KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI

GENDER DIFFERENCES ON THE RISK OF MOTHER TO CHILD TRANSMISSION OF HIV-1 DURING POSTPARTUM PERIOD IN GHANA.

Case Study: Korle-Bu Teaching Hospital, HIV Unit

BY

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DECLARATION

I hereby declare that this submission is my own work towards the award of the MSc. degree and that, to the best of my knowledge, it contains no material previously published by another person nor material which had been accepted for the award of any other degree of the university, except where due acknowledgement had been made in the text.

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DEDICATION

This projected work is dedicated to my dear mother, Madam Evelyn Frempong and brother Nana Kena Frempong and my entire family. And to all babies who through no faults of theirs had been infected with the HIV virus through motherto-child transmission of HIV.

ABSTRACT

This study sought to find the association of some risk factors with the detection of HIV in infants born to HIV positive mothers in Ghana.

A secondary data, from April 2011 to April 2014, from the Korle-Bu Teaching Hospital in Accra was used in this study. The data obtained involved some two thousand and seventy eight (2,078) mothers with clinical and outcome of birth history. For the purpose and interest of this study, only mothers on the PMTCT program were considered and this brought the total number of subjects to 950. Due to inconsistencies and missing information for some data points, some were dropped and this finally brought the total number of observations to 244 infants. The Chi-square test (p-value of 0.7211) showed that the type of delivery does not associate with detection of HIV; the test also showed (p-value of 0.1584) that breastfeeding practices was not associated with the outcome of detection of HIV. Gender of baby and the outcome of the HIV detection were associated (p-value of 0.0184). It was observed that there was an association between breastfeeding and gender of baby. In the final model, gender was significant with a p-value of 0.0198 at 5% level of significance.

From the maximum likelihood estimates, the effect of gender based on the odds ratio estimate was 2.127 with 95% confidence interval between 1.127 and 4.012.

The log-rank test showed border line significant results with (p-value of 0.0495) that there existed a significant time to detection of HIV between female babies and male babies, with male babies showing a shorter duration for HIV positive detection than females in general.

This study concludes that delivery mode and breastfeeding practices are not significant routes through which HIV is transferred from mother to child, for mothers on PMTCT. The study again showed that male babies have almost twice the risk of HIV-1 infection compared to female babies and that the time to positive detection is

shorter for male babies than female babies with a median time to detection of 343 days for male babies.

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CONTENTS

LIST OF ABBREVIATION

AIDS ..... Acquired Immune Deficiency Syndrome

ANC .....Antenatal Care

ARV .....Antiretroviral

ART .....Antiretroviral Therapy CAART

.....Combination Antiretroviral Therapy HAART

.....Highly Active Antiretroviral Therapy

HIV ..... Human Immunodeficiency Virus

IATT .....Interagency Task Team IMPAC .....

Integrated Management of Pregnancy and Childbirth

IHP+ ..... International Health Partnership and Related Initiatives

MCH .....Maternal and Child Health

MDG ..... Millennium Development Goal

MMR .....Maternal Mortality Ratio

MNCH ..... Maternal, Newborn and Child Health MTCT

.....Mother-to-Child Transmission (of HIV)

NGO .....Non Governmental Organizations

PCR ..... Polymerase Chain Reaction PMTCT .....

Prevention of Mother-to-Child Transmission (of HIV)

RH .....Reproductive Health RNA .....Ribonucleic Acids ROM ..... Rapture of Membranes SRH ..... Sexual and Reproductive Health

STI ..... Sexually Transmitted Infection

UN .....United Nations UNAIDS .....Joint United Nations Programme on HIV/AIDS

UNFPA ..... United Nations Population Fund

UNICEF ..... United Nations Children's Fund

WHO ..... World Health Organization

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CHAPTER 1

INTRODUCTION

1.1 Overview

This chapter gives a background of the study, statement of problem, purpose of the study, objectives and hypothesis guiding of the study, methodology and significance of the study.

Limitations and organization of the study is also included in this chapter.

1.2 Background of study

Human Immunodeficiency Virus infection / Acquired Immunodeficiency Syndrome (HIV/AIDS) is a disease of the human immune system caused by infection with Human Immunodeficiency Virus (HIV). The term HIV/AIDS represents the entire range of disease caused by the human immunodeficiency virus from early infection to late stage symptoms. During the initial infection, a person may experience a brief period of influenza-like illness. This is typically followed by a prolonged period without symptoms. As the illness progresses, it interferes more and more with the immune system, making the person much more likely to get infections, including opportunistic infections and tumors that do not usually affect people who have working immune systems.

HIV is transmitted by three main routes: sexual contact, exposure to infected body fluids or tissues, and from mother to child during pregnancy; delivery, or breastfeeding (known as vertical transmission). There is no risk of acquiring HIV if exposed to faeces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomit unless these are contaminated with blood.

In addition to the already existing 1.5 million human immunodeficiency virus (HIV) infected infants of sub-Saharan Africa, many of the infants being born in the region lately are at an additional risk of HIV acquisition through mother to child transmission (MTCT). Paediatric and maternal research have underscored the importance of breastfeeding on the risk of MTCT of HIV according to Ba Olayinka et al. (2000).

The first case of AIDS was reported in Ghana in 1986, since then, there has been a rise in the number of cases. The estimated adult national HIV prevalence in 2009 was 1.9%.The estimated number of persons living with HIV and AIDS in 2009 was 267,069, made up of 154,612 females and 112,457 males giving a female: male ratio of 1.4:1. In the same year, there were 25,666 children living with HIV and an estimated 3,354 children were newly infected. The annual AIDS deaths were 20,313. Sexual spread remains the main mode of transmission accounting for an estimated 80% of all transmissions, Mother-to-child (vertical) transmission accounts for 15% of infections and blood and blood products 5%, according to the Ghana AIDS Commission.

In the 2009 HIV sentinel survey (HSS), the median prevalence of HIV infection among antenatal clinic clients was 2.9%. This constituted a rise from the previous year's prevalence of 2.2%, following two consecutive drops in 2007 and 2008. Trend analysis of ANC HIV prevalence since 2000 shows three peaks in 2003, 2006 and 2009, the lowest being in 2009. The age group with highest prevalence of 4.0% in 2009 was the 40-44 year group. Also in this survey both HIV 1 and 2 were found in the Ghanaian population, with HIV 1 occurring in 91.8%, HIV-2 in 5.2% and dual HIV-1/2 infections in 3.0% of all infections. Aggregate HIV-2 infection therefore was 8.2% compared to the previous year's figure of 5.5%. Again in 2009, an estimated 370,000 children contracted HIV during the perinatal and breastfeeding period, down from 500,000 in 2001. An estimated 2.5 million children around the world are living with HIV/AIDs, according to the Joint United Nations Program on HIV/AIDS (JNAIDS), 2010 Report on the Global AIDS Epidemic.

The response to the epidemic included priority interventions which initially focused on promotion of safe sex, condom use, and improved management of STIs, safe blood

transfusion, infection prevention and control, nursing/clinical care and counselling, home based care and Prevention of Mother-To-Child Transmission (PMTCT). These interventions were geared towards reducing the number of new infections and improving on the quality of life of Persons Living with HIV (PLHIV). Antiretroviral Therapy (ART) has been available in Ghana since June 2003. The number of treatment sites has increased from 2 to over 138, and the cumulative number of people with HIV infection receiving ART was 33,745 as at December 2009. This has contributed significantly to the reduction of HIV-related morbidity and mortality, according to the Ghana AIDS Commission.

1.2.1 TIMING OF MOTHER TO CHILD TRANSMISSION (MTCT)

Mother-to-child transmission is the primary route of HIV infection in children under 15 years of age. Since the beginning of the HIV epidemic, more than 5 million children worldwide have been infected with HIV. Clinical trials in several countries have shown that mother-to-child transmission of HIV can be greatly reduced through administering a short, affordable course of antiretroviral therapy to pregnant women. These trials culminated in a recommendation by UNAIDS and its partners in the Interagency Task Team for the Prevention of Mother-to-Child Transmission that prevention of perinatal transmission should be a part of the standard package of care for HIV-positive women and their children. Moreover, it is quickly becoming clear that mother-to-child transmission prevention programs can enhance communities' understanding of and response to HIV. As a result, governments in Africa, Asia, and Latin America in collaboration with international and nongovernmental organizations have moved rapidly to improve antenatal care and incorporate interventions to prevent mother-to-child transmission of HIV into clinical and community-based care, Nyblade et al., (2001).

Mother-to-child transmission of HIV (MTCT) accounts for more than 90% of pediatric Acquired Immunodeficiency Syndrome (AIDS) cases. Prevention of mother to child transmission (PMTCT) programs has now become a priority both politically and medically worldwide. Most HIV infections in children are passed from mother to child during pregnancy, labor and delivery, or breastfeeding. However, thanks to preventive treatment regimens, the incidence of mother-to-child HIV transmission is decreasing.

HIV transmission from mother to infant can occur antepartum (in utero), intrapartum (during labor or delivery), or postpartum (through breast-feeding), Report of a Consensus Workshop, (1992). Available data suggest that at most 25-30% of perinatal HIV transmission occurs in utero, Rogers et al., (1989);

Ehrnst et al., (1991). The World Health Organization (WHO) and United Nations Programme on HIV/AIDS (UNAIDS) estimated that an additional 370 000 new human immunodeficiency virus type 1 (HIV-1) infections occurred in children in 2009, mainly through mother-to-child transmission (MTCT). Intrapartum transmission contributes to approximately 20–25% of infections, in utero transmission to 5–10% and postnatal transmission to an additional 10–15% of those cases.

Evidence of infection in aborted first trimester fetal tissues has been reported, Sprecher et al., (1986), though potential contamination with maternal blood has not always been excluded. The intrauterine transmission of HIV is also suggested by the occasional isolation of HIV from amniotic fluid and cells. Finally, the isolation of HIV from, or the detection of the HIV genome in, blood samples obtained at birth from some HIV-infected infants also suggests intrauterine HIV transmission, Rogers et al., (1989); Ehrnst et al., (1991).

The proportion of infants infected during each trimester of pregnancy is unknown. Indirect evidence suggests that 70-75% or more of vertical HIV transmission can occur during delivery, Ehrnst et al., (1991); Rogers et al., (1994). Increased risk of vertical HIV transmission has been correlated with increased duration of rupture of the

membranes prior to delivery, particularly in the presence of acute chorioamnionitis, Landesman et al., (1996).

A higher risk of transmission to the firstborn twin, particularly following prolonged labor, Duliege et al., (1995), also supports the concept of intrapartum transmission. The mechanism(s) of intrapartum transmission are unknown, but might include transplacental microtransfusion or infection through mucocutaneous exposure to maternal blood or cervical secretions. The establishment of infection following the inoculation of the simian homolog of HIV (simian immunodeficiency virus) into the conjunctival sac or oropharynx of newborn macaque monkeys also supports the mucocutaneous route of human neonatal infection, Baba et al., (1994).

HIV RNA and proviral DNA have been detected using the polymerase chain reaction (PCR) in breast milk; viral load appears to be particularly high in colostrum, Ruff et al., (1994). Large, prospective cohort studies suggest an increased risk of transmission associated with breast-feeding. In a meta-analysis, Dunn and colleagues (1992) have estimated that the proportion of transmission attributable to breast-feeding worldwide from an HIV-seropositive woman is 14% (95% confidence interval, 7-22%). The risk of breast milk transmission appears to be particularly high when maternal primary infection occurs within the first few months following delivery, Palasanthiran et al., (1993).

1.2.2 POLYMERASE CHAIN REACTION (PCR)

Because infants have maternal antibodies circulating in their bloodstream, an infant's HIV infection status cannot be ascertained by antibody assays. Instead, HIV RNA (Ribonucleic Acid) or DNA PCR (polymerase chain reaction) assays are used to detect HIV infection.

PCR assays quantify the concentration of the HIV-1 virus circulating in the infant's bloodstream and have a lower limit of detection. If circulating viral levels are below a certain limit, the assay produces a false negative result. Since early in infection, viral levels are too low to be detected, and as time progresses viral levels increase to

detectable levels, the assay shows a positive result. Mathematical models tell us that viral levels in untreated individuals increase over time Perelson and Nelson, (1999).

1.2.3 TREATMENT OF INFANTS

As per the WHO recommendations, co-trimoxazole prophylaxis should be given to all HIV-exposed infants and children until HIV infection is excluded and to all HIV-infected infants and children.

