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Time Intervalbetween Onset of Symptoms of Severe Preeclampsia to Delivery: Effect on Pregnancy Outcomes at Mbarara Regional Referral Hospital, South Western Uganda

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Abstract
Background: Hypertensive disorders of pregnancy (HDP) account for nearly 18% of all maternal deaths worldwide. Preeclampsia is a leading cause of direct maternal mortality worldwide, and the second in Uganda contributing about 9.1% of total maternal death. Expectant management of severe pre-eclampsia at 30–34 weeks is associated with good perinatal outcome and risk reduction for the mother. **Methods:** This was a retrospective cohort study done by reviewing maternal medical records from September 2009 to September 2011 and all mothers who had delivered at Mbarara Hospital with a diagnosis of severe pre-eclampsia (SPE) during study period were included in the study. **Results:** Primigravidae accounted for about 42.6% of the cases of severe pre-eclampsia studied and majority (66.7%) of the women were aged between 20-30 years. The overall good fetal outcome rate in this study was 47.5% and 68.3% of the women studied were more than 28 weeks of amenorrhoea and 31.2% had still births. The most common symptom was headache (47%) and over 35% of these women presented for delivery more than 72hours from onset of symptoms. Delivery between 0-18 hours was protective, (OR0.43, 95%CI : 0.29-0.5), p-value=0.013)**. Conclusions:** The complication rate associated with severe preeclampsia is high and worsens with longer duration of symptoms before delivery. Delivery within 18 hours of onset of symptoms is associated with good fetal outcomes and this stresses the importance of early presentation for care by the mothers and timely decision making by the clinicians.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) account for nearly 18% of all maternal deaths worldwide, with an estimated 62,000–77,000 deaths per year. The incidence of hypertensive disorders in pregnancy in a survey by WHO was found to be 2.73% with pre-eclampsia accounting for the bulk of these cases. However, data on the incidence of HDP are scarce, as shown in a recently published systematic review, [4] where just 74 studies from 40 countries reported the incidence of pre-eclampsia and eclampsia, only seven of these with data on national coverage. Preeclampsia is a leading cause of direct maternal mortality worldwide, and the second in Uganda contributing about 9.1% of total maternal death, only after haemorrhage and sepsis Maternal near-miss cases are eight times more frequent in women with pre-eclampsia, and increased to up to 60 times more frequent in women with eclampsia, when compared with women without these conditions[1'2]. Preeclampsia and eclampsia are major causes of fetal mortality and morbidity[9].

HDP fall into four categories: chronic (pre-existing) hypertension, gestational hypertension or pregnancy-induced hypertension (PIH), pre-eclampsia / eclampsia and pre-eclampsia superimposed on chronic hypertension[3]. For every woman who dies, it is estimated that 20 others suffer severe morbidity or disability[5]. The proportion of women surviving severe maternal complications (also called 'near-miss' cases) has been proposed as a useful gauge for the evaluation of the quality of maternal health care and its determinants, with the potential to complement the information obtained from the reviews of maternal deaths[6],[7].

The risk factors associated with a greater risk of severe preeclampsia and, or eclampsia include personal history of preeclampsia, personal history of pre-existing hypertension, primi-parity, and fewer than four antenatal care visits[8]. Expectant management of severe pre-eclampsia at 30–34 weeks is associated with good perinatal outcome and risk reduction for the mother[10].

In areas where careful intensive monitoring of the mother is possible these complications are relatively rare. Data are not sufficient to decide whether it is better to intervene or to apply a policy of expectant care for women with early onset of severe pre-eclampsia. Lack of human and material resources to monitor women intensively for a prolonged period may render expectant management difficult to implement in resource-poor settings. Expectant management of SPE in gestation age between 18-27 weeks was associated with perinatal mortality 87%, no mothers died, placental abruption, eclampsia, consumptive coagulopathy, renal failure, intracerebral haemorrhage, ruptured hepatic hematoma. SPE in gestation age between 28-32 week was associated with prolonged mean of 15.4 days of gestation sustained 4% placental abruption (Sibai et al, 1994).

