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An audit of mother to child HIV transmission rates and neonatal outcomes at a tertiary hospital in South Africa

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2020
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An audit of mother to child HIV transmission rates and neonatal outcomes at a tertiary hospital in South Africa.

MMed (Paediatrics and Child Health)

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APRIL 2019

ACKNOWLEDGEMENTS

I would like to thank my supervisor, Professor Daynia Ballot, for her big heart and her patience, in guiding me diligently through this process. I would also like to thank my co-supervisor, Dr. Tanusha Ramdin. To my husband, Dr. Mohamed Dao, thank you for all of your support. This process would have been much harder without you by my side. I would also like to thank my editor, Karen Gwamba, and last but not least, I would like to acknowledge Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) for their cooperation, and for allowing me access to their database for the purposes of this research.

DECLARATION

I declare that the work presented in this article is authentic and original, unless clearly indicated otherwise; and in such instances, full reference to the source is provided. I do not presume to receive any credit for such acknowledged quotations, and there is no copyright infringement in my work. I declare that no unethical research practices were used or material gained through dishonesty. I also declare that this is my own work and this it has not been submitted for degree purposes at any other institution.

Signed at _____on this _____day of _____20___.

Signature_____

Print name____DR. GHAD BENALI_____

DEDICATION

I would like to dedicate this paper to the three men in my life:

My father, Mr. Ahmed Benali, for believing in me and providing me with the means to pursue my dreams. Your spirit lives on in my heart.

My husband, Dr. Mohamed Dao, for being my rock and always being there for me.

My son, Ali Dao, for the times I couldn't spend with you because of my research, Mummy will always love you.

LIST OF ABBREVIATIONS

ANC	Antenatal care
ARV	Antiretroviral
CD4	T-lymphocyte cell bearing CD4 receptor
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
EMTCT	Early Mother to Child Transmission
HIV	Human Immunodeficiency Virus
MTCT	Mother to Child Transmission
NHLS	National Health Laboratory Service
PCR	Polymerase Chain Reaction
PMTCT	Prevention of Mother to Child Transmission
REDCap	Research Electronic Data Capture

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MMED Paediatric and child health

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Abstract

Background: With nearly half of all HIV infections occurring in women of child bearing age, one of the main challenges surrounding the HIV pandemic is the prevalence of mother to child transmission (MTCT), with the majority of HIV infections in children being as a result of MTCT.

Objective: The aim of this study was to explore the prevalence of congenital HIV infection of neonates at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) between 2015 and 2017, as well as compare the HIV PCR positive and HIV PCR negative neonates, using data from the CMJAH neonatal databases.

Methods: This was a retrospective, cross sectional descriptive study of all neonates admitted to the neonatal unit, between January 2015 and December 2017, at CMJAH. All HIV exposed neonates were included. All neonates who had no HIV PCR test at birth, or, who had indeterminate HIV PCR results, were excluded.

Results: A total number of 1443 HIV exposed neonates was examined for the study period out of a total of 5029 admissions (HIV exposure 25.3%) The study found that the rate of HIV transmission at birth was 2.52%. The majority of infants had low birth weight and were also born prematurely.

Conclusion: HIV transmission is high, despite the introduction of the early mother to child transmission (EMTCT) programme. However, there is no difference between the two groups of neonates under study; except for maternal syphilis, as the study shows a higher rate of infection in neonates with positive HIV PCR.

Keywords: HIV positive mother, HIV exposed neonate, HIV prophylaxis, ANC visit, HIV transmission.

Introduction

Human Immunodeficiency Virus (HIV) disease has been, and continues to be, a health challenge to overcome globally. One of the main challenges with HIV is the high prevalence of HIV infections in mothers and children. Nearly half of all HIV-infected adults are women of child bearing age, and as a result of this, the majority of HIV infections in children are a result of MTCT [1]. According to the Foundation for AIDS Research, 91% of the world's HIV-positive children live in sub-Saharan Africa [1]. The majority of MTCT of HIV takes place during pregnancy and/or delivery; therefore, interventions to prevent mother-to-child transmission are urgently needed to reduce the future incidence of paediatric HIV [2].

The HIV transmission rate has been shown to be twice as high in Africa as in Europe. This difference is not yet fully understood, but contributory factors include: primary HIV infection occurring during pregnancy [3]; lower maternal CD4 count; differences in use of antiretroviral (ARV) drugs (e.g. less extensive availability, lower adherence rates, higher drug abuse rates); differences in virulence of the virus according to geographical origin; co-existence with other sexually transmitted diseases; concomitant infections in the mother; invasive intra-partum procedures (e.g. foetal scalp electrodes and forceps); chorioamnionitis [3]; vaginal delivery; rupture of membranes (especially if delivery is more than four hours after the membranes ruptured); advanced maternal age; lack of prevention of mother-to-child transmission (PMTCT) services; and mixed feeding regimes [4,5]. This shows that the transmission of HIV from mother to child is a multi-factorial event. A number of these factors cannot be controlled or reduced in a meaningful manner in a resource limited setting, but the availability of ARVs and preventative MTCT services are two areas that can be influenced.

