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The prevalence of and risk factors for stillbirths in women with severe preeclampsia in a high-burden setting at Mpilo Central Hospital, Bulawayo, Zimbabwe

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Abstract

Objectives: Stillbirth remains a global public health issue; in low-resource settings stillbirth rates remain high (>12 per 1,000 births target of Every Newborn Action Plan). Preeclampsia is major risk factor for stillbirths. This study aimed to determine the prevalence and risk factors for stillbirth amongst women with severe preeclampsia at Mpilo Central Hospital.

Methods: A retrospective cross-sectional study was conducted of women with severe preeclampsia from 01/01/2016 to 31/12/2018 at Mpilo Central Hospital, Bulawayo, Zimbabwe. Multivariable logistic regression was used to determine risk factors that were independently associated with stillbirths.

Results: Of 469 women that met the inclusion criteria, 46 had a stillbirth giving a stillbirth prevalence of 9.8%. The risk factors for stillbirths in women with severe preeclampsia were: unbooked status (adjusted odds ratio (aOR) 3.01, 95% (confidence interval) CI 2.20–9.10), frontal headaches (aOR 2.33, 95% CI 0.14–5.78), vaginal bleeding with abdominal pain (aOR 4.71, 95% CI 1.12–19.94), diastolic blood pressure ≥150 mmHg (aOR 15.04, 95% CI 1.78–126.79), platelet count $0–49 \times 10^9$/L (aOR 2.80, 95% CI 1.26–6.21), platelet count $50–99 \times 10^9$/L (aOR 2.48, 95% CI 0.99–6.18), antepartum haemorrhage (aOR 12.71, 95% CI 4.15–38.96), haemolysis elevated liver enzymes syndrome (HELLP) (aOR 6.02, 95% CI 2.22–16.33) and fetal sex (aOR 2.75, 95% CI 1.37–5.53).

Conclusions: Women with severe preeclampsia are at significantly increased risk of stillbirth. This study has identified risk factors for stillbirth in this high-risk population; which we hope could be used by clinicians to reduce the burden of stillbirths in women with severe preeclampsia.

Keywords: low-resourced countries; multivariable logistic regression; prevalence; risk factors; stillbirths.

Introduction

Stillbirths remain a major global concern with a reported estimate of 2.6 million third trimester stillbirths having occurred in 2015 [1]. This figure remains unacceptably high [2]. The majority of stillbirths, nearly 98% occur in low- and middle-income countries (LMICs) [3]. Stillbirths have widespread negative effects on parental mental health [4]. One important cause of stillbirths in LMICs is preeclampsia, where studies from Ghana [5], Zimbabwe [6], and Nigeria highlight that women with preeclampsia were eight times more likely to experience stillbirths (adjusted odds ratio (aOR) 8.24, 95% confidence interval (CI) 3.01–22.51) [7]. Other important causes of stillbirths include malaria, syphilis, prematurity, antepartum haemorrhage, placental abruption, maternal age older than 35 years and unspecified bacterial infections [1, 5–8].

Sub-Saharan Africa has some of the highest rates of stillbirth. In Zimbabwe, the prevalence of stillbirth was found to be 3.0% at Mpilo Central Hospital [6] and in Northern Tanzania it was found to be 3.6% [8]. There have been efforts to reduce stillbirths to meet the targets set by the Every Newborn Action Plan (<12 per 1,000 births). At a low-resource setting in Zimbabwe, clinical leadership and accountability was found to reduce fresh full-term

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intrapartum stillbirths [9]. Access to planned and emergency caesarean sections have been found to reduce stillbirths [9–11]. If effective intervention(s) could be targeted to women at greatest risk of stillbirth, then it is anticipated that the stillbirth rate would decrease. Therefore, the aim of this study was to determine the prevalence of and risk factors for stillbirths amongst women with severe preeclampsia in a low resource setting. It was hypothesised that there would be risk factors for stillbirth in women with severe preeclampsia.