Insufficient data for reliable conclusions on maternal and fetal outcome and there is need for in-depth

research on this topic (The Cochrane Database of Systematic Reviews 2002).
This study therefore aimed at determining the effect of time duration from onset of symptoms to delivery on maternal and perinatal outcomes of mothers at Mbarara Regional Referral Hospital (MRRH) and will therefore contribute towards evidence based recommendations on management protocols of severe preeclampsia in resource limited settings.

METHODS AND MATERIALS:

Study site: The study was conducted on maternity ward at Mbarara Regional Referral Hospital. The hospital is a 265 bed capacity and is government owned and funded through the ministry of Health and it doubles as a teaching hospital for Mbarara University faculty of medicine and regional referral hospital for south western Uganda. There is a neonatal intensive care unit on paediatrics ward and a busy maternity ward with labour suite, antenatal, postnatal wards and operating theatres. The hospital delivers about 10,000 mothers annually.
Study design: Retrospective cohort study was done by reviewing maternal medical records from September 2009 to September 2011.
Study population: All mothers who had delivered at MRRH from September 2009 to September 2011 with a diagnosis of severe pre-eclampsia (SPE) during study period were included in the study.
Outcome variables included the following**:**
*Maternal outcomes***:** Abruptio placenta, HELLP syndrome, loss of blood pressure control, severe renal impairment, eclampsia, admission to intensive care unit, pulmonary oedema and cerebrovascular incident, disseminated intravascular coagulopathy (DIC), intracerebral haemorrhage, ruptured hepatic hematoma, caesarean delivery, need for transfusion of blood products, and death.
*Fetal outcomes***:** Prematurity and its complications (including Respiratory Distress Syndrome, necrotising enterocolitis, LBW), intra uterine growth restriction, chronic fetal distress, intra uterine fetal death, early neonatal death.
Exposure variables: Maternal age, parity, previous preeclampsia, chronic hypertension, gestational age at diagnosis, blood platelet count and peak serum levels of aspartate aminotransferase, creatinine, uric acid and lactate dehydrogenase.
Sampling method and sample size calculation: Consecutive case sampling was done and a total of 105 cases were calculated using the Fleiss formula.
Data collection: Review of case records was done for those that met the criteria and target parameters were recorded on the data collection tool including patient demographics, signs and symptoms of PET severity and their duration, interventions, time interval between onset of symptoms and delivery, maternal and foetal outcomes and factors associated with the outcome. Good outcome was considered as a live mother without complications and a live baby without complications whether term or premature while a poor outcome was a maternal death or a live mother with complications and stillbirth or live baby with low Apgar score.
Statistical analysis plan: The data was entered in an EXCEL spreadsheet and analysed using SPSS statistical software, version 20 (SPSS, Chicago, IL, USA). Cross tabulations was conducted to obtain descriptive statistics which were presented as frequencies, percentages and Pearson Chi-square statistics. Bivariable and multivariable logistic regression models were used to test the association of the independent variables with the dependent (outcome) variable. Variables with p-value <0.05 at bivariable analysis were included in multivariable logistic regression analysis. Results were presented with odds ratios and the corresponding 95% Confidence Intervals and significance was accepted at $p < 0.05$.
Quality assessment of the data: The completed data abstraction forms were checked by the principle investigator for missing data or discrepancies. An independent Obstetrician, not part of the research team would check every tenth form. All data were double entered and cross-checked in EXCEL spreadsheet. The study tool was pre-tested before commencement of the research process. Research assistants were trained on the use of the questionnaires
Ethical approval: Ethical approval to carry out the study was obtained from Mbarara University of Science and Technology research ethics committee (MUST REC) and the Uganda National Council for Science and Technology (UNCST). Permission to carry out the research was sought from the administration of MRRH.
Limitations: Inability to get complete information due to incomplete recording and loss to follow up, detailed information could not be obtained by this method.