The transmission of HIV can be trans-placental during early or late gestation, and the prevalence of trans-placental transmission is high, especially in African countries as compared with global rates [5,6]. A number of researchers have shown a higher mortality rate among babies born to HIV positive mothers, as compared to those born to seronegative mothers [7]. Prematurity, low birth weight, and intrauterine growth retardation, are also higher in HIV exposed infants [7]. HIV Polymerase Chain Reaction (PCR) screening was introduced in South Africa in 2015 as part of the early mother to child transmission (EMTCT) programme. The aim of this study was to review HIV exposed neonates admitted to a tertiary hospital in Johannesburg, South Africa, after the introduction of EMTCT.

Method

This was a retrospective, cross sectional descriptive study conducted in the neonatal unit at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) from 1st of January 2015 to the 31st of December 2017. The study population included all neonates admitted to the neonatal unit during the study period. All HIV exposed neonates were included. All neonates with indeterminate or no HIV PCR results, were excluded. All HIV exposed neonates were screened using a HIV PCR test at birth.

Data Collection

This was a secondary analysis of an existing database. The data of all patients was entered into the neonatal computer database for the purpose of quality control. Data was managed using the Research Electronic Data Capture (REDCap) database [8] and was exported into Excel for data cleaning.

Statistical Analysis

Neonates were divided on the basis of the PCR test into birth HIV positive and negative. Outcome, clinical and demographic data was compared between the two groups.

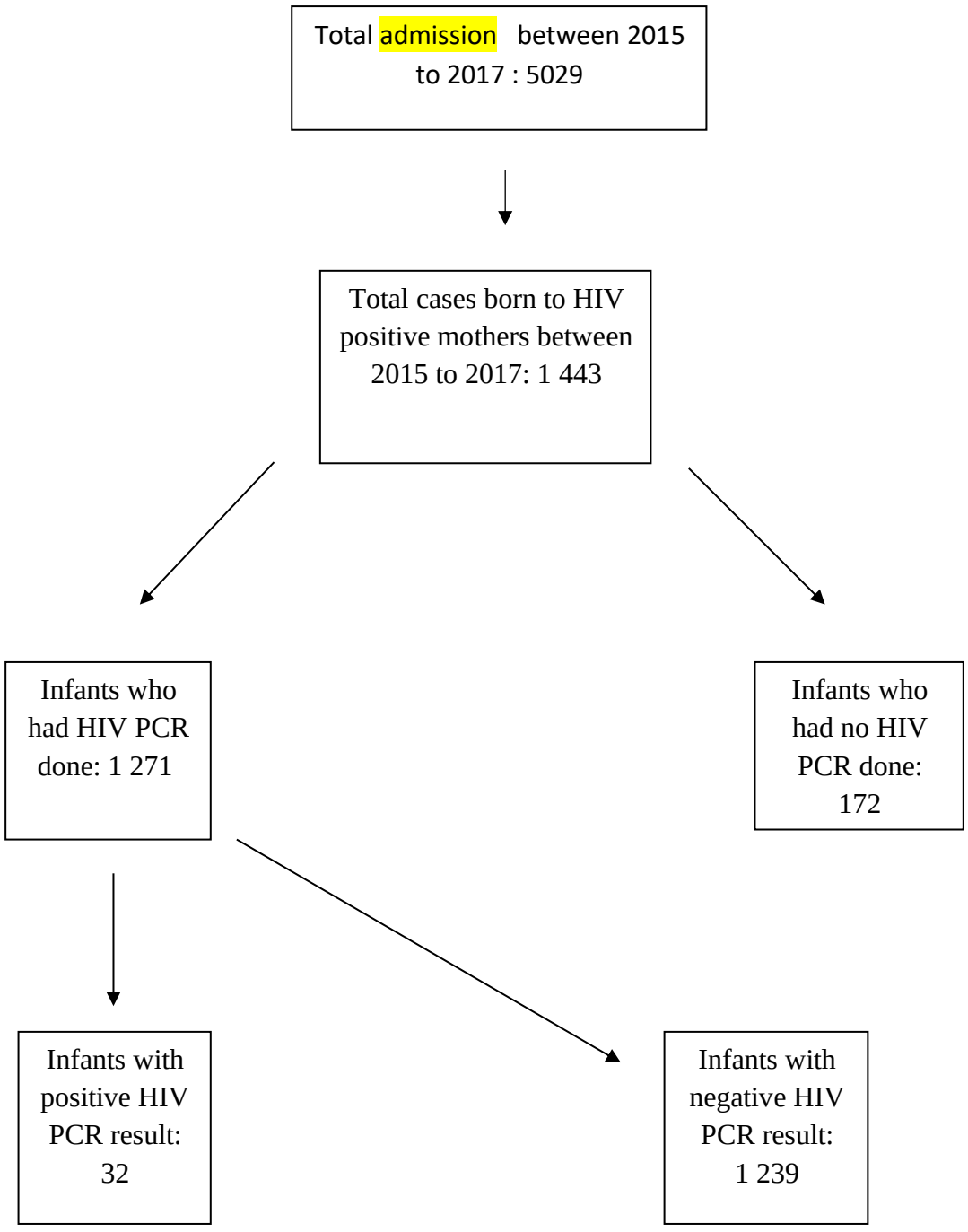
Data was analysed using IBM SPSS 25. Missing values were excluded in the analysis of each variable. Continuous variables, such as birth weight and gestational age, were described using mean and standard deviation, depending on the distribution of the data. On the other hand, categorical variables, such as gender and mode of delivery, were described using percentages.

