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Research Article

Predictors of Maternal and Perinatal Outcomes in Women with Hypertensive Disorders of Pregnancy: A Prospective Observational Study

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Abstract

***Objective**: to determine the predictors of maternal mortality and morbidity and perinatal mortality in hypertensive disorders with pregnancy.*

***Methods:** This was a prospective observational study carried out between January 2016 to December 2018 in Tanta University hospital, Obstetrics and Gynecology Department included all pregnant women admitted with hypertensive disorders after 28 weeks gestation. All data regarding the maternal risk factors at admission were recorded, the maternal and neonatal data at delivery were recorded. The study included 960 women admitted to our hospital.*

***Results:** The rate of mortality in our study was (2.08%). The most common cause of morbidity was HELLP syndrome (40.0%). multivariate regression analysis of risk factors of neonatal death in study population. With highly significance with age of mother, previous history of PE, chronic hypertension and high blood pressure at admission, also APGAR score and weight of fetus.*

***Conclusions:** Predictors of maternal and neonatal morbidity and mortality are including personal, familial and medical risk factors that should be screened during early gestation.*

Keywords: preeclampsia; morbidity; mortality; neonatal outcome.

Introduction

In general, hypertensive disorders of pregnancy (HDP) may complicate 5%-10% of pregnancies in the general population and are known to increase the risks of maternal and perinatal morbidity and mortality (1). Hypertensive disease occurs in approximately 12–22% of pregnancies, and it is directly responsible for 17.6% of maternal deaths in the United States (2).

Although the rate of eclampsia in the United Kingdom (UK) appears to have fallen, hypertension in pregnancy remains one of the leading causes of maternal death in the UK. One-third of severe maternal morbidity was a consequence of hypertensive conditions (3). However, there is a significant variation in the proportion of maternal mortality due to these disorders between the low- and high-income countries. It was noted that most maternal deaths associated with hypertensive disorders occur in the low- and middle-income countries (4).

Hypertensive disorders are the leading cause of complications in pregnancy and, together with hemorrhage, are among the major contributors to maternal death in developed and developing countries (5). Although there is a large body of literature that described the magnitude and associated complications of HDP, little is done to assess the predictors of maternal and perinatal mortality, particularly in low- and middle-income countries (6).

Many genetic risk factors, clinical features and biomarkers have been proposed but none of these seems able to prevent pre-eclampsia onset (7). The present study was designed to determine the predictors of maternal mortality and morbidity and perinatal mortality in hypertensive disorders with pregnancy.

Patients & Methods

This was a prospective observational study carried out in Tanta University hospital, Obstetrics and Gynecology Department, in the period from January 2016 to December 2018, included all pregnant women admitted with hypertensive disorders after 28 weeks gestation.

Exclusion Criteria were pregnant women with hypertensive disorders who refused to participate in the study and pregnant women with hypertensive disorders before 28 weeks gestation. For all women included in the study the following data were collected: Maternal age, parity, gestational age at admission, number of fetus, antenatal care in the current pregnancy, onset of HDP. history of HDP in previous pregnancy, history of chronic hypertension, history of DM or any other medical disorders.

Blood pressure measurement, Presence or absence of proteinuria, Presence or absence of symptoms like headache, blurred vision, epigastric pain or vomiting, Presence or absence of pitting edema, Presence or absence of convulsions were recorded. Duration of hospital stay, medications given (e.g. Mg. Sulfate, antihypertension and corticosteroid), Admission to ICU, indication & duration, Highest and lowest BP measurements achieved, Clinical or laboratory complications.

Delivery data included labor onset. "Spontaneous or induced, gestational age and indications" and Mode of delivery. Perinatal data included fetal weight at admission, fetal weight at delivery, still birth & neonatal death, Admission to ICU, APGAR scores (1minute & 5minutes). Maternal state of discharge either mortality or morbidity were recorded.

Outcomes:

- Primary outcomes
- The relation between different clinical & laboratory factors affecting maternal and perinatal outcome.
- Secondary outcomes
- Rate of maternal mortality and morbidity.
- Rate of perinatal mortality.
- Ethical considerations
- Ethical approval: An approval for the study was obtained from the institutional ethical committee. Any data taken from the patient either from the history, the examination or from the investigations dealt with in confidential manner. Informed consent: Written informed consent form obtained from patient.

Statistical analysis

Data were collected and analyzed by computer program SPSS" ver. 21" Chicago. USA. Data expressed as mean, Standard deviation and number, percentage. T-test or Mann-Whitney if necessary was used to determine significant for numeric variable. Chi. Square or Fisher exact test was used to determine significance for categorical variable. All possible factors affecting maternal mortality were entered in a multivariate logistic regression model to determine which of them remain in the equation. The same was affected for perinatal mortality as a dependent outcome. * $P < 0.05$ is significant, ** $p< 0.001$ moderate significance, *** $P<0.000$ highly significance, n.s $P>0.05$ non-significance.

