have access to this piece of information. The article will be dissected based upon its authority, accuracy, currency, relevance, objectivity and stability in that order.

The review will also delve into the article's accessibility and credibility. Upon over all appraisal the article has been found to be well penned -- clear and pertinent.

REVIEW OF LITERATURE

A cure for HIV has always been the holy grail of AIDS researchers and naturally we have plenty of literature available on the various aspects of cure from HIV—like the quest for cure, cracking a consensus about it, need for cure, barriers to cure, sources of residual virus, latent and activated CD 4 cells, viral latency, different reservoirs, different approaches to cure and torch bearers of cure and to many of them find a mention over here though to have accommodated all of them was itself a difficult task.

AIDS is a disease of staggering numbers, of tragically recursive desolation. Since the first diagnosis 32 years ago by Dr Michel Gotleib (reported in Morbidity and Mortality Weekly Report MMWR-CDC, 5th. June 1981) HIV has infected more than 60 million people, around 30 million of whom have died. For another 5 million, anti-retroviral therapy has made their infection a manageable though still chronic condition. In late nineties the two events have shaped the evolution of the thought of Cure or 'Eradication' of AIDS. With the advent of effective combination ART (cART) in the mid-1990s, some researchers suggested that given enough time, antiretroviral drugs might eventually wipe out all HIV in the body. At the XI International AIDS Conference in Vancouver in 1996, Dr David Ho from the Aaron Diamond AIDS Research Center proposed that a "hit early, hit hard" strategy using a potent combination regimen could potentially eradicate virus-infected T-cells—and with them, the virus—within two to three years.

Dr Robert Siliciano and his team at Johns Hopkins who conducted research that would yield a more sobering finding: In the May 8, 1997, issue of Nature, they reported that HIV can hide in a "reservoir" of long-lived resting CD4 T-cells. Because it is not actively replicating, this virus is invisible to the immune system and out of reach of antiretroviral drugs. HIV's genetic blueprint, known as proviral DNA, can lie dormant for years or even decades within a host cell's chromosomes, ready to produce new virus when the cell is activated.

Dr. Siliciano also suggested that the size of the viral reservoir will determine how long the treatment needs to be continued for a functional cure to be possible and how long it may take for a latent virus to recur once treatment has stopped if a functional cure has not occurred.

A baby has a tiny (if any) reservoir of latently infected cells, then 15-18 months of combination ART may have been sufficient to reduce that reservoir to allow for a functional cure (as has been unfolded at the 2013 Conference on Retroviruses and Opportunistic Infections –CROI-- as a case report of a "functional cure" in an infant (Mississippi baby') who started a full antiretroviral therapy regimen within the first days of birth, --- illustrating—and putting to the test—the evolving thought about the possibility of curing HIV infection and sparking new interest in the possible implications of this concept for the future of HIV treatment.

In 1997 Tae-Wook Chun and Anthony Fauci from the National Institutes of Allergy and Infectious Diseases (NIAID) recorded that they could still find integrated HIV DNA in resting CD4 cells from a small group of patients who started treatment early and had suppressed plasma viral load after a year on combination anti-retro viral therapy. Ten years down, based on the half-life of latently infected T-cells, Chun's group approximated that early treatment might wipe out all virus in these cells in about 7.7 years.

In the 5th International AIDS Society (IAS) Conference on HIV Pathogenesis, Treatment and Prevention 2007, the consensus around the ineffectiveness of a cure was starting to crack and with the approval of two novel classes of antiretroviral drugs—integrase inhibitors and CCR5

antagonists—there came in hand some armory for the first time in years the ability to target HIV at more stages of its life cycle.

The prospect of a cure came into its existence in 2010. At the XVIII International AIDS Conference in Vienna, Sharon Lewin from Monash University said "We should not and cannot continue to accept that HIV is a chronic illness that commits patients to lifelong treatment, In the absence of an effective vaccine, we must seriously pursue the possibility of cure."

The International AIDS Society patronized a workshop titled "Towards a Cure: HIV Reservoirs and Strategies to Control Them," which ushered together 200 researchers and advocates to discuss the latest advances in the field.

At the 18th Conference on Retroviruses and Opportunistic Infections (CROI 2011), researchers presented the first data from a human trial of an experimental gene therapy approach that deletes CCR5 receptors from T-cells in an attempt to halt HIV entry.

In the April 2010 issue of *Nature Medicine,* Maria Buzónsetal from Spain declared that adding the integrase inhibitor 'raltegravir (Isentress) to a suppressive ART regimen led to accumulation of bits of viral DNA known as 2-LTR circles, suggesting that HIV is still copying its genetic material but cannot insert it into host cell chromosomes. Using novel assays, UnaO Doherty's group at the University of Pennsylvania also detected un-integrated HIV DNA, suggesting continued viral replication.

In the April 2010 issue of *Nature Medicine,* Christoph Carteretal from the University of Michigan at Ann Arbor recorded that latent HIV can camouflage in CD34 hematopoietic stem cells, which give rise to all types of blood cells. When these stem cells were forced to differentiate in the laboratory, proviral DNA was activated and began producing new virus. According to Fauci, starting ART even within the first several months after infection can help keep viral reservoirs low, improving prospects for a functional cure.

Overall, intensification studies have not produced impressive results. Some researchers have found that raltegravir and the CCR5 antagonist maraviroc may reduce immune activation and inflammation. But so far there is no conclusive evidence that any combination of current antiretroviral drugs can eradicate HIV, Siliciano has to here to state, "We have reached the theoretical limit of antiretroviral therapy." But researchers have not yet given up on treatment intensification. The German New Era Study (by Dr Hans Jaeger) is looking at treatment-experienced patients with viral load suppressed for three years who add both maraviroc and raltegravir to their existing boosted protease inhibitor regimen. The EraMune trials are evaluating whether an intensified ART regimen with either interleukin 7 or a therapeutic vaccine can eliminate HIV from the body.

