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ORIGINAL ARTICLE

Determinants of small for gestational age among HIV exposed infants delivered at the Women and Newborn hospital, Lusaka, Zambia

Ndui A[1], Kasonka L[1], Vwalika B[2]

[1]*University Teaching Hospitals, Women and Newborn Hospital, Lusaka – Zambia*

[2]*University of Zambia, School of Medicine, Department of Obstetrics and Gynaecology, Lusaka - Zambia*

ABSTRACT

Objectives: To explore the factors that influence small for gestational age outcome among HIV exposed infants delivered at the Women and Newborn Hospital, Lusaka, Zambia.

Materials and Methods*:* This was a facility-based unmatched case control study nested in the Zambia Preterm Birth Prevention Study (ZAPPS) conducted at the Women and Newborn Hospital in Lusaka district between October 2017 and February 2021. Convenience sampling was used to select all the 53 HIV exposed small for gestational age infants (as cases) and 152 HIV unexposed small for gestational age infants (as controls). An excel data extraction tool was used to extract categorised variables from the ZAPPS data set into Stata version 13. Chi-square test was used to test for association, foetal and maternal variables with a p-value of 0.2 at univariate analyses were entered into a multiple logistic regression model.

Results: The proportion of SGA, though not statistically significant, was found to be19.9% among the HIV exposed infants compared to 17, 3% in the unexposed group (p= 0.34). More than three quarters of participants in both the HIV positive arm (71.7%) and HIV negative arm (81.3%) were aged between 20-35years. On multivariate analysis, Maternal chronic illness [AOR: 4.39, 95% CI :(1.66- 11.6), p=0.003] and spontaneous preterm delivery[AOR: 1.58, 95% CI :(1.02 - 2.46), p=0.040] had a strong association with small for gestational age. Tertiary level of education [AOR: 0.45, (0.24 - 0.85), p=0.014] was found to be significantly protective against small for gestational age. Maternal factors such as married status [AOR: 0.74, (0.48 - 1.13), p=0.164], secondary level of education [AOR: 0.82, (0.54 - 1.24), p=0.743], history of stillbirth [AOR: 1.31, (0.92-1.85), p=0.123] and the mid-upper arm circumference [AOR: 0.96, (0.92-1.00), p=0.064] was not associated with small for gestational age.

Conclusion: There was no association between maternal HIV infection and SGA. Maternal chronic illness and spontaneous preterm birth increase the odds of SGA outcome while tertiary level of education is protective. Further research is needed to broaden the evidence base for addressing small for gestational age as a gateway to improve perinatal mortality, and for policy implementers to devise

Corresponding Author:
Augustus Ndui,
University Teaching Hospital,
Women and Newborn Hospital,
PO Box RW 1X, Lusaka,
Email: nduiaugustus@yahoo.com

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cost-effective and sustainable ways of reaching the at-risk population.

INTRODUCTION

Small for gestational age (SGA) is defined as weight below the 10th percentile for the gestational age compared to a gender-specific reference population.[1]SGA is an important global problem with consequences for child survival, health, growth and development, and is even a more critical problem for low and middle-income countries like Zambia with high perinatal mortality.[2]SGA is a major health problem due to its association with increased risk of neonatal and infant death, non-communicable diseases and growth retardation.[3]

A pooled analysis of datasets from middle and low income countries showed that SGA was associated with increased risk of neonatal mortality compared to appropriate for gestational age infants.[4]This risk of morbidity and mortality increases further as the SGA infant becomes more preterm.[5]Globally, it is estimated that 32.4 million infants were born SGA in low and middle-income countries with Sub-Saharan Africa accounting for 43% of SGA infants globally.[6] In low to middle income countries like Zambia, some researchers estimate that the prevalence of SGA may be as high as twice the prevalence of low birthweight births.[7]

The factors that influence SGA outcome in women delivering in Lusaka at the Women and Newborn hospital remains unknown. Deciphering the foetal and maternal characteristics that are associated with small for gestational age outcome in HIV exposed infants is an essential step to reduce the high perinatal morbidity and mortality which is very high for Zambia. This research will broaden the evidence base for addressing the scourge of SGA as a gateway to improve the perinatal morbidity and mortality and enable policy implementers to devise cost-effective ways of reaching the at-risk population.

MATERIALS AND METHODS

This was a facility-based case control study nested in the Zambia Preterm Birth Prevention Study (ZAPPS). The ZAPPS study was an observational cohort study at the Women and Newborn Hospital, Lusaka, Zambia that recruited 1450 mother/infant pairs for the sole purpose of characterising the determinants of adverse birth outcomes. A total of 205 mother-infant pairs met the inclusion criteria of our study; comprising 53 SGA infants born to mothers with HIV and 152 HIV unexposed SGA infants. Where data was missing, the numbers of available observations were reported. All baseline data was categorised and association tested with the Chi-square test. All variables with $p< 0.20$ on univariate analysis were included in the final multivariable logistic regression. Stata version 13 was used for data analysis.