1.2.4 DIAGNOSIS OF HIV INFECTION

Early detection of HIV infection is important both for early intervention and optimizing individual therapeutic choices. This would significantly enhance survival and quality of life. Early Infant Diagnosis (EID) via HIV DNA PCR will facilitate early detection of HIV infected infants among all exposed babies for regular follow up and early treatment initiation.

Where virologic tests are not available however, exposed children must be followed up regularly till 18 months when the child's HIV sero-status will be confirmed. A child who tests negative after 18 months is not infected provided breastfeeding has stopped for at least 3 months earlier. In all cases, it is important for clinicians to have a high index of suspicion to clinically detect children who have HIV and AIDS and initiate early management to improve survival.

1.3 Problem Statement

Families and communities around the world hope for healthier babies, it is therefore a problem for an innocent child to be born infected or faced with the chances of being infected with HIV. Mother-to-child transmission (MTCT) of HIV has become a major area of concern since it is the primary route of HIV infection in children under 15 years of age according to the WHO.

Since the onset of the HIV epidemic, more than 5 million children worldwide have been infected with the disease. Each year, over half a million newborns are infected

with HIV in sub-Saharan Africa through MTCT. However, in spite of programs for the prevention of mother-to-child transmission of HIV which includes antenatal HIV testing and counselling, avoiding unintended pregnancy, provision of appropriate antiretroviral (ARV) regimen for mothers and newborns, and support for safer infant feeding options and practices, there is significant infections of HIV for newborns.

Clinical trials in several countries have shown that mother-to-child transmission of HIV can be greatly reduced through administering a short, affordable course of antiretroviral therapy to pregnant women. In the absence of treatment, the chances of HIV passing from mother to child is 15-45 percent. However antiretroviral treatment (ART) and other effective interventions for preventing mother-to-child transmission (PMTC) can reduce the risk below 5 percent according to the WHO.

One of the most promising victories in the battle against AIDS was the finding, in 1994, that administration of the antiretroviral drug zidovudine (known as ZDV, and previously as AZT) during pregnancy and childbirth could reduce the chance that the child of an HIV-positive mother would be infected by about two-thirds, Connor et al., (1994).

The PMTC program and its renewed hope it brings that MTCT can be eradicated at some point in time has seen many prospective mothers join despite the social stigma that accompanies it. This even led the WHO to launch a global plan in 2011 to reduce the number of new infections via MTCT by 90 percent in 2015.

With the advancements in drugs and treatment of HIV/AIDS to ensure that an AIDS free generation is possible, it has become necessary to ensure that newly born babies are HIV free or face a very low risk of acquiring HIV from mothers. However mother-to-child transmission continues to be a problem since it remains a significant route of HIV infections in children under 15 years of age.

1.4 Objectives Of Study

- To determine the association of breastfeeding practices and HIV detection of infants through MTCT.
- To determine the association of delivery mode and HIV detection of infants through MTCT.
- To determine the effect(s) of sex on the probability of mother-to-child transmission of HIV
- To determine which of the sex groups has a better surviving rate to infection of HIV-1.

CHAPTER 2

LITERATURE REVIEW

In an attempt to investigate gender-specific risks of mother-to-child transmission (MTCT) at birth and at 6 to 8 weeks among infants born to HIV-infected African women, (Taha TE et al., 2005) reported that the rate of HIV transmission at birth was 9.5% (187 of 1964 infants). However, at birth significantly more girls (12.6%) than boys (6.3%) were infected with HIV. This association remained significant after controlling for maternal viral load and other factors. Among infants who were uninfected at birth, 8.7% (135 of 1554 infants) acquired HIV by 6 to 8 weeks; of these infants, more girls acquired HIV (10.0%), compared with boys (7.4%). This led to a conclusion that female infants may be more susceptible to HIV infection before birth and continuing after birth. Alternatively, in utero mortality rates of HIV-infected male infants may be disproportionately higher and thus more HIV-infected female infants are born. In areas of sub-Saharan Africa, where HIV infection rates are high among women of reproductive age, the magnitude of the gender transmission differences observed in this study could have clinical, preventive, and demographic implications.

Biggar et al. 2006, analyzed mother-to-child HIV transmission rates by sex and exposure time for babies born to HIV-infected and untreated African women. Data were analyzed from 2 independent studies done in Malawi during the 1990s. Infections were established by polymerase chain reaction on blood samples. Odds ratios (ORs) for transmission were examined by period at risk: in utero (infected in umbilical cord blood), perinatal (infected in 1st postnatal blood Q4 weeks), and postnatal (later postnatal infection). Among 1394 singleton births, girls were more likely to become infected than boys. For in utero transmission, the OR was 1.4 (95% CI: 0.9 to 2.2). For transmission during early life (umbilical cord blood not available) the OR was 2.7 (95% CI: 1.5 to 4.9). However, transmission risks in the perinatal and postnatal infection periods did not differ in boys and girls. Among 303 tested twin-birth pairs, girls were at higher risk than boys for in utero (OR: 2.6; 95% CI: 1.2 to 5.8) and perinatal (OR: 1.9; 95% CI: 1.0 to 3.7) infection. Recognized mother-to-child transmission risk factors did not explain the higher risk of infection in girls. They therefore concluded that girls were at higher risk of early (in utero and perinatal) HIV infection than boys. To assess gender differences in the risk of mother-to-child transmission (MTCT) of HIV, Brahmbhatt et al., (2008), conducted a study where HIV-positive mothers were identified from a population cohort followed from 1994 to 2000. HIV infection in mothers was detected using two independent enzyme immunoassays and infant HIV infection was diagnosed using RNA- polymerase chain reaction. Birth weight was determined by anthropometry. Logistic regression was used to assess the univariate and multivariate risk factors of MTCT. Approximately 16% of 371 infants were HIV-positive in the in-utero and intrapartum periods and an additional 16% were infected via breastfeeding. Female infants were significantly more likely to be HIV infected perinatally compared with male infants (20.8% vs. 12.4%, respectively, P = 0.035), but there was no significant sex differences in postnatal risk of MTCT. In adjusted analyses, among mothers with higher than median HIV viral loads, there was no significant difference in the risk of MTCT by gender, but among mothers with lower than median HIV viral loads, female infants were

significantly more likely to be HIV infected (odds ratio = 4.1, confidence interval = 1.04-16.1). Low birth weight was more frequent in female than male infants born to HIV-positive mothers. Female infants could be more susceptible to HIV infection in the in-utero and peripartum period compared with male infants. Alternatively, this sex association could be due to higher in-utero mortality rates of male infants or to increased susceptibility of female infants. In a study of infants born to HIV-infected women in South Africa, (Coutsoudis and colleagues, 2000), found that HIV infection was detected at 6months in identical proportions of exclusively breastfed infants (19%) and never breastfed infants (19%), and that infants who received mixed feeding had a higher rate of infection (26%). By 15 months, the infection rate was higher in exclusively breastfed children than in never-breastfed children, and the rate remained highest in children who received mixed feeding. Data on Rapture of Membranes (ROM) duration and infant's HIV status was available for 1973 pregnancies.

In a study to investigate the impact of rapture of membranes(ROM) duration on mother-to-child transmission(MTCT) rates in the combination antiretroviral therapy (cART) era, data on rapture of membranes (ROM) duration and infant's HIV status was available for 1973 pregnancies. The MTCT rate was 0.3% (6/1973), with no evidence of an association with ROM (≥4 vs <4 hours) overall, among term deliveries (≥37 weeks), or term deliveries with viral load <1000 copies/ml. There was only one transmission in 237 preterm deliveries; this was also the only transmission among the 97 deliveries where ROM was ≥24. However, Studies from the pre-cART era showed an association between duration of rupture of membranes (ROM) and mother-to-child transmission (MTCT), (Townsend et. al, 2014).

Two patterns of HIV-1 MTCT now exist. In industrialized nations, dramatic declines in perinatal HIV infections were observed after integration of prenatal HIV counseling and testing into prenatal care and widespread implementation of ARV prophylaxis. Reducing the MTCT rate to below 1% appears within reach. By contrast, many resource-poor countries face a perinatal HIV epidemic as a result of increasingly

devastating levels of HIV infection, a crumbling maternal and child health care infrastructure, and limited HIV counseling and testing programs. Clinical trials and observational epidemiologic studies conducted in the developing and the developed world are leading to the development of practical, affordable, and innovative approaches to reduce infant HIV infections worldwide, including in populations where prolonged breastfeeding is currently the norm, Bulterys et al., (2002). Also in their study, in the absence of ARV prophylaxis, the risk of MTCT of HIV-1 appears to have decreased in a number of locations around the world. Early reports from case studies in the United States, for instance, from Miami, Florida, estimated the MTCT rate to be as high as 50% to 65%. However, these early studies focused on HIV-infected women identified because of obvious clinical symptoms or the prior birth of a child with AIDS. Relatively high HIV-1 MTCT rates (40% to 48%) were also reported in several early cohort studies from Africa and India. In most locations where multiple prospective cohort studies have been conducted over time (e.g., France, Kenya, Malawi, Rwanda, South Africa, Thailand, and the United States), a decreasing trend appears evident, with the highest MTCT rate recorded during the early years of the HIV-1 epidemic.

Petraro et. al, 2014 found that out of 795 HIV-infected Tanzanian women with singleton newborns, the proportion of women breastfeeding declined from 95% at 12 months to 11% at 24 months. The multivariate analysis showed breastfeeding cessation was significantly associated with increasing calendar year of delivery from 1995 to 1997 [risk ratio (RR), 1.36; 95% confidence interval (CI) 1.131.63], having a new pregnancy (RR 1.33; 95% CI 1.10-1.61), overweight [body mass index (BMI) ≥25 kg m(-2) ; RR 1.37; 95% CI 1.07-1.75], underweight (BMI <18.5kg m(-2) ; RR 1.29; 95% CI 1.00-1.65), introduction of cow's milk at infant's age of 4 months (RR 1.30; 95% CI 1.04-1.63). Material and social support was associated with decreased likelihood of cessation (RR 0.83; 95% CI 0.681.02). Demographic, health and nutritional factors among women and infants are associated with decisions by HIV-infected women to cease breastfeeding. The impact of breastfeeding counselling programs for HIV-

infected African women should consider individual maternal, social and health contexts.

To determine the predictors of breastfeeding cessation among HIV-infected women in Southern Ethiopia, Demewoz et al. (2014), found out that the mean duration of breastfeeding among HIV positive mothers was 13.79 [95% CI: (12.97-14.59)] months. The Kaplan-Meier estimate showed that proportions of women who were breastfeeding at 6, 9, 12 and 17 months were 89.3%, 75.3%, 66% and 17%, respectively. Those mothers having a monthly income of *leq*500 ETB [AHR = 0.16, 95% CI :(0.03-0.76)], having a family size of three and below [AHR = 0.12, 95%CI: (0.02-0.68), four and above [AHR = 0.07, 95%CI: (0.01-0.35)] and bottle feeding [AHR = 3.95, 95%CI: (1.64-9.51)] were also independent factors associated with breastfeeding cessation and thus concluded that Above one third of HIV positive mothers stopped breastfeeding before 12 months. Monthly income, bottle feeding and family size were the independent predictors of breastfeeding cessations. Strengthening the current counseling and promotion modality on avoidance of bottle feeding and continued breastfeeding is recommended for improved HIV free survival.

A systematic review to assess the effect of integrated perinatal prevention of mother-to-child transmission of HIV interventions compared to non- or partially integrated services on the uptake in low- and middle-income countries showed that, a cluster randomized controlled trial reported higher probability of nevirapine uptake at the labor wards implementing HIV testing and structured nevirapine adherence assessment (RRR 1.37, bootstrapped 95% CI, 1.04-1.77). A stepped wedge design study showed marked improvement in antiretroviral therapy (ART) enrolment (44.4% versus 25.3%, p<0.001) and initiation (32.9% versus 14.4%, p<0.001) in integrated care, but the median gestational age of ART initiation (27.1 versus 27.7 weeks, p = 0.4), ART duration (10.8 versus 10.0 weeks, p = 0.3) or 90 days ART retention (87.8% versus 91.3%, p = 0.3) did not differ significantly. A cohort study reported no significant difference either in the ART coverage (55% versus 48% versus 47%, p = 0.29) or eight weeks of ART duration before the delivery (50% versus 42% versus 52%;

p = 0.96) between integrated, proximal and distal partially integrated care. Two before and after studies assessed the impact of integration on HIV testing uptake in antenatal care. The first study reported that significantly more women received information on PMTCT (92% versus 77%, p<0.001), were tested (76% versus 62%, p<0.001) and learned their HIV status (66% versus 55%, p<0.001) after integration. The second study also reported significant increase in HIV testing uptake after integration (98.8% versus 52.6%, p<0.001) and a conclusion was then made that limited, non-generalizable evidence supports the effectiveness of integrated PMTCT programs and as such more research measuring coverage and other relevant outcomes is urgently needed to inform the design of services delivering PMTCT programs, Car et al., (2012).