In 2004, Ronald Mitsuyasu etal at the University of California at Los Angeles (UCLA) announced that a ribozyme or "molecular scissors" that disrupts the HIV *Tat* gene was

successfully inserted into human hematopoietic stem cells. A follow-up study with 74 HIV positive patients who interrupted ART showed that while the altered stem cells did not significantly reduce viral load, recipients had higher CD4 cell counts over two years. There have been two revolutionary stories about two patients–have changed the scenario for pessimism to hope and anticipation in the arena of cure from HIV (both named as Berlin patients, but we shall call them Berlin 1 and Berlin 2 for our convenience) The first Berlin Patient was a young German man who in 1996, sought care due to flu-like symptoms about three weeks after having unprotected sex. His doctor, Heiko Jessen, started him on ART and hydroxyurea, a cancer drug. Hydroxyurea expert Franco Lori described the case at an AIDS conference in Hamburg in 1997.

After starting combination therapy, the man rapidly reached an "undetectable" viral load according to an older test with a lower limit of 500 copies/mL. When he stopped his drugs a few months later due to a bout of hepatitis A, his HIV viral load stayed undetectable. About five weeks later, he decided to permanently discontinue therapy and his virus remained suppressed. This Berlin Patient no 1 was the first individual known to have achieved "remission" of HIV 'ala' cancer model, and the case made headlines around the world, including a reporting in the *New York Times Magazine.* Lori's team presented further details at CROI 1999 and in the May 27, 1999, *New England Journal of Medicine.* By that time, this Berlin Patient had been left treatment for about two years, still with no plasma viral rebound. But traces of HIV RNA were detected in his lymph nodes, and replication-competent virus was isolated from a small number of resting CD4 T-cells after Robert Siliciano developed a sensitive test to measure such. Although his HIV was not wiped out the man's immune system managed to control the virus, showing that a functional cure is within the reach of possibility. The second Berlin Patient came to the world's notice some ten year later.

One American man living in Germany, took treatment for acute myeloid leukemia (AML) at Berlin's Charité Medical University in 2006. At that time, he had been HIV positive for more than a decade and on c- ART for four years, and had undetectable viral load, having a history of high viral load and disease progression, excluding himself from being a natural elite controller. After initial chemotherapy failed, the next step was a bone marrow transplant. The man received a bone marrow transplant containing hematopoietic stem cell after taking strong chemotherapy and the donated stem cells essentially built a new immune system.

The man's doctor, Gero Hütte had learnt that individuals with the CCR5- delta-32 genetic variation were protected against HIV infection. He could find a bone marrow donor who was both a genetic match and carried two copies of the uncommon variation, meaning the donor's cells did not express CCR5 receptors. This Berlin Patient no 2 stopped ART one day before his first bone marrow transplant in 2007 and afterward got immunosuppressant drugs to prevent the donor cells from attacking his body. The transplant was successful and, as hypothesized, the newly reconstituted CD4 T-cells lacked CCR5 receptors.

A year later, the man had a recurrence of AML and the patient received a second transplant after chemotherapy and whole-body radiation from same donor. The man kept off from ART, two months after the first procedure maintained undetectable plasma HIV RNA and undetectable proviral DNA in resting CD4 T-cells. Dr Hütter presented this Berlin case study at CROI 2008 and in the February 12, 2009, *New England Journal of Medicine.* The case generated interest from both HIV researchers and the public at large after an in-depth article by Schools in the *Wall Street Journal.*

In an update at the IAS Reservoirs workshop and in the March 10, 2011, issue of *Blood,* Hütter's team reported that four years after the first transplant and still off ART, the man remains in remission from AML and demonstrates no signs of HIV. Using the best available technology, Siliciano and others have found no HIV RNA or DNA in his blood plasma, lymph nodes, rectal mucosa, cerebrospinal fluid, brain tissue, or resting CD4 T-cell samples. What's more, his CD4 T-cell count has increased to a normal level. This Berlin Patient revealed his identity as Timothy Brown, now in overall good health and living in San Francisco. Zinc finger gene therapy technology developed by Sangamo BioSciences is furthest along in development. This technique uses a zinc finger nuclease (ZFN), a synthetic protein carried by an adenovirus vector that can cut DNA strands at a specific location.

The nuclease causes a double-strand DNA break in the CCR5 gene, and the ensuing repair process permanently disrupts the gene, passing along to daughter cells. At CROI 2011, Jay Lalezari from Quest Clinical Research and Carl June presented findings from the first pilot studies of the Sangamo zinc finger technique in HIV positive people, assessing whether autologous (self-donated) CD4 T-cells with deleted CCR5 (dubbed SB-728-T) would proliferate, persist, and behave like normal T-cells in the body. At CROI, Craig Wilen from the University of Pennsylvania presented the first data on gene therapy to interfere with CXCR4 expression. Laboratory studies found that the zinc finger procedure did not impair CD4 T-cell proliferation.

Altered cells exposed to HIV were protected from infection and showed a significant survival advantage. In mice with a humanized immune system, altered CD4 cells were protected from infection by CXCR4-tropic HIV. In the August 2010 issue of *Nature Biotechnology,* Nathalia Holt and Paula Cannon from the University of Southern California and colleagues recorded that the Sangamo zinc finger technique can disrupt the CCR5 gene in CD34 hematopoietic stem cells from humanized mice. Since these stem cells give rise to all types of blood cells, the resulting CD4 T-cells lacked the CCR5 coreceptor and therefore were protected against HIV infection. Researchers are studying various methods of activating quiescent cells in order to awaken hidden proviral DNA, with the goal of purging or flushing out the viral reservoir And as per David Margolis, this may be done either by directly activating resting cells and their resident HIV, or by disabling mechanisms that keep them inactive—that is, by "giving them a push" or "taking the brakes off."

Sandrina Da Fonseca et al from VGTI showed that CD4 T-cells containing proviral DNA express more of a surface antigen known as programmed death 1, or PD-1. Interactions between PD-1 and its receptor, PD-L1, help maintain these cells in a resting state and keep integrated virus latent, they reported at CROI 2011. Conversely, agents that block this interaction can stimulate HIV reactivation and release.