Categorical variables were compared using Chi Square. Continuous variables were compared using an independent sample t test, as the data was normally distributed. A P value ≤ 0.05 was considered statistically significant.

Results

There were 1 443 HIV exposed neonates who were admitted during the study period. The results were broken down as shown in Figure 1.

Figure 1. Breakdown of Study Sample



From the 1 443 cases, only 1 271 cases had a birth PCR done (88.1%). 172 cases had no PCR documented (11.9%). Overall, HIV transmission at birth was 32/1271 (2.52%).

There were significantly more neonates with congenital HIV born to mothers who had syphilis (p=0.006). There were no major differences in mortality (p=0.408), and there were also no

differences in other aspects such as ANC, maternal chronic illnesses, mode of delivery, major birth defect and neonatal sepsis. See Table 1.

Table 1. Maternal and neonatal characteristics compared betwean HIV PCR positive and negative neonates

Characteristic	HIV PCR Negative	HIV PCR Positive	p Value
Gender			
Male	666/1234 (54.0%)	14/32 (43.8%)	0.252
Antenatal care	957/1136 (84.2%)	21/28 (75.0%)	0.187
Normal Vaginal Delivery	570/1176 (48.5%)	18/29 (62.1%)	0.348
Multiple gestation	162/1227 (13.2%)	3/30 (10.0%)	0.608
Nulliporous	148/1065 (13.9%)	3/27 (11.1%)	0/944
Chorioamnionitis	318/1085 (3.5%)	1/27 (3.7%)	0.955
Maternal hypertension	143/1091 (13.1%)	3/27 (11.1%)	0.761
Maternal Tuberculosis	28/1113 (2.5%)	1/28 (3.6%)	0.726
Maternal Diabetes mellitus	12/1139 (1.1%)	0/32 (0%)	0.578
Maternal syphilis	44/1135 (3.9%)	4/28 (14.3%)	0.006
Resuscitation at birth	307/1239 (24.7%)	9/30 (30.0%)	0.523
Ventilatory support			
CPAP	410/1037 (39.5%)	11/24 (45.8%)	0.533
Mechanical ventilation	207/1039 (19.9%)	3/24 (12.5%)	0.367
Major Birth Defect	77/1224 (6.3%)	1/32 (3.1%)	0.464

Sepsis on or before day 3	55/1211 (4.5%)	1/30 (5.3%)	0.753
Sepsis after day 3	227/1227 (18.5%)	9/32 (28.1%)	0.168
Neonatal Jaundice requiring phototherapy	364/1196 (30.4%)	8/31 (25.8%)	0.586
Necrotising enterocolitis	66/1220 (5.4%)	1/30 (3.3%)	0.618
Hypoxic Ischemic Encephalopathy	79/822 (9.6%)	1/23 (4.3%)	0.395
Died	136/1239 (11.0%)	5/32 (15.6%)	0.408

Unexpectedly, the study also revealed that there were no differences in gestational age, birth weight, length of stay in hospital and the maternal age between the two groups under study. See Table 2.

Table 2. Mean and Standard Deviation of Patients' Characteristics

Characteristic	HIV PCR Negative	HIV PCR Positive	p Value
Gestational age	34.7 weeks (SD 4.1)	32.6 weeks (SD 3.9)	0.786
Birth weight (kg)	2.04kg (SD 0.9)	1.96kg (SD 0.78)	0.615
Length of stay	17.7 days (SD 21.6)	18.7 days (SD 19.9)	0.783
Maternal age (Years)	30.4 yrs (SD 5.9)	30.5 yrs (SD 6.8)	0.128

Discussion

This review of HIV exposed neonates, admitted to a tertiary neonatal unit, after the introduction of EMTCT, found that 2.52% of neonates had congenital HIV. In 2014, the National Health Laboratory Service (NHLS) estimated the rate of transmission to be 1.7% [9]. This shows that the rate of transmission at CMJAH is quite high. However, it should be kept in mind that the study focused only on sick neonates who required admission to the hospital.