Results

Table (1) shows the clinical characteristics data in study population. With high in percentage of family history in both groups with significance difference ($P<0.03$). Also, about chronic diseases there were (11.97%) of cases have diabetes and there was moderate significance difference about hypertension with (51.30%) in eclampsia group ($P<0.001$) and 9.89% of cases have kidney diseases with significance difference ($P<0.05$). As regard higher percentage in both groups were delivered CS with significance difference ($P<0.05$). Also, there were high percentage in no. of fetus in both groups in twins and multiple fetus than normal with significance difference ($P<0.05$).

Item	Total "n=960"	GI Preeclampsia "n=845"	GII Eclampsia "n=115"	p-value
1-Family History:				
• Yes	299(31.14%)	261(30.89%)	38(33.04%)	P<0.03*
• No	661(68.85%)	584(69.11%)	77(66.95%)	
2-Chronic disease:				P<0.04*
• Diabetes	115(11.97%)	89(10.53%)	26(22.60%)	P<0.001**
• Hypertension	277(28.85%)	218(25.79%)	59(51.30%)	P<0.04*
• Kidney diseases	95(9.89%)	77(9.11%)	18(15.65%)	
3-Previous mode of delivery:				P<0. 04*
• NVD	99(10.31%)	94(11.12%)	5(4.34%)	
• CS	861(89.68%)	751(88.87%)	110(95.65%)	
4- No. of fetus:				P<0.01*
• Single	672(70%)	618(73.13%)	54(46.95%)	
• Twins	259(26.97%)	211(24.97%)	48(41.73%)	
• Multiple	29(3.02%)	16(1.89%)	13(21.3%)	
5- Antenatal Care of current pregnancy:				P<0.03*
• No	151(15.72%)	127(15.02%)	24(20.86%)	
• Once	689(71.77%)	601(71.12%)	88(76.52%)	
• Regular	120(12.25%)	117(13.84%)	3(2.60%)	

Table 1: Clinical Characteristic at admission in study population.

Table (2) shows signs & symptoms at admission in study population. With high percentage in value in systolic& diastolic blood pressure >160 in both groups with moderate significance (P<0.001). In Albumin & protein in urine there were (20.0%) of cases have ++++ in preeclampsia and 100% in cases in eclampsia with highly significance difference (P<0.000). As regard there were significance difference (P<0.05) with platelets count (P<0.05) and moderate significance difference with highest creatinine (P<0.001). Also there were highly significance difference (P<0.000) in headache, convulsion and visual disturbance. As regard about edema there were moderate significance (P<0.001) edema. About convulsion there were significance difference.

Item	Total "n=960"	GI Preeclampsia "n=845"	GII Eclampsia "n=115"	p-value
1- Systolic Blood Pressure:				
<160	417(43.43%)	405(47.92%)	12(10.43%)	P<0.001**
>160	543(56.56%)	440(52.07%)	103(89.56%)	
2- Diastolic Blood pressure		253(29.94%)	0.0	P<0.001**
<95	253(26.35%)	592(70.05%)	115(100.0%)	
>95	707(73.64%)	169(20.0%)	115(100%)	P<0.000***
3- Albumin & protein in Urine:		676(80.0)	0.0	
++++	284(29.58%)	0.0	0.0	P<0.04*
+++	676(70.41%)	185(21.89%)	25(21.73%)	
++	0.0	660(78.10%)	90(78.26%)	P<0.001**
6- Platelet count in mm3:	210(21.87%)	338(40.0%)	94(81.73%)	
• <100	750(78.12%)	507(60.0%)	21(18.26%)	P<0.000***
• >100	432(45.0%)	625(73.96%)	115(100%)	P<0.000***
7- Highest creatinine (gm/dl":	528(55.0%)	3(0.35%)	67(58.26%)	P<0.001**
• <1.0	740(77.08%)	667(78.93%)	115(100%)	P<0.000***
• >1.0	70(7.29%)	0.0	115(100.0%)	P=0.385n.s
	782(81.45%)	43(5.08%)	8(6.95%)	
8-Headeche	11.97%)	169(20.0%)	40(34.78%)	
9-Visual disturbance	51(5.31%)	392(46.39%)	60(52.17%)	P<0.04*
10- Edema in lower limp	209(21.77%)	241(28.52%)	7(6.08%)	
11- Convulsions	452(47.08%)	50(5.91%)	15(13.04%)	
12- Gestational age at admission:	248(25.83%)	795(94.08%)	100(86.95%)	
• <28wks.	65(6.77%)			
• 28-34wks.	895(93.22%)			
• 34-36wks.				
• >36wks.				
13- Fetal Condition:				
• IUFD				
• Live				

Table 2: Baseline clinical data at admission in study population.