A class of agents known as protein kinase C activators activates transcription of latent HIV without prompting activation of uninfected cells. Frank Wolschendorf et al stated the dubbed HIV-1-reactivating protein factor, which stimulates a brief pulse of NF-kB that activates Tat and sets off viral production—portrayed as "hit and run stimulation"

The way to "take the brakes off" is chromatin remodeling, or changing how HIV DNA binds to histones in host cell chromosomes, a chemical reaction called acetylation which keeps DNA accessible, while a complementary reaction, methylation, has the opposite effect. Histone deacetylase enzymes keep DNA tightly bound and unusable; HDAC inhibitors and methylation inhibitors release DNA so it can be used to direct virus production. In the June 19, 2008, issue of *AIDS*, Margolis et al reported from a larger follow-up study using Valproic acid. Here, 11 HIV positive people with stable viral suppression added 1,000 mg valproic acid to their standard ART regimen. Four participants (36%) showed a reduction in latently infected CD4 cells, including three who also experienced further reductions in viral load; the rest, however, had no significant change.

These studies indicate that valproic acid is not potent enough—or perhaps does not target the right forms of HDAC—to appreciably reduce the size of the latent HIV reservoir; they offer proof of concept that this approach may have some benefit.

Sophie Reuse et al (Belgium) reported at the IAS Reservoirs workshop that a combination of clinically available HDAC inhibitors plus prostratin synergistically activated the HIV promoter element, leading to enhanced viral gene expression.

In the June 2009 issue of *Retrovirology*, Savarino's group reported a "shock and kill" approach using Class I HDAC inhibitors plus the pro-oxidant agent buthionine sulfoximine (BSO). The HDAC inhibitors activated latent HIV in cell cultures, but only at toxic doses; adding BSO enabled the HDAC inhibitors to work at lower, more tolerable doses.

In the April 5, 2011, issue of *PLoS ONE*, Michael Kovochicheta l (UCLA) mentioned an approach using nanotechnology to deliver drugs more precisely to desired targets. A nanoparticle with the protein kinase C activator bryostatin-2 activated resting T-cells and stimulated latent virus production *in vitro* and in humanized mice. Adding the HDAC inhibitor sodium butyrate enhanced activation, and the particles could also be loaded with the antiretroviral drug nelfinavir to simultaneously activate latent virus and inhibit its replication.

The resting cell activation approach aims to purge latent HIV from reservoirs, but the opposite strategy—keeping integrated viral DNA permanently silenced—could also be another way to achieve a functional cure.

In the April 15, 2010, *Journal of Infectious Diseases, Siliciano's group* recorded that minocycline selectively interrupts signaling pathways critical for T-cell activation.

In 1999, Cynthia McCoigetal from the University of Texas disclosed that genetically engineered immune toxins targeting the CD45RO marker on memory CD4 T-cells killed HIV-containing memory cells while sparing naive CD4 T-cells and certain other memory cells with different marker configurations.

Abraham Loyteretalat Hebrew University expressed that a combination of peptides plus saquinavir (Invirase) increased integration of HIV DNA into host cells to such an extent that they underwent apoptosis, or cellular suicide. They further stated that in a laboratory study this lethal mix led to death of infected T-cells and "total extermination" of the virus, but it did not appear to have an effect on uninfected cells.

Other research aims to boost the immune system's response to HIV. Dozens of therapeutic vaccine candidates have been tested, but despite some promising activity in laboratory and animal studies, none have been shown to consistently and significantly decrease—much less eliminate —HIV over the long term in clinical trials.

Researchers have also tied to find many other immune-based therapies, including gene therapy to make CD8 T-cells respond more strongly to the virus, but with every method tested so far HIV comes back after ART is stopped.

Finally, reducing the harm caused by HIV could be another way to implement a functional cure. A growing school of thought evidences that persistent immune activation and inflammation are responsible for much of the damage related to chronic HIV infection. If investigators could find a way to abandon this response, the virus might be rendered harmless, in the same way some monkey species harbor persistent replicating SIV without disease progression.

ARTICLE SUMMARY

'Cure does have philosophical, and programmatic connotations in the context of HIV/AIDS. Many developments and strategies have been evolved to tame this virus, since its reporting - some 32 years ago and after the arrival of the combination medicines against this virus, called Anti retroviral therapy (ART) in 1996 (now known as 'highly active antiretroviral therapy - HAART). The advent of HAART has almost reversed a scenario -- a disease equated with death warrant -- to a chronic and manageable illness with a dramatic decrease in mortality and morbidity of AIDS-related symptoms in infected patients. But HAART has not been able to find the cure of HIV infection, There are hurdles to HIV eradication--- the main being the existence

of dormant or quiescent reservoirs. Several other problems have been found with HAART (such as side effects, adherence to medication, emergence of resistance and cost of treatment), and these inspire the search for new ways to treat these patients. Medical fraternity is reacting with guarded appreciation and anticipation, more so after the publication of reports of Sterilizing functional cure of a man (known as Berlin patient') following BMT from a donor having deficient chemo co receptor CCR5 (vital for HIV entry) gene and one baby, known as 'Mississippi Baby' who was infected with HIV at birth but is now apparently free of the virus. through a hit hard, hit early approach taken by researchers and doctors in relation to antiretroviral therapy These findings hold out the hope that treatment during acute HIV infection (ala – Mississippi baby) has the potential to transform the outcome of HIV infection in at least some individuals. The use of early and aggressive treatment could be a paradigm shift in HIV/AIDS treatment in children in the developing world, where mothers are typically treated during pregnancy to lower the risk of passing the virus on to the child. Both long-term survivors and those who have been exposed to HIV but remain seronegative (called Elite Controllers and Slow/Non-progressors) offer a great opportunity to study the mechanisms of resistance to HIV infection and disease. Recent advances hold promise for the ultimate cure of HIV infection. Besides these new strategies aiming to eliminate the virus, efforts must be made to upgrade the current HAART. The medical scientists believe that the cure of HIV infection is not going to be achieved in short term and that a HAART strategy based on purging the reservoirs has to be done aggressively. Till 'Cure' is not achieved we will have to remain steadfast in working towards it. This article fulfills its objectives of sending messages to the readers about the optimism of HAART and its prospective abilities to achieve a cure for HIV, albeit with a question mark.