RESULTS

Descriptive variables were subjected to Chi-square, univariate and multiple regression models. A p-value of 0.05 was considered statistically significant.

Table1: Baseline characteristics of the study participants

Variable	HIV positive SGA N (%)	HIV negative SGA N (%)	Total N (%)
Maternal age (years)			
	4 (7.55)	5 (2.36)	9 (3.4)
	38 (71.7)	172 (81.3)	210 (79.3)
	11 (20.8)	35 (16.5)	46 (17.4)
Marital status			
Not married	12 (22.6)	27 (12.8)	39 (14.8)
Married	41 (77.4)	184 (87.2)	225 (85.2)
Education level			
Primary	20 (37.7)	50 (23.7)	70 (26.5)
Secondary	31 (58.5)	146 (69.2)	177 (67.1)
Tertiary	2 (3.8)	15 (7.1)	17 (6.4)
Employment status			
Unemployed	28 (52.8)	107 (50.0)	135 (50.6)
Employed	25 (47.2)	107 (50.0)	132 (49.4)
Preterm delivery			
No	45 (84.9)	185 (86.5)	230 (86.1)
Yes	8 (15.1)	29 (13.6)	37 (13.9)
Body mass index			
Low	2 (3.9)	11 (5.4)	13 (5.1)
Normal	46 (90.2)	166 (81.1)	212 (83.1)
High	3 (5.9)	27 (13.24)	30 (11.8)
Abuse in pregnancy			
No	52 (98.1)	205 (97.6)	257 (97.7)
Yes	1 (1.89)	5 (2.4)	6 (2.3)
Anaemia in pregnancy	31 (77.5)	113 (75.8)	144 (76.2)
No	9 (22.5)	36 (24.2)	45 (23.8)
Yes			
Hypertension			
No	44 (86.3)	186 (89.9)	230 (89.2)
Yes	7 (13.7)	21 (10.1)	28 (10.9)

HIV=Human immunodeficiency virus, SGA= small for gestational age

Table 2: Relationship between HIV and small for gestational age

Variable	HIV exposed + SGA (%)	HIV unexposed + SGA (%)	P value
Maternal age			
<20	4(7.6)	5(2.4)	0.118
20-35	38(71.7)	172(81.1)	
>35	11(20.6)	35(16.5)	
Marital status			
Single	12(22.6)	27(12.8)	0.071
Married	41(77.4)	184(87.2)	
Education level			
Primary	20(37.7)	50(23.7)	0.100
Secondary	31(58.5)	146(69.2)	
Tertiary	2(3.4)	15(7.1)	
Employment			
Unemployed	28(52.8)	107(50)	0.712
Employed	25(47.2)	107(50)	
Gravidity			
1	11(20.8)	25(11.7)	0.102
2-3	21(39.6)	115(53.7)	
>4	21(39.6)	74(34.6)	
Body Mass Index			
Low	2(3.9)	11(5.4)	0.297
Normal	46(90.2)	166(81.4)	
High	3(5.8)	27(13.2)	
Abuse in pregnancy	1(1.9)	5(2.4)	0.830
Yes	52(98.1)	205(97.6)	
No			
Anaemia in pregnancy	9(22.5)	36(24.2)	0.827
Yes	31(77.5)	113(75.8)	
No			
Hypertension			
Yes	7(13.7)	21(10.1)	0.462
No	44(87.3)	186(89.9)	
Birth interval			
<24 months	8(21.6)	28(18.8)	0.697
>24 months	29(78.4)	121(81.2)	
Preterm Delivery			
Preterm	8(15.1)	29(13.6)	0.771
Term	45(84.9)	185(86.4)	
Infant sex			
Male	27(51.9)	103(48.8)	0.190
Female	25(48.1)	108(51.2)	

Table 3: Univariate analysis for foetal and maternal determinants of small for gestational age

Variable	COR	95% CI	P-value
Parity	1.01	0.91 – 1.13	0.836
Gravidity	1.03	0.93 – 1.13	***0.190***
Maternal age			
	Ref		
	0.91	0.49 - 1.71	0.776
	1.19	0.58 – 2.42	0.640
Marital status			
Single	Ref		
Married	0.69	0.47 – 1.02	***0.060***
Education level			
Primary	Ref		
Secondary	0.87	0.59 – 1.28	0.486
Tertiary	0.47	0.26 – 0.87	***0.016***
History of abuse			
No	Ref		
Yes	1.99	1.10 – 3.57	***0.022***
MUAC			
<23	0.94	0.90 – 0.98	***0.003***
≥23	Ref		
Chronic illness			
No	Ref		
Yes	3.84	1.49 – 9.84	***0.005***
HIV status			
Negative	Ref		
Positive	1.18	0.84 – 1.68	0.340
Preterm delivery			
No	Ref		
Yes	1.69	1.13 – 2.52	***0.011***
Prior stillbirth			
No	Ref		
Yes	1.44	1.06 – 1.97	***0.020***
Birth interval			
< 24months	Ref		
≥24months	1.32	0.82 – 2.10	0.253