Table (3) shows causes of maternal death. The rate of mortality in our study was (2.08%). The high percentage in HELLP syndrome (40.0%). As regard there were (20.0%) of cases in hemorrhage. and lowest percentage brain edema (10.0%).

Item	No. of death "n=20"
1- HELLP syndrome	7(40.0%)
2- Pulmonary Oedema	4(20.0%)
3- Hemorrhage	4(20.0%)
-Concealed Hge	1(5.0%)
-DIC	1(5.0%)
-Cerebral He	1(5.0%)
-P.P Hge	1(5.0%)
4- Renal failure	3(15.0%)
5- Brain oedema	2(10.0%)

Table 3: Causes of maternal death in study population.

Table (4) shows neonatal data in study population. With non-significance difference (P<0.05) in single and multiple fetus and birth weight. But there was significance difference (P<0.05) with APGAR score, Sex of fetus and admission to NICU and gestational age at discharge.

Item	Total "n=960"	GI Preeclampsia"n=845"	GII Eclampsia "n=115"	p-value
1- Single Pregnancy:				
Living baby	613(63.85%)	574(67.92%)	39(88.63%)	P=0.395n.s
IUFD	59(6.41%)	54(6.39%)	5(11.36%)	
2-Multiple pregnancy:	246(25.62%)	185(21.89%)	61(53.04%)	P=0.583n.s
Living baby	42(18.22%)	32(3.78%)	10(50.0%)	
IUFD				
3-Birth weight:	399(41.56%)	380(44.97%)	19(39.58%)	
<2500gm	561(58.43%)	465(55.0%)	96(83.47%)	P=0.386n.s
>2500gm	275(28.64%)	228(26.98%)	47(40.86%)	
4-APGAR score:	685(71.35%)	617(73.01%)	68(59.13%)	P<0.04*
<7	670(69.79%)	581(68.75%)	89(77.39%)	
>7	290(30.20%)	264(31.24%)	26(22.60%)	P<0.03*
5-SEX of fetus:	112(11.67%)	84(9.94%)	28(24.34%)	
Male	848(88.33%)	761(90.05%)	87(75.65%)	P<0.03*
female				
6-N.I.C.U admission:	26(2.70%)	18(2.13%)	8(6.95%)	P<0.01*
Admitted	934(97.29%)	827(97.86%)	107(93.04%)	
Not admitted				
7-Neonatal resuscitation:	49(5.10%)	42(4.97%)	7(6.08%)	P<0.03*
Done	211(21.67%)	169(20.0%)	42(36.52%)	
Not done	446(46.45%)	387(45.79%)	59(51.30%)	
8- **Gestational age at delivery:**	254(25.41%)	247(29.23%)	7(6.08%)	
• <28wks.				
• 28-34wks.				
• 34-36wks.				
• >36wks.				

Table 4: Neonatal data in study population.

Table (5) shows causes of neonatal death in study population. With highest percentage in respiratory distress (58.62%) with significance difference (P<0.05).

Item	Total "n=145"	GI Preeclampsia "n=102"	GII Eclampsia "n=43"	p-value
1-Neonatal outcome				
-Placenta insufficiency "SGA"	60(41.37%)	39(38.23%)	21(48.83%)	P<0.04*
-Respiratory distress "preterm"	85(58.62%)	63(61.76%)	22 (51.16%)	P<0.03*

Table 5: Causes of neonatal death in study population.

Table (6) shows multivariate regression analysis of risk factors of neonatal death in study population. With highly significance with age of mother, previous history of PE, chronic hypertension and high blood pressure at admission, also APGAR score and weight of fetus.

Model	Standardized Coefficients	T	Significance
Age	.302	.612	0.000***
Previous PE history	.583	.211	0.000***
Chronic hypertension	.635	.824	0.000***
High BP at admission	.559	-.572	0.000***
APGAR score	.629	.217	0.000***
Fetus weight	.510	.337	0.000***
Antenatal care	-.821	.673	0.001**
Multiple pregnancy	.466	.276	0.02*
Diabetes	.472	-1.922	0.03*
Residence	.263	.167	0.03*
Education	.708	.447	0.04*
Gestational age	.683	.412	0.04*
Family History	.538	.723	0.582n.s
Parity	.265	.344	0.860n.s
Albumin & protein in urine	.427	.334	0.493n.s

Table 6: Multivariate regression analysis of risk factors of neonatal mortality in study population.

Discussion

The causes of hypertensive diseases in pregnancy are still uncertain, thus the effective primary prevention is not available in this stage. However, several risk factors have been identified and modification of some of these risk factors might result in the decreasing of its frequency (8). In our data overall maternal mortality was (2.08%). Similar studies in India and Pakistan revealed a high maternal mortality associated with HDP. Few hospital-based studies in Ethiopia have also shown that hypertensive disorders are among the top three causes of maternal mortality. Furthermore, a national survey in Ethiopia demonstrated that 11% of all maternal deaths and 16% of direct maternal deaths occurred due to HDP and the cause-specific case fatality rate was 3.6% (9).

