Section: Pharmacology

Original Research Article

EVALUATION OF ANTIRETROVIRAL THERAPY IN REDUCING VERTICAL TRANSMISSION OF HIV AMONG PREGNANT WOMEN: A COMPREHENSIVE STUDY

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Abstract

Background: This study delves into the effectiveness of Highly Active Antiretroviral Therapy (HAART) in mitigating vertical transmission of HIV from pregnant women to infants. HAART, particularly when commenced during pregnancy, has significantly lowered HIV transmission rates, now ranging from 1% to 22% in well-resourced countries. Additionally, the study examines breastfeeding practices, an important aspect considering HAART's influence on infant mortality and HIV transmission. Adherence to HAART during breastfeeding has been linked with a reduction in both infant mortality and HIV transmission. However, the initiation of postpartum maternal HAART is associated with an increased risk of multiclass drug resistance in breastfeeding infants, particularly when started close to delivery or during exclusive breastfeeding. **Materials and Methods:** The study observed 130 HIV-positive women on HAART, resulting in 150 births (including 5 twin pairs). Follow-up for infants spanned up to 20.5 months, with a focus on breastfeeding practices and infant HIV status. HIV testing was conducted using HIV DNA or RNA PCR, supplemented by ELISA in some cases. **Result:** Of the 146 infants tested for HIV, none were positive by the study's end. Maternal HAART duration before delivery averaged 22.4 months, and 95% of mothers exclusively breastfed for around 5.3 months. A notable finding was the lower survival probability among weaned or never-breastfed infants. Bivariate analysis indicated a reverse correlation between infant mortality and duration of exclusive and total breastfeeding. The final multivariate model reinforced the inverse association between breastfeeding duration and infant mortality, even after adjusting for maternal death. **Conclusion:** HAART was highly effective in preventing vertical HIV transmission. Extended breastfeeding duration significantly reduced infant mortality risk. However, infant mortality was inversely related to breastfeeding status, highlighting the need for comprehensive care strategies encompassing both antiretroviral treatment and breastfeeding guidance for HIV-positive mothers.

INTRODUCTION

The transmission of the Human Immunodeficiency Virus (HIV) from an HIV-positive mother to her child during pregnancy, childbirth, or through breastfeeding, commonly referred to as vertical transmission, represents a significant public health challenge[1,2]. This issue is particularly acute in regions with high HIV prevalence, posing a serious threat to maternal and child health[3,4]. Despite global efforts to curb the spread of HIV, vertical transmission continues to play a major role in perpetuating the disease's burden. It profoundly impacts families and communities, creating a cycle of health and socio-economic challenges[5]. The advent and widespread use of Highly Active Antiretroviral Therapy (HAART) have marked a pivotal shift in managing this critical issue, offering a means to significantly

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reduce the risk of mother-to-child transmission (MTCT) of HIV.

Study Rationale

This comprehensive study is designed to meticulously evaluate the effectiveness of HAART in mitigating the vertical transmission of HIV among pregnant women. It delves into the intricacies of HAART initiation and adherence during pregnancy and assesses its impact on lowering the HIV transmission rate to infants. Furthermore, the study addresses the complex interplay between HAART and breastfeeding practices. Breastfeeding, while a crucial aspect of infant nutrition and development, poses unique challenges in the context of HIV due to its potential as a transmission route. This study seeks to unravel these complexities, aiming to provide a clearer picture of HAART's role in reducing the incidence of HIV in newborns and improving overall maternal and child health outcomes.

Aim and Objectives

The primary aim of this study is to provide empirical evidence on the efficacy of HAART in preventing the vertical transmission of HIV during pregnancy and in the postpartum period. This research seeks to:

Assess the effectiveness of HAART in reducing the rate of vertical HIV transmission from pregnant women to their infants.

Examine the impact of HAART on maternal health outcomes and its influence on reducing HIV transmission risks during breastfeeding.

Explore strategies to improve HAART adherence among pregnant women and evaluate the outcomes on both maternal and infant health.