ARTICLE STRUCTURE

The article commences with an abstract that overtures - an effective overview of the article by establishing the background to the issue of achieving a cure from HIV and relevant points. The article itself is very qualitative in nature and is twelve pages long. It is accessible online as a PDF/html document and the contact details for the authors are adequately provided. There is a logical ordering of points and both the paragraphs and the sentences are just instructive making the availability of the information, its reading and understanding - all that effortless. The conclusion is a straightforward summary of the points made There are more than adequate references, provided in a reference section (in fact a huge list follows --186-One hundred eighty six - in total,) but can be considered taking into the account relevance of the topic. Overall the abstract is concise and terse. The structure of the article makes it easier to interpret and understand.

ARTICLE CRITIQUE

AUTHORITY

The article has been featured in an extremely illustrious ***source 'The Journal of Antimicrobial Chemotherapy'*** This is a peer-reviewed medical journal which covers laboratory aspects and clinical use of antimicrobial agents and is published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy, The Journal of Antimicrobial Chemotherapy is among the foremost international journals in antimicrobial research and its readership includes representatives of academia, industry and health services, and includes those who are influential in formulary decisions. This journal is abstracted and indexed in *Biological Abstracts, BIOSIS Previews, CAB International, Chemical Abstracts Service, Current Contents, EMBASE, MEDLINE/Index Medicus, ProQuest Medical Library, and the Science Citation Index and as per* the *Journal Citation Reports*, this journal received a 2012 impact factor of 5.338, ranking it 7th out of 69 journals in the category *Infectious Diseases*, which makes it more plausible.

The article has been equally contributed by all of the authors as has been suggested in the article and their affiliations to Institute of Parasitology University of Strasbourg, Strasbourg, France speaks their class as the University of Strasbourg in Strasbourg, Alsace, France, is the second largest university in France (after Aix-Marseille University), with about 43,000 students and over 4,000 researchers. All of this information indicates that the article is highly credible and persuasive

ACCURACY

Being published as a 'review article in a distinguished medical journal of the stature of '*The Journal of Antimicrobial Chemotherapy* proves its correctness and exactitude. The article has more than enough (186) references of articles written by some of world famous HIV Experts connotes its great accuracy and credibility.

CURRENCY

The Journal of Antimicrobial Chemotherapy with this article was published in May 2012 in print and went online on January 31 2012. Its references date from 1998 to 2010. The recent publication of the article and the recent references indicate that the article is very topical and contemporary, as does the content of the article which deals with the current advancements in the field AIDS cure.

RELEVANCE

It has been written to furnish information to an educated sector (Medical doctors) and published in a reputable journal (The Journal of Antimicrobial Chemotherapy) and it is relevant to its main intended audience–the HIV health care providers. The topic (HIV Cure) covered too is a

significant one in the context of HIV, which has been long cherished dream. In the conclusions of the article authors asks the question-Are there reasons to be optimistic that a cure for HIV infection may be achieved and themselves answer with guarded affirmation as the cure from HIV will not be achieved in the short term. They discuss the exciting advances offering new opportunities to achieve a cure, using gene therapy to confer HIV resistance (including the CCR5 gene therapy) which is a valuable approach compared with chemotherapy, but fraught with several drawbacks, including toxicities, development of resistance and cost. They surmise that the 'holy grail' for scientists is to achieve a sterilizing cure with total eradication of the virus from the body, although we have got functional cure, with few patients who control HIV-1 infection (the elite controllers). The 'shock and kill' strategy has too emerged as an exciting potential way to eliminate the virus. The German case is the only example where a we have a possible sterilizing cure, incidentally indicating a weakness of HIV. The authors compare these strategies with a war and declare that the war against this virus is far from over and will need much more work. They equate the current therapeutic strategies that could lead in the long term to a cure as the first front line but, to win a war usually a second front line is needed to open which they analogize with the development of an HIV vaccine. They believe that even if in practice this approach (vaccine research) is not yet yielding –(ongoing vaccine trials) not very optimistic results, efforts in this direction must be continued, but the scientists might require new avenues in HIV immunology research They feel that research aiming at a therapeutic cure will benefit from research aiming to develop a vaccine, and vice versa. Finally they cite reasons to be optimistic coming from the intensive efforts made in different fields of research, that of a multidisciplinary approach, including immunologists, virologists, molecular biologists, clinicians, pharmacologists, chemists, physicists and mathematicians, who they feel, have already initiated new ways and amplified new concepts for therapies that are currently being tested in clinical trials. These are global issues (HIV, Cure research) and undoubtedly relate to the global community.

OBJECTIVITY

The information in the article was derived from team of authors' extensive experience working at higher centres of excellence in HIV field – the Institute of Parasitology University of Strasbourg, Strasbourg, France, with over 4,000 researchers. All of this information indicates that the article is highly plausible and trustworthy.

The article shows research decisions, and contains both facts and evidences, opinions have been presented, on the both sides of the argument (availability of strategies of cure vs obstacles in achieving it) are adequately elucidated. The article raises question itself in achieving a cure. The majority of the claims and arguments made have been supported, in the articles and References. The article serves its purpose as an objective presentation of achieving a cure from HIV to the medical community in general and HIV Care providers in particular.

STABILITY

The article has been published in a reputed medical journal and available in both print and electronic forms. The article and all 186 references have been duly been cited by other articles in PMC (The PMC -PubMed Central is a free digital *database* of full-text *scientific literature* in biomedical and life sciences which has grown from the online *Entrez PubMed* biomedical literature search system and developed by the U.S. *National Library of Medicine* (NLM) as an online archive of biomedical journal articles. The full text of all PubMed Central articles is free to read, with varying provisions for reuse. Some participating publishers delay the release of their articles on PubMed Central for a set time after paper publication (often six months). The archive contains approximately 2.6 million items, including articles, editorials and letters. For these reasons, the article is stable as a resource and being accessible through a credible and reliable academic database like PMC.