A substantial proportion of perinatally acquired infections with the human immunodeficiency virus type 1 (HIV-1) occur at or near delivery, which suggests that obstetrical factors may have an important influence on transmission. An evaluation of the relation of such factors and other variables to the perinatal transmission of HIV-1revealed that, among mothers with membranes that ruptured more than four hours before delivery, the rate of transmission of HIV-1 to the infants was 25 percent, as compared with 14 percent among mothers with membranes that ruptured four hours or less before delivery. In a multivariate analysis, the presence of ruptured membranes for more than four hours nearly doubled the risk of transmission (odds ratio, 1.82; 95 percent confidence interval, 1.10 to 3.00; P = 0.02), regardless of the mode of delivery. The other maternal factors independently associated with transmission were illicit-drug use during pregnancy (odds ratio, 1.90; 95 percent confidence interval, 1.14 to 3.16; P = 0.01), low antenatal CD4+ lymphocyte count (<29 percent of total lymphocytes) (odds ratio, 2.82; 1.67 to 4.76; P<0.001), and birth weight <2500 g (odds ratio, 1.86; 1.03 to 3.34; P = 0.04). This led to a conclusion that the risk of transmission of HIV-1 from mother to infant increases when the fetal membranes rupture more than four hours before delivery, Landesman et al, (1996).

Garcia et al., (1999) in a study of the relation of maternal plasma HIV-1 RNA levels to the risk of perinatal transmission and the timing of transmission showed that Increasing geometric mean levels of plasma HIV-1 RNA were associated with increasing rates of transmission: the rate was 0 percent among women with less than 1000 copies per milliliter (0 of 57), 16.6 percent among women with 1000 to 10,000 copies per milliliter (32 of 193), 21.3 percent among women with 10,001 to 50,000 copies per milliliter (39 of 183), 30.9 percent among women with 50,001 to 100,000 copies per milliliter (17 of 55), and 40.6 percent among women with more than 100,000 copies per milliliter (26 of 64) (P<0.001). The treatment status of one woman was unknown. The highest rate of transmission was among women whose plasma HIV-1 RNA levels exceeded 100,000 copies per milliliter and who had not received zidovudine (19 of 30 women, 63.3 percent). Neither higher HIV-1 RNA levels early in pregnancy nor higher levels late in pregnancy were associated with the timing of infection in the infants. And then lead to a conclusion that, in pregnant women with HIV-1 infection the level of plasma HIV-1 RNA predicts the risk but not the timing of transmission of HIV-1 to their infants.

A number of 645 mothers were enrolled to a study where 313 were assigned 200 mg at labour onset and 2mg/kg for babies within 72 h of birth; regimen A or zidovudine, 313 were assigned 600 mg orally at labour onset and 300 mg every 3 h until delivery, and 4 mg/kg orally twice daily for babies for 7 days, regimen B or nevirapine and 19 placebo. Eight mothers were lost to follow-up before delivery. The following findings were made: 99% of babies were breastfed (median duration 9 months). Estimated risks of HIV-1 transmission in the zidovudine and nevirapine groups were 10.3% and 8.1% at birth (p=0.35); 20.0% and 11.8% by age 6-8 weeks (p=0.0063); 22.1% and 13.5% by age 14-16 weeks (p=0.0064); and 25.8% and 15.7% by age 18 months (p=0.0023). Nevirapine was associated with a 41% (95% CI 16-59) reduction in relative risk of transmission through to age 18 months. Both regimens were well-tolerated with few serious side-effects. These findings led to the interpretation that Intrapartum/neonatal nevirapine significantly lowered HIV-1 transmission risk in a

breastfeeding population in Uganda compared with a short intrapartum/neonatal zidovudine regimen. The absolute 8.2% reduction in transmission at 6-8 weeks was sustained at age 18 months (10.1% [95% CI 3.5-16.6]). This simple, inexpensive, well-tolerated regimen has the potential to significantly decrease HIV-1 perinatal transmission in less-developed countries, Jackson, (2003).

Another study that was restricted to live births among women not on ART at conception but receiving antenatal HAART. The risk of detectable viral load at delivery was compared to mother-to-child transmission in two pregnancy groups: 'ART-naive' and 'HAART-experienced' (≥7 days of HAART during previous pregnancy). Multivariable analyses conducted using logistic regression showed that out of 5,372 pregnancies in the ART-naive group and 605 in the HAARTexperienced group, there was weak evidence of an increased risk of detectable viral load in the HAART-experienced group (adjusted odds ratio [aOR] 1.27; 95% CI 1.01, 1.60); however, the increased risk was apparent only among women who previously received non-nucleoside reverse transcriptase inhibitor-based HAART (aOR 1.81; 95% CI 1.25, 2.63), and not among those with previous proteaseinhibitor-based HAART exposure (aOR 1.08; 95% CI 0.81, 1.45). There was no difference in mother-to-child transmission risk between the ART-naive and HAART-experienced groups (aOR 0.42; 95% CI 0.10, 1.78), although the number of transmissions was small. In conclusion, it was found that there was no increased risk of detectable viral load at delivery among women exposed to shortcourse, protease-inhibitor-based HAART during a previous pregnancy. However, women with prior exposure to non-nucleoside reverse transcriptase inhibitorbased HAART appeared to be at increased risk of not adequately suppressing the virus. These findings highlight the need for careful management of HIVinfected women presenting with repeat pregnancies, French et al., (2012).

Women with HIV-1 infection who were breast-feeding infants were enrolled in a randomized, phase 3 trial in Blantyre, Malawi. In this study, the infants were randomly assigned to one of three regimens at birth: single-dose nevirapine plus 1

week of zidovudine (control regimen) or the control regimen plus daily extended prophylaxis either with nevirapine (extended nevirapine) or with nevirapine plus zidovudine (extended dual prophylaxis) until the age of 14 weeks. Using KaplanMeier analyses, we assessed the risk of HIV-1 infection among infants who were HIV-1-negative on DNA polymerase-chain-reaction assay at birth. Among 3016 infants in the study, the control group had consistently higher rates of HIV-1 infection from the age of 6 weeks through 18 months. At 9 months, the estimated rate of HIV-1 infection (the primary end point) was 10.6% in the control group, as compared with 5.2% in the extended-nevirapine group (P<0.001) and 6.4% in the extended-dual-prophylaxis group (P=0.002). There were no significant differences between the two extended-prophylaxis groups. The frequency of breast-feeding did not differ significantly among the study groups. Infants receiving extended dual prophylaxis had a significant increase in the number of adverse events (primarily neutropenia) that were deemed to be possibly related to a study drug. This led to the conclusion that extended prophylaxis with nevirapine or with nevirapine and zidovudine for the first 14 weeks of life significantly reduced postnatal HIV-1 infection in 9-month-old infants. Kumwenda, (2008).

In a study to assess risk and predictors of HIV transmission among HIV-exposed infants on follow up at a PMTCT clinic in a referral hospital, a total of 509 infant records were included in the analysis. The median age of infants at enrolment to follow up was 6 weeks (inter quartile range [IQR] = 2 weeks). A total of 51(10%, 95% CI: 7.8% - 13%) infants were infected with HIV. Late enrolment to the exposed infant follow up clinic (Adjusted Odds Ratio [AOR] = 2.89, 95% CI:1.35, 6.21), rural residence (AOR = 5.05, 95% CI: 2.34, 10.9), home delivery (AOR = 2.82, 95% CI: 1.2, 6.64), absence of maternal PMTCT interventions

(AOR = 5.02, 95% CI: 2.43, 10.4) and mixed infant feeding practices (AOR = 4.18, 95% CI: 1.59, 10.99) were significantly and independently associated with maternal to child transmission of HIV in this study. It was then concluded that there is a high risk of MTCT of HIV among exposed infants on follow up at the PMTCT clinic of the

University of Gondar referral hospital. The findings of this study will provide valuable information for policy makers to enhance commitment and support for rural settings in the PMTCT scaling-up program, Digsu Negese et al., (2013).

In another study in KwaZulu Nata, South Africa, of the 1,034 exclusively breastfed infants for whom HIV test results were available, 175 were diagnosed as HIVpositive before six months of age; survival analysis found cumulative infection rates of 14% by six weeks and 20% by six months. Four percent of breast-fed infants who were uninfected at six weeks of age were infected by six months. Among exclusively breast-fed infants, estimated mortality at three months was 6%; among the infants given replacement feeding from birth, estimated mortality at three months was 15%.Infants who received mixed feeding during their first six months were at higher risk of HIV infection than those who had breast-fed exclusively (hazard ratio, 10.9). Among the latter infants, transmission risk was associated with maternal CD4 cell counts: In a multi-variate analysis, those whose mothers had counts of fewer than 200 cells or 200-500 cells per microliter had a higher risk of HIV infection (3.8 and 2.4, respectively) than those whose mothers had counts of more than 500 cells per microliter. Other factors associated with an elevated risk of infection were having a mother aged 20-30 versus one younger than 20 (1.9), having a birth weight of less than 2,500 g versus a weight of more than 3,500 g (1.8) and being born after labor that lasted more than 12 hours versus less than four hours (2.2). In contrast, infants delivered by cesarean section rather than vaginally had a lower risk of infection (0.5).Among infants who had breast-fed exclusively, the risk of not surviving HIV-free for six months after birth was similar to the risk of infection. Those whose mothers had counts of fewer than 200 cells or 200-500 cells per microliter had a higher risk of not surviving HIV-free (hazard ratios, 4.0 and 2.3, respectively) than those whose mothers had counts of more than 500 cells per microliter. An elevated risk was also found for infants whose mothers were aged 20-30 (1.5), who had a birth weight of less than 2,500 g (1.9) and who were born following labor that lasted more than 12 hours (2.3). Infants delivered by cesarean section were at lower risk of not surviving

HIV-free for six months than those delivered vaginally (0.5).According to the researchers, their findings on mother-to-child transmission of HIV confirm that exclusive breast-feeding is safer for infants of HIV-positive women than mixed feeding for the first six months after birth. Furthermore, the researchers believe that these findings "warrant revision of the present UNICEF, WHO, and UNAIDS infant feeding-guidelines," which recommend that HIV-infected women feed their infants commercial or home-prepared formula rather than breast milk when possible, Coovadia et al., (2007).

In another study to determine the magnitude of the contribution of infant feeding practices on the risk of mother to child transmission (MTCT) of the HIV-1 infection in Zimbabwe ,it was found that the incidence of HIV-1 through MTCT was greatest among breastfed (8.33 per 100 child-months) and mixed fed (8.64 per 100 child-months) infants by 3 months. After adjustment for maternal age, marital status, education and infant antibody HIV-1 status, the cumulative relative risk of MTCT of HIV-1 was 4.19 (95% confidence interval (CI) 3.44, 5.09) among breastfed and 1.10 (95% CI 0.97, 1.25) among mixed fed infants. The overall MTCT rate of HIV-1 in this study was 40.3%. Hence leading to a conclusion that breastfed infants had the greatest cumulative relative risk of MTCT of HIV-1, followed by mixed fed infants, with the highest incidences occurring within the first 3 months, Olayinka et al., (2000).

Chaimay et al., ()2013, in a study to investigate clinical risk factors of survival among HIV-infected children born to HIV-infected mothers in the Southern region of Thailand, data from routine prospective cohort studies between 1990 and 2010 were analyzed. In these studies, 1,549 HIV-infected children born to HIVinfected mothers were enrolled at birth and followed longitudinally. Information on demographic, clinical manifestations, and HIV-infection status factors was collected and Survival analysis was used to determine risk factors associated with mortality. Results found that one-fourth of HIV-infected children died (434, 28.02%) during the follow-up period. The follow-up available equals to 135,295 person-months. The incidence rate was 1.03 times per 100 person-months (95% CI: 0.97 to 1.08). The median survival

time among HIV-infected children from diagnosis to death was 87.34 months (95% CI: 87.32 to 87.36). HIV-infected children were diagnosed to confirm as AIDS (88. 44%) and symptomatic HIV positive (11.56%). Clinical risk factors on survival among HIV-infected children were found HIV-infected children were more likely to die if they were infected with candidiasis (HR: 1.47, 95% CI: 1.07 to 2.00), Mycobacterium tuberculosis (HR: 1.51, 95% CI: 1.26 to 1.81), and Pneumocystis jiroveci (HR: 1.50, 95% CI: 1.27 to 1.76) as compared to HIV-infected children without clinical manifestation. The study concluded that mortality among infected children born to HIV-positive mothers is high in the Southern region of Thailand Consequently, health service system related to prevent mother-to-child HIV-transmission is needed to improve child survival.