Surprisingly, there were no significant differences between HIV PCR positive and HIV PCR negative babies, especially when compared with the high-risk babies and the outcome, which was unexpected.

About three quarters of the mothers attended ANC. Unexpectedly, this attendance was almost the same between the mothers of the HIV PCR positive (75%) and HIV PCR negative (84.2%) babies. However, it is not clear whether those mothers also started visiting the ANC before or after 28 weeks of gestation. This number shows that there is still a large number of mothers who are not aware of the importance of attending the ANC, despite the efforts made by the government and other organizations to educate women.

A large number of mothers had a variety of pre-existing diseases, including hypertension, diabetes mellitus, tuberculosis, syphilis and chorioamnionitis. Unpredictably, there was no increase in the rate of transmission of HIV among those neonates born to the mothers who had these diseases, except in the case of syphilis. The study shows high congenital HIV infection among neonates born to mothers who were infected with HIV and syphilis; which is to be expected as syphilis is a co-morbidity with HIV [10].

In addition, there were no differences in neonatal sepsis, in both cases of early and late sepsis. Early sepsis was shown to be 4.5% in HIV PCR negative neonates, compared to 5.3% in HIV PCR negative neonates (p=753). Late sepsis was 18.5% in HIV PCR negative, while in HIV PCR positive neonates, it was shown to be 28.1% (p=0.168). These high percentages show that both groups are vulnerable to a variety of neonatal infections due to maternal HIV disease [11]. In every instance, a mother passes on her immunity to her baby. However, when the mother's immunity is already low, as in the case of an HIV positive mother, especially with a concurrent disease; the baby's immunity level also becomes compromised, more so because the infant also has HIV disease; hence resulting in increased vulnerability to infection [11].

The majority of the babies under study were born with low weight. This is mainly as a result of the gestational age, as most of the infants were born prematurely. This high number of premature births may be attributed to the HIV status of the mothers. Because HIV is a chronic illness, it contributes to an increased metabolic demand. This may be a contributing factor to a decreased supply of intra-uterine nutrition to the baby; thereby leading to low birth weight [12]. In addition, there was no significant difference in the continuous variables between neonates who were HIV PCR positive at birth, as compared to those who were negative (see Table 2). Of all the neonates under study, 26.6% died, with 15.6% being HIV PCR positive neonates.

Limitations

Since the data being used is from an existing clinical data repository, the variables to be assessed were limited by the data that is routinely collected. The study only considered babies who were admitted. Therefore, the actual transmission rate could not be determined.

There is no way of knowing post discharge mortality rates and complications. Some of the HIV infected neonates may have been discharged directly to their mothers at birth. Therefore, data from these infants was not available.

Also, the VL and CD4 count for the HIV infected mothers was not collected on the database, hence, that was excluded, together with whether the mother is receiving ARV treatment or not.

Conclusion and recommendations

The main focus of the study was to examine the prevalence of HIV transmission from HIV positive mothers to neonates. The research found that 2.52% of babies born are tested positive. This shows a high prevalence of HIV transmission. However, there is no difference between the two groups of neonates, apart from maternal syphilis in mothers of positive HIV PCR neonates.

It should also be considered to add more information to a hospital's database, such as maternal HIV VL, CD4 count, whether they are on ARVs or not, and the timing of ANC visits, in order to enable more in-depth studies regarding HIV transmission. Another aspect to consider is that of the economic statuses of the mothers. In research, this information will aid in determining attribution, in instances such as showing whether low birth weight is as a result of HIV exposure, or poverty.

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Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

- May include up to 6 illustrations or tables.
- A max of 20 - 25references

Structured abstract

- This should be no more than 250words, with the following recommended headings:
  - Background: why the study is being done and how it relates to other published work.
  - Objectives: what the study intends to find out
  - Methods: must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - Results: first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - Conclusion: must be supported by the data, include recommendations for further study/actions.
  - Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
  - Do not include any references in the abstracts.

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting..*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 not 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
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- Manuscript
- Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
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  All manuscripts are reviewed initially by the Editor-in-Chief and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by either one or two reviewers selected on the basis of their expertise in the field. A double blind review process is followed at SAJCH.

  Authors are expected to receive feedback from reviewers and an editorial decision within approximately 6 weeks of submission. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

  Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit

will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion.

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The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
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