ANALYSIS OF GRAPH

Not applicable

RECENT ADVANCES RELATED TO THE TOPIC

The Berlin Patient, the VISCONTI cohort and the "cured" baby in Mississippi provide tantalizing hope that a "functional cure" may be possible. A "functional cure" essentially means that people can remain HIV free without the need for antiretroviral therapy. While HIV treatments are effective at controlling the active virus, HIV also persists in the body by hiding in long-lived cells (resting CD4+ memory T cells). In this state, HIV resides in a latent reservoir undetectable by the immune system and unaffected by antiretroviral treatments. Flushing latent HIV from these hiding places has been proposed as a key step towards a cure.

On March 14th, 2013 results from the Visconti trial conducted in France (the name is a contraction of "***Virological and immunological studies in controllers after treatment interruption***") were published, It has made the possibility of using antiretroviral drugs to produce something akin to a cure.

The Visconti trial, which was reported in the Public Library of Science's journal *PLoS Pathogens* by Christine Rouzioux et al of Paris Descartes University has followed the fates of 14 people treated with antiretroviral drugs shortly after they were infected with HIV, and for several years thereafter, who then (under medical supervision) had their drug treatments withdrawn. As the trial's investigators reported to the International AIDS Conference in Washington, in July 2012, this procedure has turned these people into what are known as "elite controllers"—(they still have detectable levels of HIV in their bodies years after infection, but even in the absence of drug treatment those levels do not rise significantly, and certainly not to a point where they are causing symptoms)

Elite controllers do occur naturally, but such people are unusual. Fewer than one person in 100 seems to have the potential to develop natural elite control. What causes natural elite control remains mysterious, but certain versions of what are known as HLA genes (which regulate cell-surface proteins in some immune-system cells) are rarely found in natural elite controllers.

The crucial feature shared by people in the Visconti study is that they were put on drugs within ten weeks of infection, a point where the virus is still establishing itself in the body. This hypothesis is akin what has been used in the "Mississippi baby" case, reported in March 2013, in which an infant girl, infected by being born to an HIV+ mother, was given antiretroviral treatment within a few hours of birth. Her doctors, however, lost touch with the child for five months when she was 18 months old, interrupting the treatment. When the mother came to health facility with the baby, researchers found her infection had regressed to the point of *undetectability*, even though she was no longer on ART. This observation, combined with the Visconti trial, leads to the question of how frequent the phenomenon of elite control following early treatment actually is.

Dr Rouzioux et al tried to estimate this frequency of 'elite controllers' from a database of French AIDS cases, and came to conclusion that about 15% of those who are infected and treated early turn into elite controllers—though with a limitation -- the database in question, the French Hospital Database on HIV, allowed them to draw this conclusion for only the first two years after the end of treatment.

It is all, extremely encouraging and if the common factor between so-called post-treatment controllers can be identified, it will allow experts to offer treatment withdrawal to those likely to benefit from it.

A scientific strategy—consisting of seven major research priorities—has been launched by an International AIDS Society working group, according to a report released July 19 and discussed in detail in a two-day symposium taking place July 21 and 22 ahead of the XIX International AIDS Conference (AIDS 2012) in Washington, DC. As per Françoise Barré-Sinoussi the strategy, baptized as "Towards an HIV Cure,--is the result of a collaborative effort which has produced a roadmap that will constructively move HIV cure research forward." Barré-Sinoussi, the co-discoverer of HIV, a Nobel laureate and researcher at the Institute Pasteur, is co-chair of the group—along with Steven Deeks, MD, of the University of California, San Francisco—consisting of 34 leading HIV scientists and clinicians.

The molecular biology regarding how HIV's DNA becomes integrated in the chromosomes of human cells is the focus of intense research. This work has already led to a number of possible interventions, some of which are being tested in clinical trials.

Recently, in a small study involving people living with HIV, David Margolis, MD, of the University of North Carolina et al demonstrated that a dose of a drug that inhibits an enzyme involved in HIV silencing leads to rapid production of HIV RNA in the patient's latently

infected cells. This could make such previously unreachable viral reservoirs susceptible to curative strategies. For example, in combination with treatments that enhance host immune defense—therapeutic vaccines are an example—unmasking latent virus might allow clearance of infection. Barré-Sinoussi, Deeks and their colleagues note that substantial resources will be required to address these priorities.

A number of clinical trials are planned, or currently underway, to study the safe elimination of latent infection in people living with HIV receiving antiretroviral therapy. These include:

Study	Intervention	Reference (clinicaltrials.gov)	Status
Optiprim ANRS 147	3 vs 5 ARVs during acute infection	*NCT01033760*	Closed, ongoing
IntensVIH	Isentress + Selzentry intensification	*NCT00935480*	Closed, ongoing
Eramune 01	IL-7 +intensifcation	*NCT01019551*	Closed, ongoing
Eramune 02	Vaccination +intensification	*NCT00976404*	Closed, ongoing
Deeks	Disulfiram	*NCT01286259*	Closed, ongoing
Margolis	Vorinostat (SAHA)	*NCT01319383*	Recruiting
Lewin	Vorinostat (SAHA)	*NCT01365065*	Recruiting
Lalezari	Zinc finger nuclease (ZFN)	*NCT01252641*	Closed, ongoing
Tebas	Zinc finger nuclease (ZFN)	*NCT00842634*	Closed, ongoing
Krishnan	Gene therapy/stem cell transplants in	*NCT00569985*	Recruiting

	HIV lymphoma patients		
Moreno	Bryostatin	N/A	Starting soon
Hatano	Anti-PD1 antibody	N/A	Starting soon
Woolfrey	Autologous HIV-resistant cells	N/A	Starting soon

NEW ERA STUDY

This study ties perhaps first time to define 'Cure/Eradication' in the context of HIV/AIDS One interesting trial is going on in Germany since May 2009 under Dr Hans Jaeger, which is a multicenter, open-label, non-randomized trial to evaluate treatment with multi-drug class (MDC) HAART and its impact on the decay rate of latently infected CD4+ T cells. (The author of this article knows Dr Hans Jaeger personally Dr Jaeger has presented a paper on eradication/cure at AIDS Society of India Conference –ASICON on 31st. Oct 2010 Hyderabad, where he tried to define 'Eradication or Cure' from AIDS on certain end points for his study. This is probably the first time that 'Eradication or Cure' has been tried to be defined scientifically. Once this study gets completed then we can learn whether Mega- HAART can have really some effect on decay of latently infected CD4+ T Cells, affecting 'a cure' at least on programmatic terms.