CHAPTER 3

METHODOLOGY

3.1 Introduction

This chapter describes the theory of models to be used, formulations and methods of analyzing the available data to satisfy the objectives of this study. The main methods employed in analyzing the data in this study are the logistic regression and survival analysis.

3.2 Likelihood - Ratio Statistic

It is an alternative test statistic for testing Ho for independence. The test determines the parameter values that maximize the likelihood function under the assumption that H_o is true. It also determines the values that maximize it under the more general condition that H_o may or may not be true. In statistics, a likelihood ratio test is done to compare the fit of two models based on the ratio of the maximized likelihoods which expresses how many times more likely the data fits one model than the other as follows:

$$\Lambda = \frac{\text{maximum likelihood when parameters satisfty } H_o}{\text{maximum likelihood when parameters are unrestricted}} \quad (3.1)$$

Properties of Λ

- Λ cannot exceed 1.
- Λ far below 1 indicates that the maximum likelihood is much larger when the parameters are not forced to satisfy H_o. Therefore it indicates strong evidence against H_o.

The likelihood ratio statistic equals: $-2\log(\Lambda)$ and is Non-negative and "Small" values of Λ yield "large" values of $-2\log(\Lambda)$.

The Likelihood-ratio statistic for a two-way contingency table is given as:

$$G^2 = 2\sum_{i=1}^{I}\sum_{j=1}^{J} O_{ij}\log\left(\frac{O_{ij}}{E_{ij}}\right) \quad (3.2)$$

And has a Minimum value of 0 when all $O_{ij} = E_{ij}$. Larger values of G^2 provide stronger evidence against H_o with approximate chi-squared sampling distribution with $df = (I - 1)(J - 1)$.

Although the Wald test is adequate for large samples, the likelihood-ratio test is more powerful and more reliable for sample sizes often used in practice. The test statistic compares the maximum L_o of the log-likelihood function when $\beta = 0$ (i.e. when $\pi(x)$ is forced to be identical at all x values) to the maximum L_1 of the log-likelihood function for unrestricted β. The test statistic,

$$G^2 = -2(L_0 - L_1)$$

also has a large-sample chi-squared null distribution with $df = 1$. Most software for logistic regression reports the maximized log-likelihoods L_0 and L_1 and the likelihood-ratio statistic derived from those maxima.

3.3 Chi-Square Test

The chi-squared test is used under the following conditions:

- When the two variables are independent of each other
- When the distribution of the sample is binomial, normal or other. That is the chi-squared becomes more appropriate when the expected value for each cell exceeds five(5)

- When the variable under study is categorical. The Pearson chi-squared statistic for testing H_o is

$$\chi^2 = \sum_{i=1}^{I}\sum_{j=1}^{J}\frac{(O_{ij}-E_{ij})^2}{E_{ij}}$$

where O_{ij} is the observed cell count and E_{ij} is the estimated expected count under the null hypothesis in the $ij-th$ cell of a (IxJ) table than two outcomes are possible. The chi-squared is specified by its degrees of freedom (df) with Mean of chi-squared distribution =df and Variance of chi-squared distribution = $2df$, it is Defined only for nonnegative values and Skewed to the right but becomes more "bell-shaped" and concentrated around larger values, as df increases.

3.4 Binary Logistic Regression Model

3.4.1 Components of a GLM

All generalized linear models have three components: The random component identifies the response variable Y and assumes a probability distribution for it. The systematic component specifies the explanatory variables for the model. The link function specifies a function of the expected value (mean) of Y , which the GLM relates to the explanatory variables through a prediction equation having linear form.

3.4.2 Random Component

The random component of a GLM identifies the response variable Y and selects a probability distribution for it. Denote the observations on Y by $(Y_1,Y_2,\cdots,Y_n)$. Standard GLMs treat $(Y_1,Y_2,\cdots,Y_n)$ as independent. In many applications, the observations on Y are binary, such as "success" or "failure." More generally, each Y_i might be the number of successes out of a certain fixed number of trials. In either case, we assume a binomial distribution for Y . In some applications, each observation is a count. We

might then assume a distribution for Y that applies to all the nonnegative integers, such as the Poisson or negative binomial. If each observation is continuous, such as a subject's weight in a dietary study, we might assume a normal distribution for Y.

3.4.3 Systematic Component

The systematic component of a GLM specifies the explanatory variables. These enter linearly as predictors on the right-hand side of the model equation. That is, the systematic component specifies the variables that are the $\{x_j\}$ in the formula

$$\alpha + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k \tag{3.3}$$

This linear combination of the explanatory variables is called the linear predictor. Some $\{x_j\}$ can be based on others in the model. For example, perhaps $x_3 = x_1 x_2$, to allow interaction between x_1 and x_2 in their effects on Y, or perhaps $x_3 = x_2$, to allow a curvilinear effect of x. (GLMs use lower case for each x to emphasize that x-values are treated as fixed rather than as a random variable.)

3.4.4 Link Function

Denote the expected value of Y, the mean of its probability distribution, by $\mu = E(Y)$. The third component of a GLM, the link function, specifies a function $g(\mu)$ that relates μ to the linear predictor as

$$g(\mu) = \alpha + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k \tag{3.4}$$

The function $g(\mu)$, the link function, connects the random and systematic components.

3.4.5 Normal GLM

Ordinary regression models for continuous responses are special cases of GLMs. They assume a normal distribution for Y and model its mean directly, using the identity link function, $g(\mu) = \mu$. A GLM generalizes ordinary regression models in two ways: First, it allows Y to have a distribution other than the normal. Second, it allows modeling some function of the mean. Both generalizations are important for categorical data. Historically, early analyses of nonnormal responses often attempted to transform Y so it is approximately normal, with constant variance. Then, ordinary regression methods using least squares are applicable. In practice, this is difficult to do. With the theory and methodology of GLMs, it is unnecessary to transform data so that methods for normal responses apply. This is because the GLM fitting process uses ML methods for our choice of random component, and we are not restricted to normality for that choice. The GLM choice of link function is separate from the choice of random component. It is not chosen to produce normality or stabilize the variance.

3.4.6 GLM for Binary Data

Many categorical response variables have only two categories: for example, whether you take public transportation today (yes, no), or whether you have had a physical exam in the past year (yes, no). Denote a binary response variable by Y and its two possible outcomes by 1 ("success") and 0 ("failure").

The distribution of Y is specified by probabilities $P(Y = 1) = \pi$ of success and $P(Y = 0) = (1 - \pi)$ of failure. Its mean is $E(Y) = \pi$. For n independent observations, the number of successes has the binomial distribution specified by the index n and parameter π. Each binary observation is a binomial variate with

$n = 1$.

We introduce GLMs for binary responses. Although GLMs can have multiple explanatory variables, for simplicity we introduce them using a single x. The value of

π can vary as the value of x changes, and we replace π by $\pi(x)$ when we want to describe its dependence on that value.

3.4.7 Logistic Regression Model

According to the Agresti (2002), the relationships between $\pi(x)$ and x are usually nonlinear rather than linear. A fixed change in x may have less impact when π is near 0 or 1 than when π is near the middle of its range. In practice, $\pi(x)$ often either increases continuously or decreases continuously as x increases.

The logistic regression or logit model takes the following form:

$$\log\left(\frac{\pi(x)}{1-\pi(x)}\right) = \text{logit}(\pi(x)) = \alpha + \beta x$$

where

$$\pi(x) = \frac{\exp(\alpha + \beta x)}{1+\exp(\alpha + \beta x)} = \frac{e^{\alpha+\beta x}}{1+e^{\alpha+\beta x}}$$

Important property

- π is restricted to 0 and 1,
- But logit(π) can take any real value except 0.
- The linear predictor that form the systematic component of a GLM also take any real value.
- Hence, this model does not have the structural problem that the linear probability model has.

3.4.8 The Simple Model

To begin, suppose there is a single explanatory variable X, which is quantitative.

For a binary response variable Y, recall that $\pi(x)$ denotes the "success" probability at value x. This probability is the parameter for the binomial distribution. The logistic regression model has linear form for the logit of this probability,

$$\text{logit}(\pi(x)) = \log\left(\frac{\pi(x)}{1-\pi(x)}\right) = \alpha + \beta x \tag{3.5}$$

The formula implies that $\pi(x)$ increases or decreases as an S-shaped function of x.

The logistic regression formula implies the following formula for the probability $\pi(x)$, using the exponential function, then

$$\pi(x) = \frac{\exp(\alpha + \beta x)}{1+\exp(\alpha + \beta x)} = \frac{e^{\alpha+\beta x}}{1+e^{\alpha+\beta x}} \tag{3.6}$$

3.4.9 Significance Testing

Wald Statistics

The Wald test is obtained by comparing the maximum likelihood estimate of the slope parameter β to an estimate of its standard error. For the logistic regression model, $H_0: \beta = 0$ states that the probability of success is independent of X.

Wald test statistics are simple. For large samples,

$$z = \frac{\hat{\beta}}{ASE_{\hat{\beta}}} \tag{3.7}$$

has a standard normal distribution when $\beta = 0$. Refer z to the standard normal table to get a one-sided or two-sided P-value. Equivalently, for the two-sided

$H_a: \beta \neq 0$

$$z^2 = \left(\frac{\hat{\beta}}{ASE_{\hat{\beta}}}\right)^2 \tag{3.8}$$

has a large-sample chi-squared null distribution with $df = 1$.

3.5 The Maximum Likelihood Estimation

In a logit model, the parameters $\beta_i\{i = 1,\cdots\cdots\cdots,k\}$ are unknown, using the maximum likelihood we estimate the parameters. This method often leads to estimators possessing desirable properties, particularly large sample properties. The idea is to use a value in the parameter space that corresponds to the largest "likelihood" for the observed data as an estimate of the unknown parameter. The method is explained as follows:

(i.) Let $X_1,X_2,\cdots,X_n$ be an iid random sample from a probability distribution function $f(x,\theta)$ where $\theta = (\theta_1,\theta_2,\cdots,\theta_k) \in \Omega$.

(ii.) Find the likelihood function i.e. the probability of the observed data, expressed as a function of the parameter, likelihood function is given as

$$L(x_1, x_2, \cdots, x_n, \theta) = \prod_{i=1}^{n} f(x_i, \theta)$$

(iii.) The estimator $\hat{\theta}(x_1,x_2,\cdots,x_n)$ for θ is that value of θ which maximizes the likelihood function $L(x,\theta) = L(x_1,x_2,\cdots,x_n,\theta)$. The estimator $\hat{\theta}$ is called the maximum likelihood estimator (MLE). That is, MLE $\hat{\theta}$ maximizes $L(x,\theta)$ for each outcome $x_1,x_2,\cdots,x_n$.

(iv.) To determine MLE, $\hat{\theta}$ the for which $L(x_1,x_2,\cdots,x_n,\theta)$ is maximized, we rather maximize $\ln L(x,\theta) = \ln L(x_1,x_2,\cdots,x_n,\theta)$ for computational convenience:

$$\frac{\partial \ln L(x,\theta)}{\partial \theta} = \frac{\partial \ln L(x_1, x_2, \cdots, x_n, \theta)}{\partial \theta} = \ell(x_1, x_2, \cdots, x_n, \theta) = 0 \qquad (3.9)$$

and solve $\hat{\theta}(x_1,x_2,\cdots,x_n)$.

DEFINITION

A value $\hat{\theta}_n$, say $\hat{\theta}_n = t(x_1,\cdots,x_n)$ which maximizes the likelihood function, $L(\theta,x_1,\cdots,x_n)$ over $\forall\theta \in \Theta$ is called a maximum likelihood estimate for θ.

Hence $\forall\theta \in \Theta, L(t(x_1,\cdots,x_n),x) \geq L(\theta;x_1,\cdots,x_n) \rightarrow \hat{\theta}_n$ is the ML – estimate, ~

so, the random variable $T_n = t(X_1,\cdots,X_n)$ is called a maximum likelihood estimator for θ.

DEFINITION

The function $l(\theta;x) = l(\theta;x_1,\cdots x_n) = \ln L(\theta;x_1,\cdots x_n)$ is called the Log Likelihood function of $x_1,\cdots,x_n$. That is taking the natural log of the likelihood function.

DEFINITION

The function $s(\theta;x) = s(\theta;x_1,\cdots x_n) = \frac{\partial}{\partial\theta} l(\theta;x)$ is called the Score function of $X_1,\cdots,X_n$. That is the first partial derivative with respect to the log-likelihood function.