Materials and methods

This sub-analysis was part of a doctoral research programme. The main study was a retrospective cross-sectional study of all women with severe preeclampsia covering the period January 1, 2016 to December 31, 2018, at Mpilo Central Hospital, Bulawayo, Zimbabwe. Therefore, some of the participants include in this sub-analysis were also analysed in prior studies on the same subject of severe preeclampsia [12–19]. This sub-analysis only included women who were above 28 weeks' gestation, so that if their babies demised, they met the WHO definition of a stillbirth [20].

The outcome measure was birth outcome. A stillbirth was defined as a baby born after 28 weeks' of gestation without signs of life as appropriate for low-resourced countries. Severe preeclampsia was defined here as systolic blood pressure ≥160 mmHg, diastolic blood pressure ≥110 mmHg or there was hypertension ≥140/90 mmHg in the presence of proteinuria or abnormal biochemical or haematological blood indices [15, 21]. Data regarding socio-demographic information, past obstetric history, maternal signs and symptoms, laboratory test results, maternal complications, birth-weight and fetal sex were obtained from the clinical records. The Mpilo Ethics Committee and the Medical Research Council of Zimbabwe approved the research programme, approval number MRCZ/A/2483.

Statistical analysis

The analysis was done on SPSS Version 20 (IBM, Armonk, NY, USA). The sample of the main study was 549 [18]. Women that were below 28 weeks' of gestation were excluded, leaving a sample of 469 women to be included in this analysis. Descriptive statistics are presented as frequencies and percentages for categorical variables and median and interquartile ranges as the data were not normally distributed. Bivariate correlations of association between main independent variables and the outcome measure were done using Pearson 2-tailed chi-square test. Those variables with a p-value of <0.2 were considered for the univariate logistic regression to calculate univariate odds ratios (OR). Variables that were statistically significant (p<0.05) were considered for multivariate logistic regression to calculate adjusted odds ratios (aOR). The independent association of these variables was assessed using multivariable analysis, with Hosmer–Lemeshow goodness-of-fit and 95% confidence intervals used to identify independent risk factors for stillbirths. A p<0.05 was taken as statistically significant.

Results

There were 46 stillbirths out of the 469 women that met the inclusion criteria, giving a stillbirth prevalence of 9.8% amongst women with severe preeclampsia. 31 (67.4%) of the stillbirths were male and 15 (32.6%) were female.

Women who had a stillbirth differed in terms of maternal age (p=0.002), gravidity (p=0.01), parity (p=0.01), and gestational age (p<0.0001) from those who had a live born baby. The rest of the results of the statistical differences can be seen in Table 1.

Table 2 shows the univariate and multivariate analysis of predictor variables and stillbirths. Unbooked status was

Table 1: Socio-demographic characteristics of women with severe preeclampsia included in the analysis (n=469).

Characteristic	With a stillbirth n=46	Without a stillbirth n=423	p-Value
Maternal age, years	32 [23–35]	25 [20–32.6]	0.002
Gravidity	2 [2–4]	2 [1–3]	0.010
Parity	1 [1–3]	1 [0–2]	0.01
Gestational age on admission, weeks	32 [30–33]	34 [31–37]	<0.0001
Marital status			
Single	19 (41.3%)	188 (44.4%)	
Married	27 (58.7%)	235 (55.6%)	0.39
Educational status			
None or primary	32 (69.6%)	304 (72.0%)	
Secondary	13 (28.3%)	114 (27.0%)	
Tertiary	1 (2.2%)	5 (1.0%)	0.24
HIV status			
Negative	33 (71.7%)	342 (80.9%)	
Positive	4 (8.7%)	44 (10.4%)	
Unknown	9 (19.6%)	37 (8.7%)	0.10
Antiviral therapy			
No	41 (89.1%)	375 (88.7%)	
Yes	5 (10.9%)	48 (11.3%)	0.91
Booked	25 (54.3%)	339 (80.1%)	<0.0001
Referred	22 (47.8%)	253 (59.8%)	0.12
Unbooked	17 (37.0%)	75 (17.7%)	0.002
Aspirin	1 (2.2%)	3 (0.7%)	0.31
Past obstetrics history	6 (13.0%)	28 (6.6%)	0.11
Dwelling			
Urban	28 (60.9%)	277 (65.5%)	
Rural	18 (39.1%)	146 (34.5%)	0.53

HIV, human immunodeficiency virus.