The purpose of this study is to decrease viral reservoirs in 40 HIV-infected patients with either primary infection (PHI) or chronic infection (CHI) and successful HAART for at least three years. All patients will be started on a multi drug HAART including two NRTI, one PI, a CCR5-inhibitor and an integrase inhibitor. Decay of viral reservoirs like latently HIV-infected CD4+ T-cells will be monitored over time. The latest reports indicate that here has been decrease in proviral DNA and no patients has stopped medicines due to toxicities, with no unexpected serious adverse events (SAE) --only 2 SAEs (kidney stones), 8 laboratory AEs (Adverse effects) (grade 3), and 32 clinical AEs (grade 1 and 2, i.e. diarrhea, fatigue) have been reported, but therapy has not been interrupted which has been all so far encouraging. We will have to wait for 2019 for its results, but this will certainly pave the way whether earlier & aggressive treatment will have any bearing on the elimination of reservoirs of HIV leading to a possible 'cure'

CONCLUSION

The review analyzes critically the article ***Achieving a cure for HIV infection: do we have reasons to be optimistic'*** written by *Valentin Le Douce,* et al The content, structure, strengths and limitations of the article were construed and dissected. The article has shared to a better understanding amongst the HIV guild, of the pros and cons of a possibility of achieving a HIV cure. It is an accessible, easier to read well researched and highly credible. One familiar axiom

'*to 'Cure occasionally, relieve often, console always* '—coming from the ancient French aphorism ***'Guirerquelquefois, soulagersouvent, consoler toujours'***, fits superbly into the natural history of HIV/AIDS leading to its much wanted 'cure, even it does portray that cure or eradication has a bit of a philosophical content (we keep telling our patients --HIV is now a treatable and controllable illness like Diabetes Mellitus and Hypertension, though a 'cure' is still elusive) thereby meaning that no body has a clear concept and we are still in a trial and error phase. Cure may have different meanings in the context of epidemiology, clinical care and programmatic evaluation and could range from 'remission (cancer model) to 'eradication' (Infectious diseases model). ***An example may be cited here*** : in RNTCP -Revised National TB Control Program in India minimum two sputum negatives (of AFB), out of three done during 'Continuation phase' are required to declare the person be cured of TB.

'Cure' -comes from Latin word 'cura' meaning –care, concern, attention'. The current use of word seemingly sprang from the belief that proper and sufficient 'care' was tantamount to 'cure'. Would that this were so!

Both these words 'care' and 'cure' are legitimately appropriate in the ambience of HIV/AIDS, more so in present scenarios. And hence this article is being recommended for medical experts especially, the HIV care providers

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LUMBAR RADICULOPATHY: RESULTS OF GRADE 3 AND 4 VERTICAL OSCILLATORY PRESSURE (VOP) IN PAIN MANAGEMENT IN A 32-YEAR-OLD FEMALE. A CASE REPORT

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BACKGROUND AND PURPOSE

Chronic low back pain is prevalent in the western world. Lumbar radiculopathy is a common presentation in physical therapy daily practice.[4] Large epidemiological studies show that: "20 to 30% of patients with chronic back pain suffer from a neuropathic pain component".[4,7] Its diagnosis and management remain an enigma. There is no conclusive evidence for the long-term efficacy of spinal manipulation for any type of low back pain.[3] There is no evidence that describes the efficacy of vertical oscillatory pressure (VOP) in the management of pain resulting from lumbar radiculopathy either. The few articles that report the effect of VOP did not quantify the intensity (grading) of the applied thrust to the spine.[3] This case report describes and observe the result of applying a submaximal and maximal central posterior-anterior thrust (grade 3 and 4) vertical oscillatory pressure to the lumbar spine in a 32-year-old female with lumbar radiculopathy. In his prospective study, Onuwe observed a statistically significant difference in pain perception before and after vertebral mobilization.[13] The purpose of this case report was to describe and observe the result of VOP in pain management of a 32-year-old female with lumbar radiculopathy.

PATIENT HISTORY AND SYSTEMS REVIEW

The patient was a 32-year-old black south African. She was a secondary school teacher, and a mother of 2. Her chief complaint was bilateral thigh and leg pain. Her pain was decribed as "burning paresthesia". The patient's Pain was reported to be aggravated by prolonged standing. She also complain of occasional lumbosacral pain, but her major concern was the pain in her lower limb. However, her personal care, sexual activity and sleeping were not affected by her pain. She is now psychologically depressed with her incessant pain, which according to her, has failed to be managed by orthodox medical interventions. She has visited six different medical

doctors in the past six months, i.e…. from January to june 2012. She has had 2 different plain radiographs of the lumbosacral area taken three month and last month respectively. The X-ray was without any pathological findings. At the time patient self-referred herself for physical therapy (precisely 3 weeks ago), she had been living with her lower limb pain for 6-months. Her past medical history was not significant. She had normal delivery and full term pregnancy on both occasion of her delivery, and labor was uneventful. No history of cancer in the family. At the time of presentation, patient was neither hypertensive, nor diabetic, nor pregnant. No active inflammation or infective arthritis. She was taking 400mg Ibuprofen, thrice daily for the management of the pain in both legs.

Goal of physical therapy intervention was to: (1) be pain free, (2) for paresthesia to stop, and (3) not to have any aggravating factor causing her symptoms of pain and paresthesia.

SYSTEMS REVIEW

Four major systems were reviewed, according to the guide. Cardiopulmonary system, CP, the heart rate HR was found to be 72 beats per minute. Blood pressure taking with analog sphygmomanometer and Litman's stethoscope was found to be 115/74mmHg. Respiratory rate was 20bpm. No pedal or peripheral edema was noted. There was full passive range of movement (PROM), and full active range of motion (AROM) of the lumbar spine during forward flexion. Active spinal extension of the lumbar was however, reduced by a difference of 0.5cm. Digital compression pressure (DCT) performed on the spinous processes of first lumbar vertebrae, L1 to fifth lumbar vertebrae, L5 was positive. Paresthesia and numbness was demonstrated on skin area corresponding to dermatome L2-L4 bilaterally. Patient was slightly overweight, with a body mass index (BMI) of 27.8kg/m^2, calculated from a height of 1.64 meters and weight of 75kilograms.