DEFINITION

The function $I(\theta;x) = I(\theta;x_1,\cdots,x_n) = -\frac{\partial}{\partial\theta} s(\theta;x) = -\frac{\partial^2}{\partial\theta^2} l(\theta;\underset{\sim}{x})$ is called the information function of $X_1 \cdots X_n$. So, in many cases, $\hat{\theta}_n$ can be found by solving the maximum likelihood equation: $s(\theta;\underset{\sim}{x}) = 0$ and by checking that $I(\hat{\theta}_n) > 0$.

3.5.1 The Maximum Likelihood – Estimator for the Poisson parameter given the random sample, $X_1, X_2, \cdots, X_n$

$$f(x,\theta) = \frac{\theta^x e^{-\theta}}{x!}, \quad x = 0,1,2,\cdots$$

$$L(x,\theta) = L(x_1,x_2,\cdots,x_n,\theta)$$

$$= \prod_{i=1}^{n} f(x_i,\theta) = \prod_{i=1}^{n} \frac{\theta^{x_i} e^{-\theta}}{x_i!} = \frac{\theta \sum x_i e^{-n\theta}}{\prod_{i=1}^{n} x_i!}$$

$$\ln L(x,\theta) = \left(\sum_{i=1}^{n} x_i\right) \ln\theta - n\theta - \sum_{i=1}^{n} \ln x!$$

$$\frac{\partial \ln L(x,\theta)}{\partial\theta} = \frac{\sum_{i=1}^{n} x_i}{\theta} - n = 0$$

$\sum_{i=1}^{n} x_i = n\theta$ from which we have $T_n = \frac{1}{n}\sum_{i=1}^{n} X_i = \bar{X}$.

3.5.2 The Maximum Likelihood – Estimator For the Bernoulli Parameter π.

$X_1,\cdots,X_n$: random sample form X.

X: Bernoulli, parameter $\pi,\pi]0,1[$

$$f(x,n) = \pi^x(1-\pi)^{1-x}, \qquad x = 0,1 \tag{3.10}$$

Then we define the log-likelihood function;

$$\begin{aligned} L(\pi;\underset{\sim}{x}) &= \prod_{i=1}^{n} \pi^{x_i}(1-\pi)^{1-x_i} = \pi^{\sum_{i=1}^{n} x_i}(1-\pi)^{n-\sum_{i=1}^{n} x_i} \\ l(\pi;\underset{\sim}{x}) &= \Sigma x_i \ln \pi + (n-\Sigma x_i)\ln(1-\pi) \\ s(\pi;\underset{\sim}{x}) &= \frac{\Sigma x_i}{\pi} - \frac{(n-\Sigma x_i)}{1-\pi} \\ I(\pi;\underset{\sim}{x}) &= \frac{\Sigma x_i}{\pi^2} - \frac{(n-\Sigma x_i)}{(1-\pi)^2} \end{aligned} \tag{3.11}$$

So solve $s(\pi;\underset{\sim}{x}) = 0$ and check $I(\pi;\underset{\sim}{x}) > 0$,

$\hat{P}_n = \frac{1}{n}\sum_{i=1}^{n} x_i$ is the ML estimate for π, then $T_n = \frac{1}{n}\sum_{i=1}^{n} X_i = \bar{X}$ is the ML-estimator for π

3.6 The Odds Ratio

The odds ratio is another measure of association for 2×2 contingency tables. It occurs as a parameter in the most important type of model for categorical data. For a probability of success π, the odds of success are defined to be

$$Odds = \pi/(1-\pi) \tag{3.12}$$

The odds are nonnegative, with value greater than 1.0 when a success is more likely than a failure. When odds = 4.0, a success is four times as likely as a failure. We then expect to observe four successes for every one failure. When odds = 1/4, a failure is

four times as likely as a success. We then expect to observe one success for every four failures. The success probability itself is the function of the odds,

$$\pi = odds/(odds + 1)$$

The odds ratio (OR) is the ratio of two "odds" of success versus failure for the two groups:

$$\frac{\frac{\pi_1}{1-\pi_1}}{\frac{\pi_2}{1-\pi_2}} \tag{3.13}$$

The odds can take any nonnegative real number, it is a skewed sampling distribution and the log-odds ratio is often used to alleviate the restrictions that the odds ratio must be positive, i.e

$$\begin{aligned}\log(OR) &= \log\left(\frac{\frac{\pi_1}{1-\pi_1}}{\frac{\pi_2}{1-\pi_2}}\right) \\ &= \log\left(\frac{\pi_1}{1-\pi_1}\right) - \log\left(\frac{\pi_2}{1-\pi_2}\right) \\ &= \text{logit}(\pi_1) - \text{logit}(\pi_2)\end{aligned} \tag{3.14}$$

where $-\infty \leq \log(OR) \leq \infty$

7→ Less skewed sampling distribution, closer to normality.

7→ Therefore, best to construct C.I for log(OR) and then transform back (by exponentiating) to obtain C.I for OR.

7→ Note that the (OR) is the difference in logits.

- The estimated OR is:

$$\frac{\frac{p_1}{1-p_1}}{\frac{p_2}{1-p_2}}$$

- The estimated variance of $\log\frac{\frac{p_1}{1-p_1}}{p_2}$ is

$$\overline{1-p_2}$$

$$\left[\frac{1}{y_1}+\frac{1}{n_1-y_1}\right]+\left[\frac{1}{y_2}+\frac{1}{n_2-y_2}\right]$$

3.7 SURVIVAL ANALYSIS

Survival analysis is the modern name given to the collection of statistical procedures which accommodate time-to-event censored data.

Survival Analysis typically focuses on time to event data. In the most general sense, it consists of techniques for positive valued random variable, such as Time to death, Time to onset(or relapse) of a disease Length of stay in a hospital etc.

3.7.1 Some definitions and notations

Failure time random variables are always non-negative. That is, if we denote the failure time by T, then. $T \geq 0$. T can either be discrete or a continuous. A random variable X is called a censored failure time random variable if $X = \min(T,U)$ where U is a non-negative censoring variable.

3.7.2 Types of censoring

Data can be censored for a number of reasons and the effect it will have on our results will vary, therefore the need to classify the types of censoring present in the data.

Right-censoring

A person's exact survival time becomes incomplete at the right side of the followup period, occurring when the study ends or when the person is lost to follow-up or is withdrawn. We generally refer to this kind of data as right-censored. For this study, if a mother dropped out of the PMTC program or could no longer be traced or even the baby dying before taking the PCR test , the complete survival time interval, which

we don't really know, has been cut off (i.e., censored) at the right side of the observed survival time interval.

We call this right-censored because the true unobserved event is to the right of our censoring time; i.e. all we know about is that the event has not happened at the end of follow-up or study.

In addition to observing X_i, we also get to see the failure indicator:

$$\delta_i = \begin{cases} 1 & \text{if } T_i \leq U_i \\ 0 & \text{if } T_i > U_i \end{cases}$$

Some software packages instead assume we have a censoring indicator:

$$c_i = \begin{cases} 0 & \text{if } T_i \leq U_i \\ 1 & \text{if } T_i > U_i \end{cases}$$

Right-censoring is the most common type of censoring assumptions we will deal with in survival analysis.

Left-censoring

Censoring mechanism prevents knowledge of when entry into the particular state occurred e.g. in medical studies, lives will be subject to regular medical examinations. Discovery of a condition only tells us that onset occurred in the period since the previous examination date so when measuring the number of days someone will survive with a certain disease we may not know when the disease actually starts e.g. we don't know the start of the left side of the time line.

We Can only observe $Y_i = \max(T_i, U_i)$ and the failure indicators:

$$\delta_i = \begin{cases} 1 & \text{if } U_i \leq T_i \\ 0 & \text{if } U_i > T_i \end{cases}$$

Left-censored data can occur when a person's true survival time is less than or equal to that person's observed survival time. For example, in this study, we may record a

failure when a neonate firsts tests positive for the virus on the PCR. However, we may not know exactly the time of first exposure to the virus, and therefore do not know exactly when the failure occurred. Thus, the survival time is censored on the left side since the true survival time, which ends at exposure, is shorter than the follow-up time, which ends when the subject tests positive.

Interval-censoring

Censoring mechanism only allows us to say that a particular event occurred within some known interval of time e.g. in this study, we may only know the period within which a baby becomes positive to HIV rather than the exact time the baby became infected.

Random censoring

Random censoring is further classified into informative and non-informative censoring. The classification is based on analyzing whether we think a life being censored gives any indication of the lifetimes T_i. For example, if we are studying mortality then individuals leaving the investigation because they are ill may indicate that the lifetime will be less than the lives that remain in the investigation. Informative censoring may therefore indicate that the survival function calculated from the remaining lives may be biased. Non-informative censoring is when people leaving the investigation is truly independent of future lifetime and hence should not affect the results.

Independent vs informative censoring

We say censoring is independent (non-informative) if U_i is independent of T_i.

3.8 Kaplan-Meier Estimator

The Kaplan-Meier estimator of the survivorship function (or survival probability) is:

$S(t) = Pr(T \geq t)$is :

$$\hat{S(t)} = \prod_{j:x_j<t}\left(1-\frac{d_j}{r_j}\right) = \prod_{j:x_j<t}\left(\frac{r_j-d_j}{r_j}\right) \quad (3.15)$$

where

- $\tau_1,\tau_2,\cdots,\tau_K$ is the set of K distinct ordered times at which failure occurred. • d_j is the number of failures at τ_j
- r_j is the number of individuals "at risk" right before the $j-th$ failure time (every baby tested positive or censored at or after that time)
- c_j is the number of censored observations between the $j-th$ and $(j+1)th$ failure times. Censorings tied at τ_j are included in
- two useful formulas are:

1. $r_j = r_{j-1} - d_{j-1} - c_{j-1}$
2. $r_j = \mathrm{P}_{i\geq j}(c_i - d_i)$

CHAPTER 4

DATA ANALYSIS AND RESULTS

4.1 Introduction

This chapter discusses the analysis of the study variables involved in this study on "gender differences on the risk of mother to child transmission of HIV-1 during postpartum period in Ghana" case study: Korle-Bu HIV Unit", we first look at the preliminary analysis, summary of the entire analysis carried out and the model specification. The multiple logistic regression model and Kaplan-Meier survival estimator were employed in the data analysis using the SAS software version 9.2.

4.2 Data Source

A secondary data was obtained from the Korle-Bu teaching hospital in 2014.The data obtained involved some two thousand and seventy eight (2,078) mothers with clinical history and outcome of birth history. There were various referrals coded as (1=Diagnostic HIV testing, 2=Walk-in VCT site, 3=PMTCT program, 4=Old patient, 5= TB, 6 = STI, 7 = others, 8=NR, 9 = Transfer in on Ois, 10= Transfer in on ART) and about fifteen variables. For the purpose and interest of this study only mothers on the PMTCT program were considered and this brought the total number of subjects to nine hundred and fifty (950). Due to inconsistencies and missing information for some data points, only infants whose last known PCR test results indicated their HIV status were used and this finally brought the total number of observations to two hundred and forty four (244).

4.3 Exploratory Analysis of the study

The data was explored using contingency tables to find the frequencies and percentages of the dependent variable as well as to investigate the association between the response of the PCR test and selected demographic and exposure variables. Summary statistics for the continuous independent variables were obtained, for example: the standard deviation, the mean, and the maximum and minimum observations of these variables.

The dependent variable is a child's response to the PCR test (0, indicator for a baby who tested negative for the HIV infection and 1, indicator for a baby who tested positive for the HIV infection

4.3.1 Preliminary analysis

Table 4.1: Frequencies and percentages of delivery mode

Delivery Mode	Frequency	Percent	Cumulative Frequency	Cumulative Percent

Spontaneous without episiotomy	118	50.64	118	50.64
Spontaneous with episiotomy	26	11.16	144	61.80
Caesarian section elective	74	31.76	218	93.56
Emergency caesarian section	15	6.44	233	100.00

Table 4.1shows the frequency, percentage, cumulative frequency and cumulative percentage of the respective mothers during delivery. The mother's delivery mode was categorized into four levels. The mode of delivery is a transmission risk factor during intrapartum. Of all mothers considered in this study, 118 representing 50.64% delivered with spontaneous without episiotomy (i.e. normal delivery), 26 women representing 11.16% delivered by spontaneous with episiotomy (i.e. a surgical cut in the muscular area between the vagina and the anus (the area called the perineum) made just before delivery to enlarge vaginal opening). 74(31.76%) delivered through elective caesarian section and 15(6.44%) through emergency caesarian section.