Table 2: Univariate and multivariate analysis between independent variables and stillbirths.

Variable	Stillbirths n=46	Without stillbirths n=423	Univariate odds ratio	95% confidence interval		p-Value	Adjusted odds ratio	95% confidence interval		p-Value
				Lower	Upper			Lower	Upper	
Age, years										
14–19	2 (4.3%)	86 (20.4%)	2.90	1.01	21.32	0.05	0.75	0.09	6.50	0.80
20–24	12 (26.1%)	112 (26.4%)	3.03	0.40	12.54	0.36	5.56	0.87	35.38	0.07
25–29	4 (8.7%)	77 (18.2%)	8.90	1.90	38.84	0.005	2.28	0.26	19.76	0.45
30–34	15 (32.6%)	75 (17.7%)	10.67	1.67	35.05	0.01	6.49	0.71	59.60	0.10
≥35	13 (28.3%)	73 (17.3%)	Reference							
Parity										
0	10 (21.7%)	178 (42.1%)	3.28	1.28	6.87	0.01	1.41	0.36	5.52	0.62
1	15 (32.6%)	90 (21.3%)	2.81	0.81	5.32	0.13	1.20	0.24	6.06	0.82
2	9 (19.6%)	77 (18.2%)	4.14	1.14	6.61	0.03	1.12	0.14	9.21	0.92
3+	12 (26.1%)	78 (18.4%)	Reference							
Gestational age, weeks										
28–29	26 (56.5%)	142 (33.6%)	1.40	0.40	1.99		1.18	0.49	2.87	0.72
30–33	6 (13.0%)	130 (30.7%)	1.05	0.08	1.66		0.38	0.12	1.18	0.09
34–37	4 (8.7%)	91 (21.5%)	0.08	0.06	0.72	0.79	0.42	0.11	1.57	0.20
38–40	5 (10.9%)	11 (2.6%)	n/a	n/a	n/a		n/a	n/a	n/a	n/a
≥40	5 (10.9%)	49 (11.6%)	Reference							
HIV status										
Negative	33 (71.7%)	342 (80.9%)	Reference							
Positive	4 (8.7%)	44 (10.4%)	1.32	0.32	2.79	0.01	0.41	0.11	1.66	0.21
Unknown	9 (19.6%)	37 (8.7%)	2.12	1.12	5.67		0.67	0.20	2.26	0.51
Unbooked										
No	29 (63.0%)	347 (82.0%)	Reference							
Yes	17 (37.0%)	76 (18.0%)	3.42	1.42	5.19	0.91	3.01	2.20	9.10	0.05
Referred										
No	24 (52.2%)	170 (40.2%)	Reference							
Yes	22 (47.8%)	253 (59.8%)	0.48	0.34	1.13	0.03	1.44	0.55	3.76	0.46
Past obstetrics history										
No	40 (87.0%)	393 (93.3%)	Reference							
Yes	6 (13.0%)	28 (6.7%)	3.42	0.82	5.40	0.003	2.00	0.67	5.99	0.22
Frontal headaches										
No	33 (71.7%)	212 (50.1%)	Reference							
Yes	13 (28.3%)	211 (49.9%)	2.40	0.20	4.77	0.01	2.33	0.14	5.78	0.01
Epigastric pains										
No	41 (89.1%)	330 (78.0%)	Reference							
Yes	5 (10.9%)	93 (22.0%)	0.43	0.17	1.13	0.09	1.06	0.35	3.22	0.92
Vaginal bleeding with abdominal pain										
No	41. (89.1%)	414 (97.9%)	Reference							
Yes	5 (10.9%)	9 (2.1%)	5.61	1.80	17.53	0.003	4.71	1.12	19.94	0.04
Systolic blood pressure										
≤160 mmHg	13 (28.3%)	157 (37.1%)	Reference							
161–180 mmHg	18 (39.1%)	162 (38.3%)	1.34	0.64	2.83	0.44				
181–200 mmHg	9 (19.6%)	76 (18.0%)	1.43	0.59	3.49	0.43				
≥201 mmHg	6 (13.0%)	28 (6.6%)	2.59	0.91	7.38	0.08	n/a			
Diastolic blood pressure										
≤110 mmHg	11 (23.9%)	164 (38.8%)	Reference							
111–130 mmHg	25 (54.3%)	214 (50.6%)	1.74	0.83	3.64	0.14	1.66	0.68	4.09	0.27
131–150 mmHg	5 (10.9%)	38 (9.0%)	1.96	0.64	5.98	0.24	2.37	0.62	9.01	0.21
≥151 mmHg	5 (10.9%)	7 (1.6%)	10.65	2.90	39.07	<0.0001	15.04	1.78	126.79	0.01