RESULTS

Table 1: Participants characteristics

Variable	Frequency, n (%)
Age(years)	
<20	14 (13.9)
20-30	67 (66.3)
>30	20 (19.8)
Gravidity	
Prime gravida	43 (42.6)
Multigravida	53 (57.4)
Magnesium sulphate	
Yes	82 (81.2)
No	14 (13.9)
Induction	
Yes	37 (36.6)
No	56 (55.4)
Distance from the health unit (km)	
>5	62 (61.4)
<5	39 (38.6)
Gestation age(weeks)	
<20	1 (1)
20-27	11 (10.9)
28-36	37 (36.6)
>36	32 (31.7)
Mean systolic BP(mmHg)	
<160	11 (10.9)
≥160	90 (89.1)
Mean diastolic BP(mmHg)	
<110	33 (32.7)
≥110	68 (67.3)
Mode of delivery	
Vaginal	43 (42.6)
C/S	49 (48.5)
Mean time lag between onset of symptoms and delivery	
0-6 hours	4 (4)
7-12 hours	1 (1)
13-24 hours	18 (17.8)
25-48 hours	2 (2)
49-72 hours	10 (9.9)
73 hours-7 days	17 (16.8)
8-14days	6 (5.9)
15-21 days	5 (5)
>21 days	8 (7.9)
Missing	30 (29.7)
Number of foetuses	
Single	88 (87.1)
Twins	6 (5.9)
Status of baby before birth	
Well	65 (64.4)
Distressed	10 (9.9)
IUFD	12 (11.9)

Table 2: Pregnancy outcome of mothers with severe Pre-eclampsia at Mbarara Regional Referral Hospital

Maternal Outcome		Fetal Outcome	
	N=92		N=93
HELLP syndrome	4 (4.3)	Normal	43 (46.2)
DIC	1 (1.1)	Birth asphyxia	7 (7.5)
Convulsions	26 (28.3)	ENND	1 (1.1)
Oliguria	2 (2.2)	FSB	13 (14.0)
IUFD	1 (1.1)	MSB	15 (16.1)
Mental confusion	1 (1.1)	Live premature	12 (12.9)
None	57 (62.0)	Abortion	1 (1.1)
-	-	Birth weight (kg)	
-	-	<1	2 (2)
-	-	1.1-1.5	8 (7.9)
-	-	1.6-2.0	13 (12.9)
		2.1-2.5	14 (13.9)
		>2.5	29 (28.5)
		Missing	35 (34.7)
Overall maternal outcome		**Overall fetal outcome**	
Good	76 (75.2)	Good	48 (47.5)
Poor	17 (16.8)	Poor	45 (44.8)
Missing	08 (7.9)	Missing	08 (7.9)

Table 3: Factors associated with maternal outcomes

		Maternal n=88		
Variable	Categories	Bad outcome	Good outcome	P-value
Age				0.2
	<20	5	9	
	20-30	10	51	
	31-40	2	16	
Gravidity	PG	8	33	0.8
	Multigravida	8	39	
Gestation age at delivery in weeks				0.1
	< 20	1	0	
	20-27	2	8	
	28-36	8	26	
	> 36	3	26	
Highest systolic BP				0.7
	<140	0	1	
	140-150	3	5	
	151-160	2	11	
	161-170	1	7	
	171-180	1	12	
	181-190	2	15	
	191-200	3	9	
	>200	5	16	
Highest diastolic BP				0.3
	<100	2	7	
	100-110	5	33	
	111-120	2	16	
	121-130	1	7	
	131-140	5	8	
	>140	2	5	
Urine protein				0.5
	Plus 1	0	3	
	Plus 2	1	1	
	Plus 3	6	20	
	Plus	3	23	
Induction of labour				0.05
	Yes	10	26	
	No	6	47	