MATERIALS AND METHODS

Study Setting and Period

The research was conducted at Andhra Medical College and King George Hospital in Visakhapatnam, Andhra Pradesh, India. The research spanned a one-year period, from January 2022 to December 2022. This timeframe was strategically chosen to allow for detailed observation and analysis of the effects of Highly Active Antiretroviral Therapy (HAART) on the vertical transmission of HIV from pregnant women to their offspring. The duration was sufficient to follow the course of pregnancies and capture relevant data post-delivery, which was crucial in assessing the effectiveness of HAART in this context.

Study Population

The focus of this study was on HIV-positive pregnant women who were receiving treatment at Andhra Medical College and King George Hospital. This particular population was selected because of their unique health needs and the potential insights they could provide into the effectiveness of HAART in preventing vertical HIV transmission. These women, being at various stages of their pregnancy and under HAART treatment, constituted an ideal group for evaluating the objectives of the study. By focusing on this specific demographic, the research aimed to gain a deeper understanding of how HAART can be optimized to reduce HIV transmission rates from mothers to their infants, while also considering the health outcomes for both mother and child.

Inclusion Criteria

Confirmed HIV-Positive Status: All participants were required to have a medically confirmed diagnosis of HIV. This was essential to ensure the study focused on the impact of HAART on preventing mother-to-child transmission of HIV.

Pregnancy: The study was limited to women who were pregnant during the study period. Pregnancy is a critical factor in the study of vertical transmission of HIV, and including only pregnant women ensured that the findings were relevant to this specific group.

Undergoing HAART: Participants needed to be currently receiving Highly Active Antiretroviral Therapy. This criterion was crucial as the study's primary aim was to evaluate the effectiveness of HAART in reducing vertical transmission of HIV.

Exclusion Criteria

Non-HAART Recipients: Women who were HIV-positive but not receiving HAART were excluded. Since the study aimed to assess the efficacy of HAART, including non-recipients could confound the results.

Significant Comorbid Medical Conditions: Women with other significant medical conditions that could interfere with the study outcomes were excluded. This was to ensure that any changes in the health of the mother or infant could be more confidently attributed to the effects of HIV and HAART, rather than other health issues.

Non-Consenting Participants: Women who declined to participate in the study were excluded.

Data Collection

Data was collected through a combination of patient medical records, direct interviews, and follow-up assessments. Key data points included:

Demographic Information: Age, socio-economic status, educational background, and obstetric history.

Clinical Data: HIV status and history, details of HAART regimen (including initiation time and adherence), and any other relevant medical information.

Pregnancy and Delivery Outcomes: Gestational age at delivery, mode of delivery, birth weight of infants, and any complications during pregnancy or childbirth.

Infant Follow-Up: HIV status of infants at birth and subsequent intervals, breastfeeding practices, and overall health status.

Data Analysis

Data was analyzed using statistical methods suitable for clinical research. The primary focus was on assessing the rate of vertical transmission of HIV from mothers to infants and evaluating the effectiveness of HAART in this context. Secondary analyses included examining the relationship between the timing and adherence to HAART during

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pregnancy and breastfeeding practices, and their impact on both maternal and infant health outcomes.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Andhra Medical College and King George Hospital,Visakhapatnam. All participants provided informed consent, and the study was conducted in accordance with ethical standards for clinical research. Confidentiality of patient information was strictly maintained throughout the study.

RESULTS

During the study period, 130 women undergoing Highly Active Antiretroviral Therapy (HAART) gave birth to 150 infants. This group included 5 sets of twins and 15 siblings, as 15 mothers experienced a second pregnancy during the study, three of which resulted in twins. The infants were typically monitored for a period of 20.5 months, with the majority (87%) being followed for at least a year.

The average duration for which mothers had been receiving HAART before giving birth was approximately 22.4 months. Twenty-five mothers began HAART during their pregnancy, with an average treatment duration of 6.1 months before delivery. Close to the time of delivery, 12 mothers had measurable viral loads, varying between 4,500 to 350,000 copies/mL, typically identified about 28 days before or after delivery(Table No. 1).

A significant majority (95%) of the mothers breastfed their infants exclusively for an average of 5.3 months, ceasing breastfeeding at about 6.2 months. At the age of 6 months, over half of the infants had been weaned, with 28% still exclusively breastfed, and 15% receiving a mix of breast milk and other foods or liquids.