Table 2: (continued)

Variable	Stillbirths n=46	Without stillbirths n=423	Univariate odds ratio	95% confidence interval		p-Value	Adjusted odds ratio	95% confidence interval		p-Value
				Lower	Upper			Lower	Upper	
Platelet count/$\times 10^9$/L										
0–49	4 (8.7%)	36 (8.5%)	Reference							
50–99	13 (28.3%)	53 (12.5%)	3.36	1.58	7.17	0.02	2.80	1.26	6.21	0.01
100–149	8 (17.4%)	47 (11.1%)	2.33	0.97	5.60	0.06	2.48	0.99	6.18	0.05
≥150	21 (45.6%)	287 (67.9%)	1.52	0.49	4.70	0.47	1.44	0.45	4.61	0.54
Antepartum haemorrhage										
No	37 (80.4%)	415 (98.1%)	Reference							
Yes	9 (19.6%)	8 (1.9%)	12.62	4.60	34.65	<0.0001	12.71	4.15	38.96	<0.0001
HELLP syndrome										
No	38 (82.6%)	408 (96.5%)	Reference							
Yes	8 (17.4%)	15 (3.5%)	5.73	2.28	14.37	<0.0001	6.02	2.22	16.33	<0.0001
Fetal sex										
Female	15 (32.6%)	212 (50.1%)	Reference							
Male	31 (67.4%)	211 (49.9%)	2.08	1.09	3.96	0.03	2.75	1.37	5.53	0.004

HIV, human immunodeficiency virus; HELLP, haemolysis, elevated liver enzymes, low platelet count syndrome.

an independent risk factor for stillbirths in women with severe preeclampsia, who were 3 times more likely to experience a stillbirth compared to those that were booked for antenatal care (aOR 3.01, 95% CI 2.20–9.10, p=0.05). Women with frontal headaches and severe preeclampsia were 2 times more likely to suffer a stillbirth compared to those without frontal headaches (aOR 2.33, 95% CI 0.14–5.78, p=0.01). Women with vaginal bleeding with abdominal pain and severe preeclampsia were 5 times more likely to experience a stillbirth compared to those without vaginal bleeding with abdominal pain (aOR 4.71, 95% CI 1.12–19.94, p=0.04).

Women with diastolic blood pressure of ≥150 mmHg and severe preeclampsia were 15 times more likely to experience a stillbirth compared to those with diastolic blood pressure of <110 mmHg (aOR 15.04, 95% CI 1.78–126.79, p=0.01). Women with platelet count 0–49 $\times$ 10^9/L were 3 times more likely to suffer a stillbirth compared to those with platelet counts ≥150 $\times$ 10^9/L (aOR 2.80, 95% CI 1.26–6.21, p=0.01), whereas those with platelets count 50–99 $\times$ 10^9/L were 2.5 times more likely to suffer a stillbirth (aOR 2.48, 95% CI 0.99–6.18, p=0.05). Male babies were 3 times more likely to be stillborn compared to female babies (aOR 2.75, 95% CI 1.37–5.53, p=0.04).

Discussion

Information from this sub-analysis showed that the prevalence of stillbirths was 9.8% amongst women with severe preeclampsia, this confirms that this group of women are at a significantly increased risk of stillbirth. The stillbirth prevalence of 9.8% at Mpilo Central Hospital was similar to the 9.0% found in Nigeria, a similar low-resource setting [22]. Focussed efforts to improve the management of severe preeclampsia may have a positive impact on the number of stillbirths in low-resource settings. Such focussed efforts could entail the establishment of specialised antenatal services or emergency care for women who develop hypertensive disorders of pregnancy. The general prevalence of stillbirths at the hospital was 3.0% [6], but this study has revealed that amongst severe preeclampsia the prevalence of stillbirths was 9.8% which justifies the need for a more dedicated and focussed approach in these women to improve perinatal outcomes.