Table 4: Factors associated with foetal outcomes in severe pre-eclampsia

		Foetal n=88		
Variable		Bad outcome	Good outcome	P-value
Age	<20 20-30 31-40	7 28 10	7 33 8	0.8
Gravidity	Prime gravida Multigravida	18 24	23 23	0.5
Gestational age, wks	< 20 20-27 28-36 > 36	1 10 19 7	0 0 15 22	0.000
Highest diastolic BP mmhg	<100 100-110 111-120 121-130 131-140 >140	3 16 11 3 9 3	6 22 7 5 4 4	0.4
Urine protein	<999 Plus 1 Plus 2 Plus 3 Plus 4	0 2 2 14 14	1 1 0 12 12	0.5
Induction of labour	Yes No	25 18	11 35	0.001
Mode of delivery	Svd C/S	10 6	33 43	0.2

Table 5: Time intervals versus fetal outcomes

Time(hours)	Feotal outcome	Odds ratio	p-Value	
	Poor	Good		
>6 0-6	38 0	29 4	0.43 (0.33-0.57)	0.027
>12 0-12	38 0	28 5	0.42 (0.32-0.56)	0.013
>18 0-18	38 0	28 5	0.42 (0.32-0.56)	0.013
>24 0-24	28 10	21 12	1.60 (0.58-4.40)	0.361
>30 0-30	28 10	20 13	1.82 (0.67-4.97)	0.240
>48 0-48	26 12	20 13	1.41 (0.53-3.47)	0.482
>60 0-60	26 12	19 14	1.60 (0.60-4.32)	0.344
>72 0-72	19 19	16 17	1.06 (0.42-2.70)	0.817

DISCUSSION OF RESULTS

Primigravida accounted for about 42.6% of the cases of severe pre-eclampsia studied and majority (66.7%) of the women were aged between 20-30 years. This compares well with a study by Parveen M et al in 2015 in south India where 46.23% of the women studied were primigravida and were about 70% of them were aged between 21 and 30 years[11]. This is probably because the two studies were done in similar settings-tertiary or referral hospitals and had similar patient characteristics.

The overall good fetal outcome rate in this study was 47.5% which is lower compared to the study by Parveen M et al in 2015 where the good fetal outcome rate was 62.3%.[11] It is possible that the population in south East India presented earlier than the ones in our study.

Of the women studied, 68.3% were more than 28 weeks of amenorrhoea and 31.2% had still births. There is evidence by L.L Simpson 2002 that suggests that beginning at approximately 36 weeks, the risk of intrauterine fetal demise increases substantially and severe preeclampsia represents significant risk factor for intrauterine fetal demise, with estimated stillbirth rate of 21 per 1000.[12,13]

The most common symptom was headache (47%) and over 35% of these women presented for delivery more than 72hours from onset of symptoms. In a study by Al-Safi Z et al 2005 where about 90% of patients studied presented within 7 days after discharge from the hospital and the most common presenting symptom was headache in 105 (69.1%) of patients.[14] In both studies, the commonest symptom was headache. Prematurity being the commonest fetal complication

Delivery between 0-18 hours was protective OR 0.43, CI=0.29-0.52), p-value 0.013. Delivery after 36weeks gestation was protective to fetus while delivery by C/S was associated with good maternal and fetal outcome p value 0.000 while induction of labour was associated with poor outcome OR 4.4, CI: 1.78-10.9. Visual blurring and headache were associated with poor outcome mainly headache and blurring of vision. P value 0.009

Conclusions and recommendations:

The complication rate associated with severe preeclampsia is high and worsens with longer duration of symptoms before delivery. Delivery within 18 hours of onset of symptoms is associated with good feotal outcomes and this stresses the importance of early presentation for care by the mothers and timely decision making by the clinicians. Survival for babies after 18 hours from onset of symptoms is by chance. Delivery by C/S is protective to both mothers and babies. There is need to enhance health education to mothers about symptoms of severe pre-eclampsia during antenatal care so that they can present early for care.

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