Out of 150 infants, 146 were tested for HIV using DNA or RNA PCR tests, and none were found positive by the end of the study or before any deaths occurred. Four infants, who passed away before testing could be conducted, were between 10 and 60 days old; two of these had negative HIV ELISA tests shortly after birth.

The PCR results for 130 of the 146 tested infants (89%) were definitive. This group included infants who were never breastfed or had stopped breastfeeding for at least six weeks. The remaining 16 results were inconclusive, with six from infants still breastfeeding at their last test and ten from deceased infants, some of whom were still breastfeeding or had been weaned shortly before testing. A notable portion of these infants with inconclusive results (63%) died with severe gastrointestinal symptoms.

The study observed 21 infant deaths, accounting for 14% of the total infants. The median age at death was around 4.1 months. None of the 17 infants who underwent PCR testing before death were HIV positive, but most of these results were not definitive. The average duration of exclusive and total breastfeeding among the deceased infants was 3.2 and 4.0 months, respectively. The majority of the deceased infants showed symptoms of gastroenteritis in the week before their death, with some also displaying respiratory symptoms or fever and convulsions(Table No. 2).

An analysis of infant mortality in relation to breastfeeding status revealed a significantly lower survival rate among infants who were weaned or never breastfed compared to those still breastfeeding. A Cox proportional hazards model indicated that longer periods of exclusive and total breastfeeding were inversely associated with infant mortality. The model also considered maternal death but found no significant correlation between it and infant mortality. However, infants breastfed for less than six months faced a higher mortality risk, suggesting the protective nature of prolonged breastfeeding against infant mortality(Table No. 3).

Table 1: Characteristics of Study Participants

Parameter	Value
Total Infants	150
Total Women	130
Twins	5 pairs
Siblings (Second Pregnancy)	15
Median Follow-up (Months)	20.5 (IQR: 11.2-29.7)
Children Followed for ≥ 12 Months (%)	87% (104/120)
Mothers' Median Time on HAART (Months)	22.4 (IQR: 15.3-30.6)
Started HAART During Pregnancy (%)	25 (of 130)
Detectable Viral Loads (%)	12 (of 130)
Median Time to Detectable VL (Days)	28 (IQR: 12-50)
Exclusive Breastfeeding (%)	95% (143/150)
Median Duration of Exclusive BF (Months)	5.3 (IQR: 4.1-7.2)
Median Age at Stopping BF (Months)	6.2 (IQR: 4.2-8.0)
Weaned at 6 Months (%)	52% (78/150)
Still Exclusively BF at 6 Months (%)	28% (42/150)
Receiving Mixed Feeding at 6 Months (%)	15% (22/150)

Table 2: Infant Testing and Mortality

Parameter	Value
Infants Tested by HIV DNA/RNA PCR (%)	97% (146/150)
HIV Positive Infants by End of Follow-up	0 (of 146)

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Infants Tested by PCR Before Death (%)	11% (17/150)
HIV Positive Infants Tested Before Death	0 (of 17)
Infant Mortality (%)	14% (21/150)
Median Age at Death (Months)	4.1 (IQR: 2.3-9.1)
Never Breastfed (%)	4 (of 21)
Weaned Before Death (%)	12 (of 21)
Died During Exclusive BF (%)	3 (of 21)
Died During Mixed Feeding (%)	2 (of 21)
Symptoms Before Death	Gastroenteritis (81%), Respiratory (52%), Fever/Convulsions (14%)

Table No. 3: Factors Associated with Infant Mortality (Multivariate Analysis)

Factor	Hazard Ratio (HR)	95% CI	p-value
Duration of Exclusive Breastfeeding (EBF)	0.65	0.51-0.82	0.001
Duration of Total Breastfeeding (TBF)	0.67	0.55-0.82	<0.001
Maternal Death	7.25	1.09-48.6	0.04
Maternal Viral Loads	1.25	1.02-1.54	0.18
CD4 Counts	300	280-320	0.12
Maternal Marital Status	Married	N/A	N/A