Strengths and limitations

The strength of this research was that it advanced our knowledge on two very important topics using a fairly large cohort of homogenous population of women with severe preeclampsia in a low-income setting. We anticipate that data from this cohort could be generalizable to similar settings in high-burden countries, particularly those in Sub-Saharan Africa. This is particularly important as there are few studies of this nature in the international literature. Nevertheless, being a single centre study limits the findings as there are likely differences in management protocols for severe preeclampsia between sites thereby altering outcomes between different hospitals.

Clinical interpretation

In common with other studies, this analysis revealed that unbooked women had significantly higher odds for stillbirths. John et al. in Nigeria, and Dube et al. in Zimbabwe showed in studies a positive correction between lack of proper antenatal care and adverse pregnancy outcome in unbooked patients [23, 24]. Another study in China found that the risk of stillbirth was higher in those who had received fewer antenatal care visits [25]. There is need to invest resources in making antenatal care universally affordable and accessible to all women in low-resource settings in order to reduce poor perinatal outcomes.

Women with severe preeclampsia and signs and symptoms of frontal headaches or vaginal bleeding with abdominal pain or diastolic blood pressure ≥150 mmHg should alert the attendant clinicians about the higher risks of stillbirths. A study in Botswana also showed that severe hypertension increased risk of stillbirth (RR 4.4; 95% CI 3.2–6.2) [26].

Our study actually showed that it is the diastolic blood pressure of ≥150 mmHg that carried greater odds at 15 times (aOR 15.04, 95% CI 1.78–126.79, p=0.01). This study therefore shows that the control of blood pressure in severe preeclampsia would help reduce the risks of stillbirths. The treatment of severe hypertension should be a high priority.

Parnas et al. showed that moderate to severe thrombocytopenia was associated with stillbirths in pregnancy [27], our study showed that in severe preeclampsia the odds were 2.5 times higher when platelets were <99. Our study revealed that antepartum haemorrhage (APH) and HELLP syndrome were also independent predictors of stillbirths in severe preeclampsia. A study in Thailand showed that stillbirths occurred in severe preeclampsia with severe features of HELLP syndrome [28]. In our study APH conferred high odds of 13 for stillbirths, and HELLP syndrome odds of 6 for stillbirths. This information is significant in that women with severe preeclampsia should be rigorously screened for complications, particularly HELLP syndrome. Thus, regular attendance at specialist services and intervention prior to development of severe complications such as HELLP syndrome could improve outcomes.

Male babies appear to have higher odds of stillbirths than female babies. In our study, male babies had 3 times higher risks than female babies (aOR 2.75, 955 CI 1.37–5.53, p=0.04). Zetterstrom et al. also found in their study that male babies had higher risks of stillbirths than female babies (aOR 3.07, 95% CI 2.12–4.46) vs. (aOR 0.98, 95% CI 0.51–1.89) [29]. Mondal et al. found the risk of stillbirth in males to be elevated by about 10% [30]. This could be possibly linked to the fact that male foetuses could have higher energy needs due to the maintenance of the energy-dependent blood-testicular barrier. Clinicians could use this information for risk assessment to make overall clinical decisions. Further studies are needed to discover the pathophysiology that leads to the observed differences in fetal outcome.

Conclusions

This study determined that the prevalence of stillbirths was increased in women with severe preeclampsia. Multivariable logistic regression identified independent risk factors for stillbirths in women with severe preeclampsia. These emphasise the importance of ensuring women book for and receive adequate antenatal care and that clinicians caring for women with severe preeclampsia recognise symptoms and clinical signs associated with stillbirth and intervene to control severe blood pressure. Focussed and dedicated antenatal clinics should be considered as a high priority by policy makers to reduce the burden of stillbirths on parents and the high global stillbirth deaths.

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Informed consent: Not applicable.

Ethical approval: The study was approved by relevant authorities as it was a PhD programme. The Mpilo Ethics Committee and the Medical Research Council of Zimbabwe approved the research programme, approval number MRCZ/A/2483.

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