In our data multivariate regression analysis of risk factors of maternal mortality in study population was highly significance with age with increase in risk of mortality with increases in age group. This agree with Ghulmiyyah et al that found that the risk of death from preeclampsia or eclampsia was higher for women aged>30 years (10).

As regard in Dalmaz et al (8) reported several risk factors have been described as predispose to hypertensive disorders in pregnancy worldwide, such as: family history of preeclampsia, preeclampsia in a previous pregnancy, multifetal gestation, obesity, nulliparity, diabetes, chronic hypertension and extremes of maternal age. In our data, family history of PE, previous PE history, nulliparity, diabetes, and chronic hypertension were significantly more frequent in patients. Our results are similar to other studies in different populations (11).

As expected, multivariate analysis showed that family history of PE, diabetes and chronic hypertension are independent risk factors for hypertensive diseases in pregnancy. The family and the previous history of PE increased the risk for this complication in our patients. These data have been reported in other studies (12).

Indeed, the genetic component in pathophysiological abnormalities of preeclampsia has been suggested (13). Preeclampsia was reported to be more common in daughters of preeclamptic women and in pregnancies fathered by sons of preeclamptic women; this data suggest the involvement of both maternal and fetal genes in the syndrome. Pregnant women with this history should be carefully monitored in the prenatal care and postpartum (14). Women with preexisting chronic hypertension also have an increased risk of preeclampsia (12).

In the present study, diabetes, and particularly, preexisting chronic hypertension were risk factors for preeclampsia same to in Southern Brazilian women. Thus, actions in the public health focused to prevent these diseases are important to also prevent preeclampsia (2).

Generally, PE is regarded as a disease of first pregnancy and its frequency ranges between 2% and 7% in healthy nulliparous women (15). Nulliparity is well established as a risk factor for hypertensive disorders in pregnancy (16).

In this study, nulliparity was confirmed as a risk factor in the conditional logistic regression analysis. Nulliparous women have a two-fold increase in the risk of developing complications of hypertensive disorders in pregnancy.

Multiple pregnancy doubles the risk of preeclampsia; however, in our findings this association was not established, likely due to low number of cases in both groups of subjects associated with a reduced sample size as a whole. Extremes of maternal age cannot be demonstrated as a risk factor in our study since our sample is matched by age; nevertheless, it is an established risk factor for PE (1).

Regardless of the indicator of social deprivation, we found that low educational level was significantly more frequent in the group of cases. Haelterman et al (2011) showed that the burden of PE is concentrated in socially disadvantaged women, thus health services should be more responsive to the specific needs of these women (17).

In present study there were (2.08%) of cases died with (40.0%) of them have HELLP syndrome and (20%) have hemorrhage. In the of study Ghulmiyyah, 2012 (10) reported severe preeclampsia is associated with increased risk of maternal mortality (0.2%) and increased rates of maternal morbidities (5%), such as convulsions, pulmonary edema, acute renal or liver failure, liver hemorrhage, disseminated intravascular coagulopathy, and stroke. These complications are usually seen in women who develop preeclampsia before 32 gestation and in those with preexisting medical conditions.

In present study there were highly significance with severe hypertension with low birthweights babies and SGA. This agree with (Mark & Megan, et al., 1997) who reported severe hypertension was confirmed by multivariate analysis to be associated with low birthweight babies, and in univariate analysis, with a higher incidence of all fetal complications and higher incidence of SGA babies. Therefore, the more severe the hypertension, the more the like hood of fetal as well as maternal complications.

Merits of the study

This is a prospective observation study determining the most significant clinical factors that can predict bad prognosis in cases of hypertensive disorders of pregnancy. Determining such factors will help in prevention of maternal and perinatal mortality & severe morbidity in this relatively unpredictable disorder. The regression model used in this study is a relatively strong tool to select factors that independently affect the outcome. Another merit of the study comes from the relatively long duration one year of recurring the cases.

Limitations of the study

Longer follow up of women might be of benefit especially for those with persistent medical problems. The diagnosis and analysis of perinatal outcome depend on data collection of the hospital records without detailed follow up of the neonates. Classification of the preeclamptic cases into mild and severe was not done but it might be compensated by entering the level of hypertension at admission as a possible independent factor in predicting the outcomes.

Conclusion

The main results of the study as regarding the most significant predictors of maternal outcome were: Age (old age ≥30), presence of pregestational hypertension (chronic hypertension), high blood pressure at admission, absence of regular antenatal care, presence of high albumin and protein in urine and low platelet count.

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