Neuromuscular system: good static and dynamic balance was demonstrated both in standing and seated positions. Deep tendon reflexes tested on both knees with the patella hammer were low. Muscle tone was globally normal. She however demonstrated a low strength on Oxford Muscle scale- a muscle power of 4. There was thermal sensory deficit to hot and cold modalities on dermatome corresponding to L2, L3 and L4.

Integumentary system shows normal skin integrity, normal consistency, and normal skin color. Patient demonstrates good communication ability. She was fully oriented in time, place and person. Her learning style was found to be auditory.

TESTS AND MEASURE

This includes, digital compression test (DCT) on the spinous processes of the first through the fifth lumbar vertebra, L1-L5. This compression test was found to reproduces patients pain.

Vertebral artery insufficiency test was done on both sides of the spine. With the patient in a supine position, the head was aligned at the edge of the bed. The neck was extended, laterally rotated and bend sideways; first to the right and then to the left. Each position was maintained for 60 seconds. There was no dizziness or any complaint from the patient. This suggest a negative outcome for vertebrae artery insufficiency[11].

Visual analog scale (VAS), score= 7, while the Oswetry disability index (ODI) score was 30%.

CLINICAL IMPRESSION #1

Based on the data collected so far on this patient, there was no contraindication to vertical oscillatory pressure (VOP), which include: "pregnancy, osteoporosis, active inflammation, infective arthritis, malignancy, fracture, joint ankylosis, rheumatoid collagen necrosis, and vertebral artery insufficiency"[11,13]. According to a prospective study by Onuwe, he observed a statistically significant difference in pain perception before and after vertebral mobilization in the management of mechanical low back pain[13]. The fact that pharmacological intervention has not helped much in relieving her pain and symptoms warrant a second opinion in terms of physical therapy. Based on the patient's history, systems review, and tests and measure (examination), especially as regards to the sensory and motor deficits on the L2-L4 dermatome, a clinical impression of **Lumbar radiculopathy** was made.

PLAN FOR EXAMINATION

Plan for examination, was to rule out any of the above mentioned contraindication to spinal mobilization. Vertebral artery insufficieny test was carried out on both sides of the spine, and was found to be negative. Brief vertebral distraction was observed to relieve her symptoms. Straight - leg raise (SLR), test assessed in supine position was positive bilaterally, suggesting a neuropathy. Supine SLR was found to be more sensitive for lumbar radiculopathy as compared to SLR in sitting position[15].

EXAMINATION AND CLINICAL IMPRESSION 2

The following tests and measures were used to confirm that the patient is appropriate for vertical oscillatory pressure (VOP); vertebral artery test, digital compression test (DCT), straight leg-raising test (SLR), visual analog scale (VAS), and Oswestry disability index (ODI).

TESTS

Vertebral artery insufficiency test was performed with the patient in the supine position, with the clinician cradling the cranium while seated at the head of the plinth. The cervical spine was slowly extended, rotated, and laterally flexed bilaterally. Each manipulation was held for 30 seconds. Patient was observed for dizziness, nystagmus, and blurred vision. Results were negative indicating that there was no partial or complete occlusion of the vertebral arteries on

both side of the cervical spine[9,11]. Positive findings to the vertebral artery insufficiency test is a contraindication for traction and joint mobilizations[9].

Straight leg-raising was performed with the patient in the supine position. Standard goniometric measurement ensured that the test was completed at 70 degrees hip flexion. The standard plastic goniometer is illustrated in fig. 1. The SLR is arguably the most commonly employed orthopedic test[2].

GONIOMETER

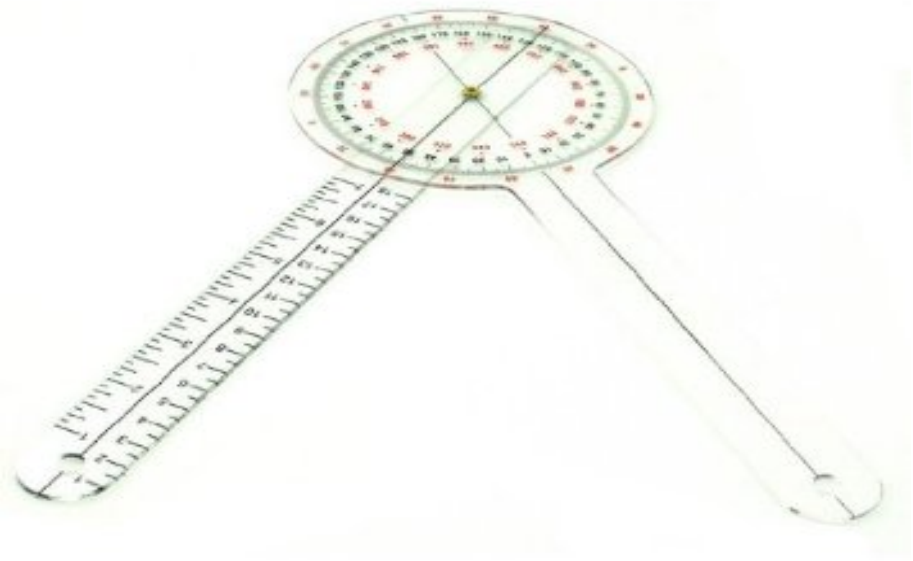

Figure 1.