Table 4.2 below shows the distribution of the various levels of breastfeeding practices adopted by the mothers on the PMTCT. Breastfeeding is also a transmission risk factor during postpartum. From Table 4.2 it can be seen that about 149(69.30%) of the infants were exclusively breastfed over a period and with 15(6.98%) of the infants on mixed breastfeeding. 51(23.72%) of the infants in this study were not breastfed at all.

Table 4.2: Frequencies and percentages of breastfeeding

BreastFeed	Frequency	Percent	Cumulative Percent
No breastfeeding	51	23.72	23.72
Exclusive breastfeeding	149	69.3	93.02
Mixed breastfeeding	15	6.98	100

In the data, about 55% of the infants were females whiles 45% were males. Gender here can be seen as fairly balanced. Almost all mothers on the PMTCT referral had HIV1 stage.

Table 4.3 below shows the distribution of the outcome of the last known PCR test. We observe that about 191(79.25%) of the infants tested positive for the HIV viral loads and 50(20.75%) tested negative for the HIV.

Table 4.3: Frequencies and percentages of HIV Detection

HIV1 Detection	Frequency	Percent	Cumulative Percent
0(No)	191	79.25	79.25
1(Yes)	50	20.75	100

Below is table 4.4, the age of subjects at last known PCR test ranges between the ages of 0 months and about 52 months with an average age of about 8 months and a standard deviation of 7.936month, which seem to be large variations in this variable. The average length of time (in days) since the mothers registered at the facility and the last known PCR test is about 141 days with a standard deviation of 127.875days. This large variation may be due to the varying timing of mothers registering to a facility. The average father's age before birth is about 39years with a standard deviation of 6.919years. The average mother's age at time of birth is about 32years with standard deviation of 5.181years. The current weight of 230 infants at the time they took the last known PCR test also ranged from 1.730 kg to 26.50kg with a standard deviation of 2.298kg. The average length of time (in days) since the infants were born and the last known PCR test was carried is about 230 days with a standard deviation of 238 days. This may be due to the different times of carrying PCR tests.

Table 4.4: Summary statistics of some continuous variables

Variable	N	Mean	Minimum	Maximum	Std Dev
Age at last PCR test(month)	241	7.65	0	56.333	7.936
Dur_register_dob(month)	241	4.025	0	51.666	6.028
Dur_pcrtest_reg(days)	241	141.34	0	553	127.875
Father's Age(years)	198	38.919	21	66	6.919
Current Weight(kg)	2302	5.138	1.73	26.5	2.297
Mother's Age(years)	39	31.786	19	46	5.181

Dur_pcrtest_dob (days)	241	229.502	0	1690	238.082

Where "age at last PCR test(months)" means the age of infants in months at the time they took the last PCR test. Also "dur_register_dob(month)" means the length of time in months, between when the child was born and when they registered to take the PCR test. "dur_pcrtest_reg(days)" represent the length of time in days, between when the mothers registered and when the infants actually took the last PCR test. Finally, "dur_pcrtest_dob (days)" represents the length of time in days, between when the infants was born and when they took the last PCR test.

4.3.2 TEST FOR NO ASSOCIATIONS

Table 4.5: Delivery Mode by detection

Delivery Mode	Detection		Total
	HIV -	HIV+	
Spontaneous without episiotomy	96	22	118
	41.2	9.44	50.64
Spontaneous with episiotomy	22	4	26
	9.44	1.72	11.16
Caesarian section elective	56	18	74
	24.03	7.73	31.76
Emergency caesarian section	12	3	15
	5.15	1.29	6.44
Total	186	47	233
	79.83	20.17	100

The table 4.5 presents the cross tabulation of delivery mode and outcome of the last known PCR test to detect the presence of HIV viral loads or not. The table shows the joint cell frequency counts and the conditional probability estimates. The Chi-square test ($\chi^2 = 1.338$ with p-value of 0.7211) shows that the type of delivery does not associate with detection of HIV viral loads. This could be the effect on best practices of antenatal care for pregnant women who are on the PMTCT. We observe from table

4.3 and table 4.5 that of the 21% of HIV positive detection about 9% positive detection were from mothers who delivered normally and had the highest frequency. From table 4.6, we observe that exclusive breastfeeding had the highest frequency of positive results (30) which is about 13.95% of the total positive detections. From the Chi-square test, breastfeeding practices are not associated with the outcome of detection of HIV positive with $\chi^2 = 3.571$ and p-value of 0.1584).

Table 4.6: Breast Feed by detection

Breast Feed	Detection		Total
	HIV -	HIV+	
No breastfeeding	42	9	51
	19.53	4.19	23.72
Exclusive breastfeeding	119	30	149
	55.35	13.95	69.3
Mixed breastfeeding	9	6	15
	4.19	2.79	6.98
Total	170	45	215
	79.07	20.93	100

From Table 5.6 and 5.7 in appendix, we observe that about 8% of female infants tested positive for HIV whiles about 13% of male infants tested positive for HIV and from the Chi-square test, gender of baby and the outcome of the HIV detection are associated with and p-value of 0.0184 respectively.

From table 4.8, one other significant result we observed was the association between breastfeeding practice and gender of baby. About 35% of female infants had exclusive breastfeeding and about 34% of male infants also had exclusive breastfeeding. About 16% of female infants had no breastfeeding and about 7% of male infants had no breastfeeding. The Chi-square test with Chi-squared value of 6.1075 and p-value of 0.0472 at 5% level of significance, indicated that the breastfeeding practices and gender of baby were associated.

4.4 The Logistic Regression Model

The demographic and exposure variables considered in the model were delivery mode, mother's age at delivery, Breastfeeding practice and gender of baby. Even though the test of association was not significant for delivery mode and breastfeeding practices, these variables were considered in the logistic regression model because of the possible joint effect on the HIV viral load detection. In a global analysis to test if all the variables considered in the study had some effect on the model in order for them to be included in the model showed that none was significant. From the type 3 analysis of effect test in table 4.7, we observe that both Delivery Mode and mothers age at delivery were highly insignificant (see appendix Table 5.1). We therefore dropped the two variables from the model using the likelihood ratio test. Further, breastfeeding was dropped because of the association with gender in the preliminary results and a final model with only gender was obtained.

Table 4.7: Type 3 analysis of Effects

Effect	DF	Wald Chi-Square	Pr > ChiSq
Delivery Mode	3	2.6178	0.4544
Breast Feed	2	4.1537	0.1253
Mother Delivery Age	1	0.0655	0.798

The type 3 analysis above with the indicated p-values, showed that, at 5% level of significance, Gender, Delivery mode, Breastfeeding and mother's age were all not significant to be included in the model. This raised the question of co-linearity since Gender was seen earlier to be associated with the detection of HIV. Further tests of association were done to see if there existed some relationships between the predictor variables considered in this study. This led to the finding, that Gender of an infant and breastfeeding mode were associated with a Chi- squared value of 6.107 and P- value = 0.0472 at 5% level of significance.

Table 4.8: Test of No Association between Breast feeding and Gender

	FEMALE	MALE	TOTAL
No Breastfeeding	35	16	51
Exclusive Breastfeeding	76	73	149
Mixed Breastfeeding	6	9	15
TOTAL	117	98	215

Chi-squared value=6.1075 P-value=0.0472

In the final model, gender was significant with a p-value of 0.0198 at 5% level of significance in table 4.9 below. From the maximum likelihood estimates, the effect of gender based on the odds ratio estimate was 2.127 with 95% confidence interval between 1.127 and 4.012. The odds of male infants being infected versus not infected is almost twice of the odds of female infants. Here, male infants are at more risk of positive detection than female infants. We recall that breastfeed practice is associated with gender.

Table 4.9: Analysis of Maximum Likelihood Estimates

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr> ChiSq
Intercept	1	-1.7228	0.2428	50.3648	<.0001
Gender	1	0.7545	0.3239	5.426	0.0198
Odds Ratio Estimates					
Effect	Point Estimate	95% Wald Confidence Limits			
Gender	2.127	1.127	4.012		

4.5 Survival Analysis

The variable dur_pcrtest_dob (days) which means time (in days) since birth and the last known PCR test was carried on the new born baby was used as the time to event

variable. This variable was chosen because WHO 2013 guidelines on mother-to-child transmission, the PCR test should be carried before baby is 18months old. About one hundred and ninety four (194) observations were eligible for the analysis. From figure 4.1, the Kaplan-Meier survival estimates showed that the median time to HIV positive detection was 549 days. In a Logrank test for testing for differences in time to HIV positive detection based on different breast feeding practices), Chisq= 0.8 on 2 degrees of freedom, p= 0.661 indicating that there is no significant difference in time to HIV detection between the three breastfeeding practices (see figure 5.1 in the appendix).

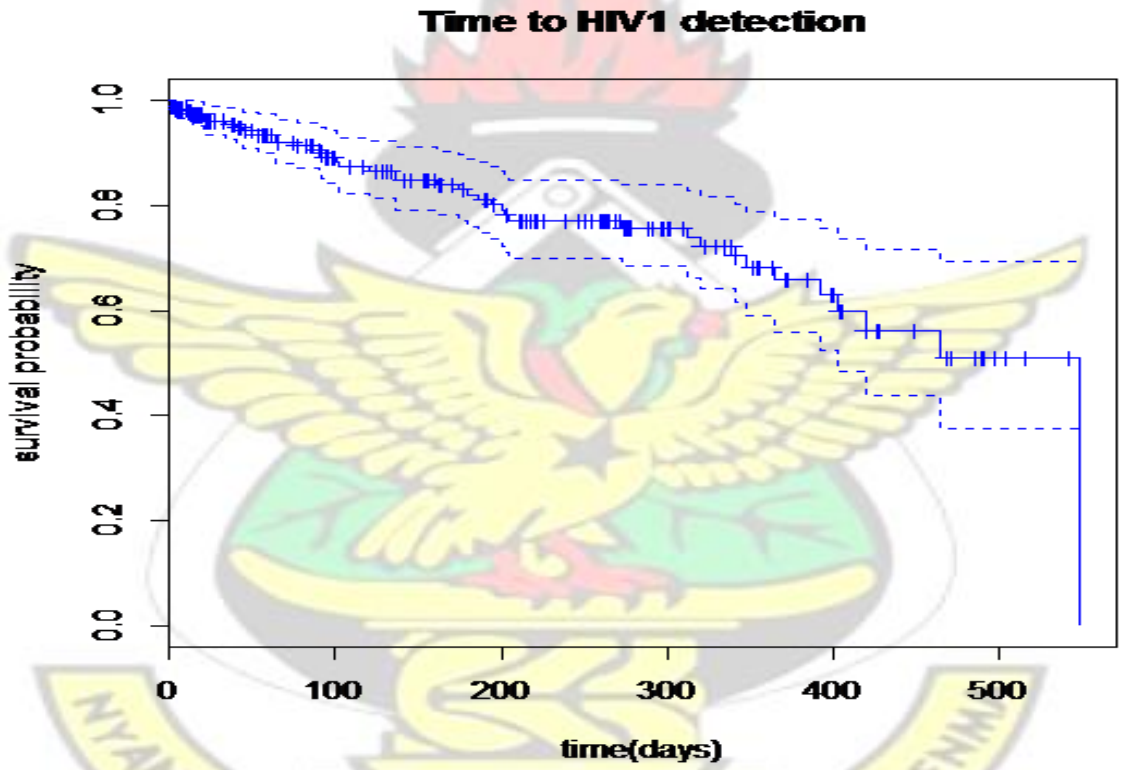

Figure 4.1: Kaplan-Meier survival estimates for entire observations

The Log-rank test for testing for differences in time to HIV positive detection based on delivery mode, Chisq= 3.3 on 3 degrees of freedom, p= 0.314 show that there is no significant difference in time to HIV positive detection.