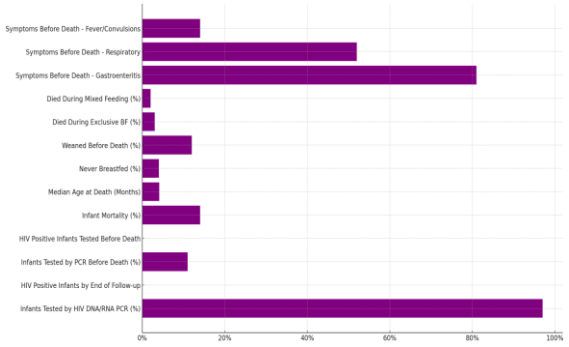

Figure 1: Infant Testing and Mortality

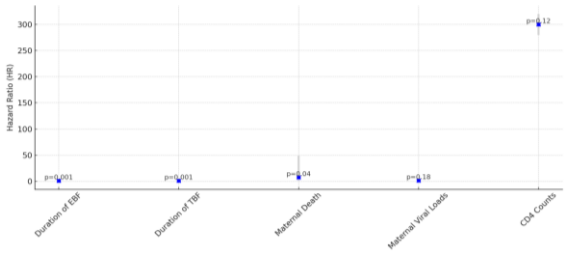

Figure 2: Factors Associated with Infant Mortality(Multivariate Analysis)

DISCUSSION

Effectiveness of HAART in Reducing Vertical HIV Transmission

The results of this study are consistent with findings by Siemieniuk RAC et al[1]. and Wang et al[2]., which highlight the significant role of Highly Active Antiretroviral Therapy (HAART) in reducing vertical transmission of HIV from pregnant women to their infants. Similar to our findings, where no HIV was detected in infants at the end of the study, these studies underscore the efficacy of HAART when properly administered and adhered to. This is particularly relevant considering the global burden of HIV and the critical need for effective interventions in maternal health.

HAART and Breastfeeding Practices

Our observation that adherence to HAART during breastfeeding is crucial in reducing both infant mortality and HIV transmission echoes the findings of Rosa MC et al[3].and Fowler MG et al[4]., who also reported on the safety and effectiveness of breastfeeding in the context of maternal HAART. This challenges earlier concerns about breastfeeding among HIV-positive mothers, as noted by Gamell A et al[10]. and reinforces the notion that with effective HAART, breastfeeding can be a viable and safe option.

Challenges and Recommendations

The study identifies the challenge of initiating postpartum maternal HAART, aligning with observations made by Lyatuu GW et al[6]. and Lyatuu GW et al[7]. regarding the risk of multiclass drug resistance. This emphasizes the need for careful monitoring and timing of HAART initiation as suggested by Naburi H et al[9].and Schnippel K et al[12]. Healthcare providers should tailor HAART regimens to balance the safety of the infant and the effectiveness of the treatment.

Global Health Implications

Our findings have significant global health implications, particularly in resource-limited settings where the burden of HIV is highest. This study contributes to the evidence base, supporting public health policies and clinical guidelines, potentially transforming the approach to managing HIV in pregnant and breastfeeding women. This aligns with the systematic review by Gumede-Moyo S et al[11]., which emphasizes the importance of implementing effective prevention strategies. The need for comprehensive care strategies that integrate both antiretroviral treatment and breastfeeding guidance, as shown in our study, is also highlighted in the work by Verma U et al[13] and Irshad U et al[14] who stress the importance of a holistic approach to managing maternal HIV.

Moreover, the study's findings are in line with Cardenas MC et al[15]., who recap the journey so far in the prevention of vertical HIV transmission,

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underscoring the ongoing need for effective strategies in this area. Our study contributes to this body of knowledge by providing specific insights into the role of HAART and breastfeeding practices in reducing infant mortality and HIV transmission rates, particularly in HIV-positive mothers.

Limitations and Future Research

While the study provides important insights, it is not without limitations. The single-center nature and the relatively small sample size may affect the generalizability of the findings. Future research should aim to replicate these findings in a multi-center study with a larger and more diverse population. Additionally, long-term follow-up studies are needed to understand the impact of maternal HAART on children as they grow, particularly regarding their long-term HIV status and overall health.

CONCLUSION

This study contributes significantly to our understanding of preventing vertical HIV transmission. The integration of Highly Active Antiretroviral Therapy (HAART) with suitable breastfeeding practices emerges as a potent approach to diminish both infant mortality and HIV transmission rates in HIV-positive mothers. This research lays the groundwork for developing more comprehensive and effective care strategies, holding extensive implications for improving maternal and child health in the milieu of HIV/AIDS.

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