The stationary arm of the goniometer was placed parallel to the edge of the plinth, while the moving arm was aligned along the lateral midline of, first the right thigh, and the axis was over the greater tronchanter. Patient leg was actively raised, keeping the knee straight, until pain/discomfort was felt along the thigh, buttock and calf. Pain was reported by the patient at an angle of 40 degree. At this point, the ipsilateral ankle was dorsiflexed. There was an additional increase in pain level or discomfort with this manipulation. The SLR or Lasegue's test is said to be positive if the angle at which pain or discomfort is reported by the patient is between 30 degree and 70 degree or if dorsiflexing the foot at pain level increases the pain[2,9,16]. This positive findings implied that there was lumbosacral nerve root irritation. This test is a neural tension test. Because it put a tensile stress on the nerve root and dura matter surrounding the nerve root[16].

Digital compression test (DCT), a provocative test, used for identification of radiculopathy was performed on the spinous processes of the lumbar vertebrae (L1-L5). Pain provocative tests are found by Sheffinger *et al* to be most reliable compared to spinal palpatory procedures in diagnosing etiology of back and neck[17]. There was a reproduction of the lower limb pain at L2-L4 segment. A positive finding to this test is indicative of nerve root irritation.

VISUAL ANALOG SCALE

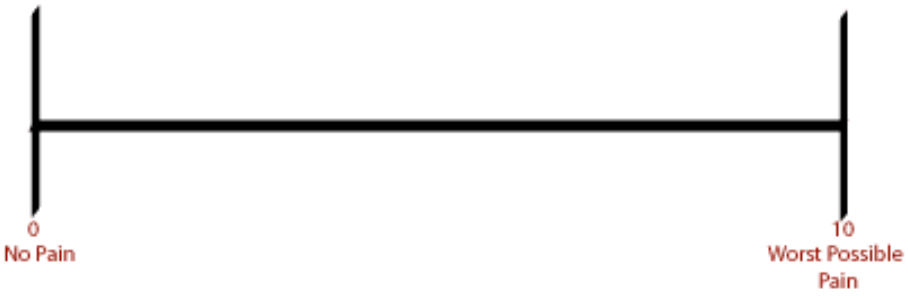

Figure 2.

Figure 2, is a visual analog scale (VAS)[5]. Operationally, this scale is usually 100mm in length, drawn horizontally with word descriptors at each end. It was used subjectively to quantify the patient's pain perception. The patient reported a pain rating of 7 on the visual analog scale indicating severe pain[5].

Oswestry disability index (ODI) was employed to assess the patient's level of disability in terms of activity performance. This measures patient's impairment, and how the pain level/intensity has affected her life. The ODI is refer to as the "gold standard" of low back pain outcome measure[14]. The patient had a total score of 30%. Calculated using the following formula: point total/50 x 100 = % disability[14]. Patient indicated a score of 5 on lifting ability, 5 on social life, and 5 on standing. A percent disability score of 30% on the ODI implies that this patient has moderate disability.

CLINICAL IMPRESSION

The examination data indicate that the patient was appropriate for grade 3 and 4 vertical oscillatory pressure (VOP). No contraindications to joint mobilization were noted in the examination. VOP is also indicated when there is no history of malignancy, osteoporosis, fracture, pregnancy and active inflammation[9]. Patient's clinical presentation and history is consistent with lumbar radiculopathy. As radiculopathy means compression of the spinal nerve root.

It therefore follows that, if the VOP is successful, the radicular symptoms and pain should completely disappear within 2-6 sessions of the intervention.

INTERVENTION OUTCOME AND DISCUSSION

The patient was treated using grade 3 and 4 vertical oscillatory pressure (VOP). VOP is a slow passive oscillatory movement employed to increase joint mobility and decrease pain. My decision was based on the outcome of the tests and measure performed; on the patient's clinical presentations which were consistent with musculoskeletal dysfunction, and on study by Sipila on the rationale for joint mobilization[18].

Patient was positioned on the treatment plinth in prone, adequately draped, with only the back exposed. The lumbar spine was in a closed pack position, i.e. resting position. The treatment plane was perpendicular to the movement. Patient and therapist were relaxed. Using both thumbs, grade 3 VOP was applied to the patient's spinous processes, from L1-L5. Based on surface anatomy, the 10th rib was palpated and 3 vertebral levels below this corresponds to the L1. A large amplitude movement performed up to the limit of the range was applied with a speed of 3-4 thrust per second. An average of 30 seconds was spent on each vertebrae. This mobilization was carried out with the PT standing on a stool in a comfortable height with the upper limbs straighten out. Force was generated from the shoulder down through the thumbs. Grade 4 (small amplitude movement performed at the limit of the range) was applied from L1-L5 with the same frequency, duration and speed.

Patient was concurrently using 400mg Ibuprofen, thrice daily, but has reported no changes in her pain and associated radiculopathy with the use of this pharmacological agent. She had 2-sessions of VOP, with lumbar active range of motion (AROM) exercise as home program.

OUTCOME

Patient was evaluated with the visual analog scale pre and post intervention. As shown in table 1 and table 2,initial assessment indicate a score of 7. After two treatment sessions, at 3 days interval patient scored 0!

Oswetry disability index was found to be 30% before treatment. After treatment it was 5%.

According to a study by Boonstra *et al* on the reliability and validity of the VAS, using a test-retest and cross-sectional design respectively for disability in patients with chronic musculoskeletal pain, it was found that reliability of the VAS for disability is moderate to good[1].

DISCUSSION

Epidemiologically, back pain causes at least 10% of the adult population to consult a physician, physical therapist, or chiropractor each year. Low back pain, was found to be the most common form of back pain and primarily affects people between the age 30 and 70[12]. It therefore follows that adequate skill is needed on the part of the PT's to manage effectively cases of back pain in general, and low back pain in particular. Leininger *et al* reported a moderate evidence of

effectiveness of spinal manipulation for the treatment of lumbar radiculopathy[10]. Similar study by Onuwe[5] found similar result with vertebrae mobilization techniques. Interestingly, in this case report, just 2-session of grade 3 and 4 VOP was able to alleviate the patient's radicular pain completely. Further studies should compare which of the grade 1-4 vertical oscillatory pressure is more effective in treating lumbar radiculopathy as compared to only grade 3 and 4 VOP.

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VISUAL ANALOG SCALE

Table 1.

VAS PRE RX	VAS POST RX
7	0

Table 2.

ODI PRE RX	ODI POST RX
30%	5%

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