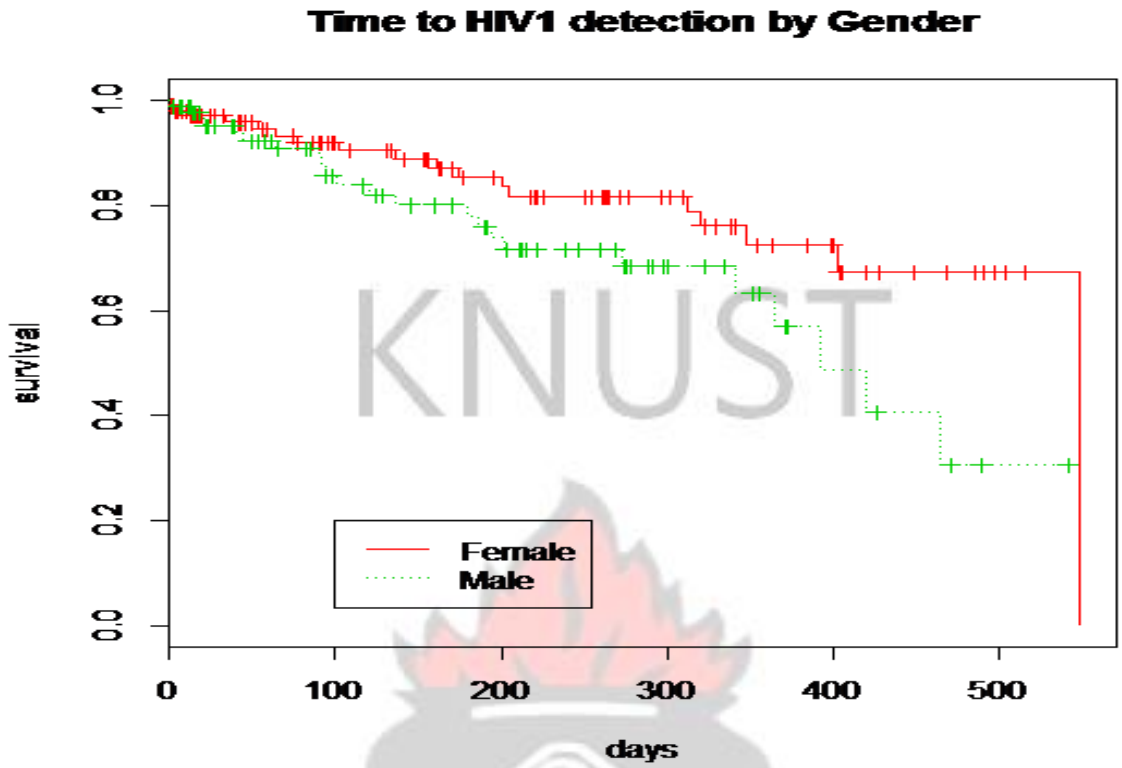

Figure 4.2: Kaplan-Meier survival estimates by gender

Figure 4.2 shows the two Kaplan-Meier survival estimates for females and males respectively. We observe that male infants showed shorter duration for HIV positive detection than females in general.

The log-rank test showed border line significant results with a Chisq of 4.8 on 1 degrees of freedom, and a p-value of 0.0292 at 5% level of significance indicated that, there exists a significance time to detection of HIV between female infants and male infants(see table 5.8 in Appendix). From Appendix table 5.5, approximately 50% of the male infants are detected with the HIV infection on the three hundred and forty third day (343rd day) after birth indicating that, the median time to detection of HIV in male infants was 343 days.

CHAPTER 5

DISCUSSION, CONCLUSION AND

RECOMMENDATION

This chapter is divided into three sections. The first section looks to discuss the primary empirical findings of the study. The second section provides some recommendations to help reduce the rates of mother to child transmission of HIV in Ghana. The final section then concludes the section.

5.1 Discussion

Out of the 241 mothers that were considered in this study, majority (118) delivered normally, 26 of them had a surgical cut at the perineum to aid in delivering, 74 women opted for caesarian section and 15 women had emergency caesarian section for various reasons. Out of the 21% positive detections, mothers who delivered normally had the highest percentage of infection of about 9% followed by those that opted for caesarian section about 8% with the least infection coming from mothers who delivered through emergency caesarian section.

Table 4.2 indicates that 51 mothers did not breastfeed their infants at all while 149 went for exclusive breastfeeding and 15 went for breastfeeding where as in table 4.3 shows that 191 infants tested negative for the HIV 1 virus and 50 tested positive. Although the WHO recommends exclusive breastfeeding for HIV positive mothers in low income countries like Ghana, it can be seen from Table 4.6 that exclusive breastfeeding had the highest percentage of infection, about 14% with mix breastfeeding having the lowest percentage of infection (3%).

From table 4.4, the age of subjects at last known PCR test ranges between the ages of 0 months and about 52 months with an average age of about 8 months. The average length of time (in days) since the mothers registered at the facility and the last known PCR test was carried is about 141 days. This large variation may be due to the varying timing of mothers registering to a facility. The average father's age before birth is about 39 years and the average mother's age at time of birth is about 32 years. The current weight of 230 infants at the time they took the last known PCR test also

ranged from 1.730kg to 26.50kg with a standard deviation of 2.298kg. The average length of time (in days) since the infants were born and the last known PCR test was carried is about 230 days with a standard deviation of 238 days. This may be due to the different times of carrying PCR tests.

The tests for no associations showed that the mode of delivery of the baby and breastfeeding were not significant in the transmission of HIV from mother-tochild in this study with p-values of 0.7211 and 0.0184 respectively at 5% level of significance. We observed that about 8% of female infants tested positive for HIV whiles about 13% of male infants tested positive for HIV. One significant result that was observed was the association of gender with the outcome of HIV detection with a p-value of 0.0184 at 5% level of significance. Another interesting observation was that, although breastfeeding was not significant in the transmission of HIV from mother to child, it was highly associated with the gender of a baby.

Although most literature reviewed concluded that female infants were more susceptible to acquiring HIV from infected mothers, the maximum likelihood estimates shows that the effect of gender based on the odds ratio estimate was 2.127 with 95% confidence interval between 1.127 and 4.012 meaning the odds of male infants being infected versus not infected is almost twice of the odds of female infants implying that male infants are at more risk of mother-to-child transmission of the HIV than female infants.

From the Kaplan-Meier survival estimates for female infants and male infants respectively, the results showed that female infants survive better than male infants, in that, male infants showed shorter duration for HIV positive detection than females in general. With the median time to detection of about 343 days for male infants and female infants showing no median time to detection.

5.2 Conclusion

The results from this study show that there is no association between breastfeeding practices and HIV detection in infants. This study concludes that the mode of delivery does not associate with detection of HIV viral loads in infants.

However, this study finds much evidence to conclude from a Chi-square value of 5.557 and a p-value of 0.0184 that the gender of an infant and the outcome of the HIV detection are associated. male infants have almost twice the risk of HIV infection than female infants. Again, a relationship was found to exist between the breastfeeding practices and gender of baby. The results again shows that there exist a significant time to detection of HIV viral loads between female infants and male infants with male infants showing a shorter duration for HIV positive detection than females in general and a median time to detection of 343 days for male infants.

The study concludes, that there is no significant impact of the exposure risk factors considered in this study on HIV infections from Mother to child transmissions (MTCT). However there exist significant gender differences on the risk to Mother to child transmissions (MTCT).

5.3 Recommendations

In a cross tabulation to test for significant association between gender and breastfeeding, it was evident that more females were breastfed in all forms of breastfeeding than males, the rate of infection in male infants was significantly higher than in female infants, we would therefore recommend that either HIV mothers breastfeeding male infants should be put on an increased recommended dosage of ARV's if possible, or HIV mothers breastfeeding male infants should have extra preventive care.

Although breastfeeding was not associated with the detection of viral load in infants, we cannot deny the fact that it may have accounted for some infections in this study,

we would therefore recommend that that male infants are weaned earlier than female infants since they (male) survive less good than the female infants.

We would also recommend a review in the practices involved in delivering infants normally (spontaneous without episiotomy) since it showed the highest frequency of infection among all the delivery modes.

REFERENCES

1. Ruptured membranes and risk of vertical transmission in women with HIV,CTownsend1, K Harding2,3, H Peters1, A De Ruiter2,3, K Francis1, G Taylor4, P Tookey1, Archives of Disease in Childhood

2. Fetal and Neonatal Editionfn.bmj.com ,Arch Dis Child Fetal Neonatal Ed2014;99:A4 doi:10Predictors of breastfeeding cessation among HIV-infected women in Dar es Salaam, Tanzania, Petraro, Christopher, Gernard Msamanga, Karen E Peterson, Donna ,Wafaie Fawzi, Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts 02115, USA. Maternal and Child Nutrition (Impact Factor: 2.11). 07/2011; 7(3):273-83. DOI: 10.1111/j.1740 8709.2009.00236.x, Source: PubMed .1136/archdischild-2014-306576.10

3. Breastfeeding Cessation among HIV Infected Mothers in Southern Ethiopia: A Survival Analysis Demewoz Haile mail, Tefera Belachew, Getenesh Birhanu, Tesfaye Setegn, Sibhatu Biadgilign ,Published: March 07, 2014,DOI: 10.1371/journal.pone.0090067

4. Integrating Prevention of Mother-to-Child HIV Transmission Programs to Improve Uptake: A Systematic Review Lorainne Tudor Car, Michelle H. M. M. T. Van Velthoven, Serena Brusamento, Hoda Elmoniry, Josip Car mail, Azeem Majeed, Peter Tugwell, Vivian Welch, Ana Marusic, Rifat Atun Published: April 27, 2012,DOI: 10.1371/journal.pone.0035268

5. Obstetrical factors and the transmission of human immunodeficiency virustype 1 from mother to child. The Women and Infants Transmission Study, Landesman1, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C, Garcia P, Fowler MG, Mofenson L, Tuomala R, N Engl J Med. 1996 Jun 20;334(25):1617-

23.

6. Maternal levels of plasma human immunodeficiency virus type 1 RNA and therisk of perinatal transmission. Women and Infants Transmission Study Group, Garcia1, Kalish LA, Pitt J, Minkoff H, Quinn TC, Burchett SK, Kornegay J, Jackson B, Moye J, Hanson C, Zorrilla C, Lew JF, N Engl J Med. 1999 Aug 5;341(6):394-402.

7. Intrapartum and neonatal single-dose nevirapine compared with zidovudinefor prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomized trial. Jackson1, Musoke P, Fleming T, Guay LA, Bagenda D, Allen M, Nakabiito C, Sherman J, Bakaki P, Owor M, Ducar C, Deseyve M, Mwatha A, Emel L, Duefield C, Mirochnick M, Fowler MG, Mofenson L, Miotti P, Gigliotti M, Bray D, Mmiro F, Lancet. 2003 Sep 13; 362(9387):859-68.

8. Extended antiretroviral prophylaxis to reduce breast-milk HIV-1 transmission,Kumwenda NI1, Hoover DR, Mofenson LM, Thigpen MC, Kafulafula G, Li Q, Mipando L, Nkanaunena K, Mebrahtu T, Bulterys M, Fowler MG, Taha TE, . Engl J Med. 2008 Jul 10; 359(2):119-29. doi: 10.1056/NEJMoa0801941. Epub 2008 Jun 4.

9. Mother-to-child transmission of HIV and its predictors among HIV-exposedinfants at a PMTCT clinic in northwest EthiopiaDigsu Negese Koye* and Berihun Megabiaw Zeleke ,Department of Epidemiology and Biostatistics, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia ,BMC Public Health 2013, 13:398 doi:10.1186/1471-2458-13-398

10. Coovadia HM et al., Mother-to-child transmission of HIV-1 infection duringexclusive breastfeeding in the first 6 months of life: an intervention cohort study, Lancet, 2007, 369(9567):1107–1116.

11. Clinical risk factors on survival among HIV-infected children born to HIV-infected mothers,Chaimay B1, Woradet S2, Chantutanon S3, Phuntara S3, Suwanna K , J Med Assoc Thai. 2013 Nov; 96(11):1434-43.

12. Gender differences in perinatal HIV acquisition among African infants.Taha TE1, Nour S, Kumwenda NI, Broadhead RL, Fiscus SA, Kafulafula G, Nkhoma C, Chen S, Hoover DR. Pediatrics. 2005 Feb;115(2):e167-72.