COR = Crude odds ratio; CI = Confidence interval; Ref = Reference category; MUAC = mid-upper arm circumference

Table 4: Multivariable logistic regression analysis for determinants of small for gestational age among HIV exposed infants

Variable	AOR	95% CI	P-value
Marital status			
Not married	Ref		
Married	0.74	0.48 – 1.13	0.164
Education level			
Primary	Ref		
Secondary	0.82	0.54– 1.24	0.342
Tertiary	0.45	0.24 – 0.95	***0.014***
History of abuse			
No	Ref		
Yes	1.76	0.94 – 3.28	0.077
Preterm Birth			
No	Ref		
Yes	1.58	1.02 – 2.46	***0.040***
Prior stillbirth			
No	Ref		
Yes	1.31	0.92 – 1.85	0.123
Chronic illness			
No	Ref		
Yes	4.39	1.66 – 11.6	***0.003***
Birth interval			
>24 months	Ref		
<24 months	1.01	0.58 – 1.76	0.979

MUAC = Mid-upper arm circumference, AOR = Adjusted odds ratio

DISCUSSION

This study found a significant associationbetween maternal chronic illness and preterm spontaneous delivery with SGA outcome in HIV exposed neonates. Maternal HIV infection does not increase the likelihood of SGA outcome, and the odds of an SGA outcome are similar among the HIV exposed and unexposed infants. Attaining tertiary level of education was found to be protective while primary level of education was associated with increased odds of SGA neonate.

Maternal HIV infection does not increase the odds of an SGA outcome (p = 0.340).This is attributed to Maternal antiretroviral treatment that was started early in pregnancy of the participants, which improved immunological status in the mothers thereby improving nutrient supply to the foetus and ultimately, results in improved foetal weight and decreases the occurrence of SGA.[8] Additionally, only stable patients on treatment for the HIV were recruited and all received standard antenatal care which may have influenced results.[9]This is in conflict with numerous other studies that found significant association between maternal HIV infection and increased odds of SGA outcome.[10,11]

Small for gestational age was strongly associated with spontaneous preterm birth [AOR: 1.58, 95% CI:(1.02 - 2.46), p=0.040] in line with findings from a global study done in the United States of America.[4]Although there is no causation link between SGA and prematurity, compromised foetuses are more likely to be delivered earlier (preterm) to avoid intrauterine demise. These infants may eventually succumb to effects of prematurity rather than SGA.[12] Global studies indicate that SGA infants in Africa and Zambia in particular are born at a later gestational age, that is, more than 30 weeks, which is consistent with our findings.[9]

Chronic maternal illness [AOR: 4.39, 95%CI :(1.66- 11.6), p=0.003] had a significant association with SGA. Main chronic conditions that contributed to this aggregate variable were chronic hypertension, maternal anaemia and diabetes. The primary pathologies lead to a common pathway, which is impaired foetal nutritional supply at placental level.[13] Chronic hypertension is a significant independent contributor to SGA but not to spontaneous preterm birth, the incidence of chronic hypertension increasing with maternal age and weight.[14] The relationship between maternal anaemia during pregnancy and SGA was not significant contrary to other studies that found significant association between first trimester maternal anaemia and SGA.[15]

Tertiary level of education was protective, and exhibited an inverse relationship with the likelihood of SGA outcome. Epidemiological studies have reported that the higher the level of education of the pregnant women, the less the odds of delivering a small for gestational age infant.[8] Low maternal education level is associated with low financial power, limited ability to purchase right food to meet

daily nutritional requirements and inability to make independent decisions concerning pregnancy health.[16]

In this study, there was no significant difference in the body mass index and mid-upper arm circumference (MUAC) between HIV infected mothers and their negative counterparts implying similar nutritional states. This may explain the lack of significant association between the MUAC, BMIand SGA outcome after adjusting for confounders. This is contrary to other studies that found that low body mass index, low MUAC and lowmaternal weight gain increased the odds of SGA.[17,18]

Our study demonstrated that maternal age, gravidity, parity,marital status, wealth index, prior still birth and delivery interval were not significantly associated with SGA contrary to findings from other epidemiological studies that established strong relationship between the aforementioned variables and increased odds of SGA outcome.[5,8,19,20]

CONCLUSION

Maternal HIV exposure does not increase the odds of an SGA outcome. Preterm birth, maternal chronic illness and preterm birth increase the likelihood of SGA outcome in the HIV exposed infants. To deal with the scourge of SGA, prompt control of chronic illnesses in pregnancy and addressing spontaneous preterm labour will improve outcomes of SGA infants. More effort is needed with other line ministries to encourage women education, as this is protective against SGA and other adverse pregnancy outcomes.

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