13. Higher In Utero and Perinatal HIV Infection Risk in Girls Than Boys, Robert J. Biggar, MD, Taha E. Taha, MD, Donald R. Hoover, PhD, Francis Yellin, MD, Newton Kumwenda, PhD,† and Robin Broadhead, MD, J Acquir Immune Defic Syndr & Volume 41, Number 4, April 1, 2006 Higher In Utero and Perinatal HIV Infection Risk in Girls

14. Advances in the prevention of mother-to-child HIV-1 transmission: currentissues, future challenges By Marc Bulterys,1 Monica L. Nolan,1,2 Denise J. Jamieson,1 Kenneth Dominguez,1 and Mary Glenn Fowler1 AIDScience Vol. 2, No. 4, February 2002

15. Influence of short-course antenatal antiretroviral therapy on viral load andmother-to-child transmission in subsequent pregnancies among HIV-infected women Clare E French1,*, Pat A Tookey1, Mario Cortina-Borja1, Annemiek de Ruiter2, Claire L Townsend1, Claire Thorne Antiviral Therapy 2013; 18:183-192,doi: 10.3851/IMP2327 ,Date published online: 22 August 2012

16. Impact of infant feeding practices on the risk of mother to child transmissionof HIV-1 in Zimbabwe Ba Olayinka, Ao Oni andFe Mbajiorgu, journal of Pediatrics and Child Health ,Volume 36, Issue 4, pages 313–317, August 2000, 24 DEC 2001, DOI: 10.1046/j.1440-1754.2000.00528.x

17. Is the risk of mother-to-child transmission of HIV higher among female compared with male infants? A case of Rakai, Uganda,Heena Brahmbhatta, Godfrey Kigozib, David Serwaddac, Fred WabwireMangend,Nelson,Sewankamboe, Maria Wawera and Ronald Graya, Journal of Pediatric Infectious Diseases 4 (2009) 275–279 275, DOI 10.3233/JPI-2009-
0168, IOS Press

18. Categorical Data Analysis, Second Edition. Alan Agresti, Copyright 2002 John Wiley & Sons,Inc. ISBN: 0-471-36093-7

19. Survival Analysis: A Self-Learning Text Second Edition, David G. Kleinbaum, Mitchel Klein, 2005, 1996 Springer Science+Business Media, Inc. ISBN-10: 0-387-23918-9 , ISBN-13: 978-0387-23918-7

20. Maternal levels of plasma human immunodeficiency virus type 1 RNA andthe risk of perinatal transmission. Women and Infants Transmission Study Group Garcia PM1, Kalish LA, Pitt J, Minkoff H, Quinn TC, Burchett SK, Kornegay J, Jackson B, Moye J, Hanson C, Zorrilla C, Lew JF, N Engl J Med. 1999 Aug 5;341(6):394-402

APPENDIX A

Table 5.1: Analysis of Maximum Likelihood Estimates (full model)

Parameter		DF	Estimate	Standard	Wald	Pr>ChiSq

				Error	Chi-Square	
Intercept		1	-1.2776	1.192	1.1489	0.2838
Sex		1	0.433	0.3687	1.3789	0.2403
DeliveryMode	1	1	0.0365	0.3321	0.0121	0.9124
DeliveryMode	2	1	-0.456	0.5265	0.7502	0.3864
DeliveryMode	3	1	0.5155	0.347	2.2071	0.1374
BreastFeed	1	1	-0.5979	0.3517	2.8905	0.0891
BreastFeed	2	1	-0.207	0.275	0.5665	0.4516
MotherDeliveryAge		1	-0.009	0.0351	0.0655	0.798

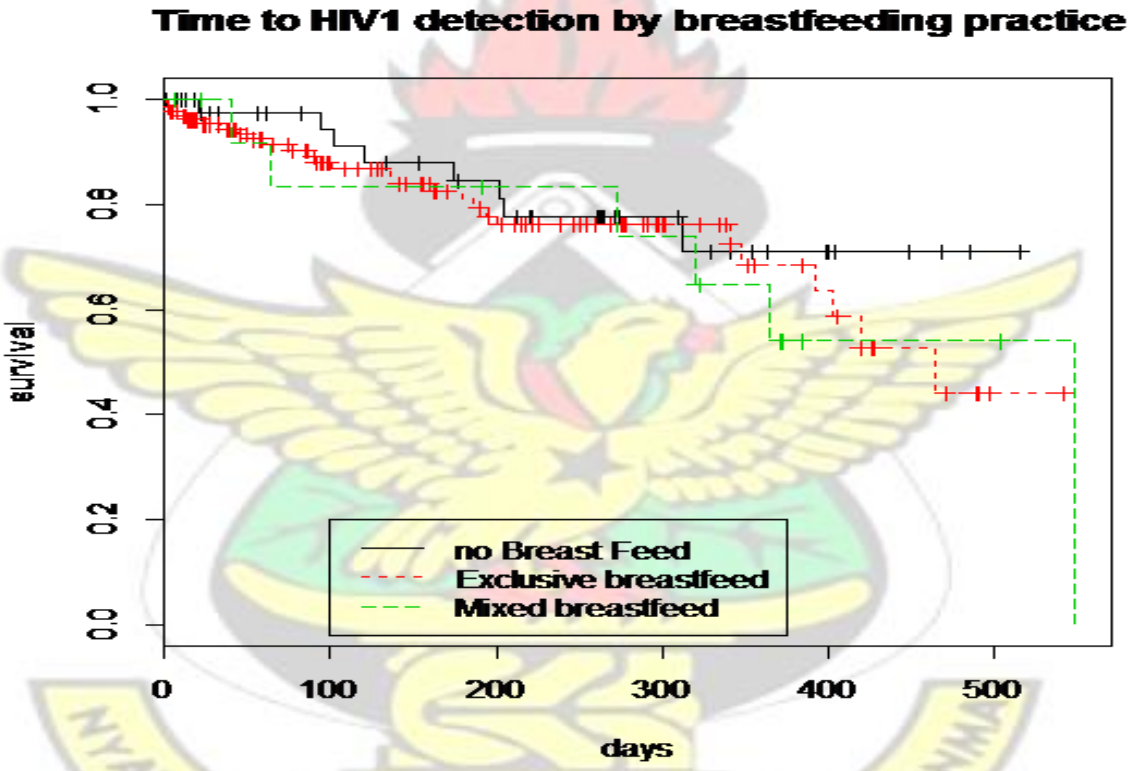

Figure 5.1: Kaplan-Meier survival estimates

Table 5.2: Test of no association between Breastfeeding against gender

Frequency Percent	Female	Male	Total
No Breastfeeding	35 16.28	16 7.44	51 23.72

Exclusive Breastfeeding	76 35.35	73 33.95	149 69.3
Mixed Breastfeeding	6 2.79	9 4.19	15 6.98
Total	117 54.42	98 45.58	215 100

Chi- squared value = 6.1075 P- value = 0.0472

Table 5.3: KAPLAN-MEIER SURVIVAL ESTIMATOR FOR OVERALL DATA

x	Number of risk	Number of events	survival	Standard error	CI(lower)	CI(upper)
7	239	1	0.996	0.00418	0.988	1
16	220	1	0.991	0.00614	0.979	1
20	219	2	0.982	0.00881	0.965	1
23	213	1	0.978	0.0099	0.58	0.997
27	212	2	0.968	0.01176	0.946	0.992
33	206	2	0.959	0.01339	0.933	0.986
35	203	1	0.954	0.01414	0.927	0.982
37	195	1	0.949	0.01489	0.921	0.979
41	194	1	0.944	0.01559	0.914	0.976
42	193	2	0.935	0.0169	0.902	0.968
44	186	1	0.93	0.01754	0.896	0.965
48	184	1	0.925	0.01816	0.89	0.961
50	177	1	0.919	0.01879	0.883	0.957
54	176	1	0.914	0.0194	0.877	0.953
56	172	1	0.909	0.02	0.877	0.953
58	163	1	0.903	0.02064	0.864	0.945
63	161	2	0.892	0.02185	0.85	0.936
68	153	1	0.886	0.02431	0.822	0.917
70	152	2	0.875	0.02364	0.829	0.922
77	138	1	0.868	0.02431	0.822	0.917
84	134	2	0.855	0.02561	0.807	0.907
97	113	1	0.848	0.02648	0.797	0.901
99	111	1	0.84	0.02732	0.788	0.889
114	104	1	0.832	0.02823	0.778	0.889
131	96	1	0.823	0.02923	0.768	0.883
152	87	1	0.814	0.03039	0.756	0.876
169	81	1	0.804	0.03163	0.744	0.868
182	76	2	0.783	0.03415	0.719	0.853
184	71	1	0.772	0.03541	0.705	0.844
217	60	1	0.759	0.03708	0.689	0.835
218	57	1	0.745	0.03875	0.673	0.825
252	53	1	0.731	0.04049	0.656	0.815

259	51	1	0.717	0.04216	0.639	0.805
294	41	2	0.682	0.0468	0.596	0.78
308	39	3	0.63	0.05209	0.535	0.74
343	27	1	0.606	0.05513	0.507	0.725
357	24	1	0.581	0.05834	0.477	0.707
400	16	561	0.545	0.06502	0.431	0.707
434	10	1	0.49	0.07807	0.359	0.67

Results showing the median time to infection for overall data to be 434 days.

Table 5.4: KAPLAN-MEIER SURVIVAL ESTIMATOR FOR FEMALE INFANTS

Time	Number of Risk	Number of event	Survival	Standard Error	CI(lower)	CI(upper)
7	113	1	0.991	0.00881	0.974	1
27	106	2	0.972	0.01569	0.942	1
33	102	1	0.963	0.01821	0.928	0.999
37	97	1	0.953	0.02055	0.914	0.994
50	91	1	0.943	0.02284	0.899	0.988
54	90	1	0.932	0.02487	0.885	0.982
58	84	1	0.921	0.02693	0.87	0.975
63	83	1	0.91	0.0288	0.855	0.968
70	79	1	0.898	0.03066	0.84	0.96
114	52	1	0.881	0.03459	0.791	0.952
131	48	1	0.863	0.03843	0.791	0.941
169	42	1	0.842	0.04266	0.763	0.93
184	36	1	0.819	0.04745	0.731	0.917
252	26	1	0.787	0.0551	0.686	0.903
259	25	1	0.75	0.06123	0.645	0.886
294	19	2	0.676	0.07638	0.542	0.844

Results showing no median time to detection for female infants.

Table 5.5: KAPLAN-MEIER SURVIVAL ESTIMATOR FOR MALE INFANTS

Time	Number of risk	Number of events	Survival	Standard error	CI(lower)	CI(upper)
16	81	1	0.988	0.0123	0.964	1
20	80	1	0.975	0.0172	0.942	1
23	77	1	0.963	0.0212	0.922	1
33	75	1	0.95	0.0245	0.903	0.999
35	74	1	0.937	0.0273	0.885	0.992
42	70	2	0.91	0.0324	0.849	0.976
44	66	1	0.896	0.0347	0.831	0.967
48	65	1	0.883	0.0368	0.813	0.958
56	58	1	0.867	0.0392	0.794	0.948
63	56	1	0.852	0.0415	0.774	0.937
77	47	1	0.834	0.0444	0.751	0.925
84	46	2	0.798	0.0493	0.707	0.9
97	37	1	0.776	0.0525	0.68	0.886
99	35	1	0.754	0.0555	0.653	0.871
152	27	1	0.726	0.06	0.617	0.854
182	25	2	0.668	0.0678	0.547	0.815
308	11	2	0.546	0.0954	0.388	0.769
343	8	1	0.478	0.1052	0.311	0.736
357	7	1	0.41	0.1101	0.242	0.694
434	3	1	0.273	0.1335	0.105	0.712

Results showing a median time to detection of 343 days for male infants.

Table 5.6: Frequencies and Percentages of Gender and detection of HIV

Table of Sex by response			
Sex	Response		Total
	No	Yes	
Female	112	20	132
	46.47	8.30	54.77
Male	79	30	109
	32.78	12.45	45.23
Total	191	50	241
	79.25	20.75	100.00

Table 5.7: Test of no association between Gender and Detection of HIV

Sex	HIV Detection	Total

	No	Yes	
Female	112	20	132
Male	79	30	109
Total	191	50	241

Chi-squared=5.557 and P-value=0.0184

Table 5.8: Log-rank test (testing for differences in time to HIV1 detection based on Gender)

	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
Female	114	18	24.9	1.92	4.76
Male	94	24	17.1	2.80	4.76

Chisq=4.8 on 1 degrees of freedom and P-value=0.0292

Table 5.9: Log-rank test (testing for differences in time to HIV1 detection based on Delivery Mode)

	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
DeliveryMode=1	105	19	21.56	0.3038	0.629
DeliveryMode=2	24	4	5.26	0.3004	0.348
DeliveryMode=3	67	17	13.58	0.8609	1.287
DeliveryMode=4	12	2	1.60	0.0979	0.103

Chisq=1.6 on 3 degress of freedom and P-value=0.663

Where Delivery modes 1,2,3 and 4 represent spontaneous without episiotomy, spontaneous with episiotomy, caesarian section (elective) and caesarian section (emergency) respectively.

Table 5.10: Log-rank test (testing for differences in time to HIV1 detection based on different breast feeding practices)

	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$
No BrestFeed	50	8	12.44	1.582	2.275

Exclusive BreastFeed=2	143	28	25.10	0.336	0.851
BreastFeed=3	15	6	4.47	0.526	0.603

Chisq=2.5 on 2 degrees of freedom and P-value=0.291