Original Article

The outcome of hypertensive disorders with pregnancy

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Abstract

Background: Hypertensive disorders (HTDs) with pregnancy remain a major health problem because of the associated adverse maternal and perinatal adverse outcomes. **Objectives:** To evaluate the outcomes of HTDs with pregnancy. **Patients and Methods:** Four hundred and five (405) hypertensive women included in this retrospective multicenter study. Data of the studied women including maternal age, parity, gestational age at delivery, pregnancy outcome [preterm delivery (PTD), birth weight (LBW), Apgar scores, neonatal intensive care unit admission (NICU), intrauterine fetal death (IUFD), intrapartum and/or early neonatal deaths] were collected. Collected data analyzed statistically to evaluate the outcome of HTDs with pregnancy. **Results:** Preeclampsia (PE)/superimposed PE group had significantly high relative risk (RR) and Odds ratio (OR) for PTD (RR 2.1; OR; 3.3; $P = 0.0001$ and $P = 0.0001$, respectively), LBW (RR 2.01; OR; 3.17; $P = 0.0001$ and $P = 0.0001$, respectively), and low Apgar score at 1st min (RR 1.7; OR 1.9; $P = 0.01$ and 0.01, respectively) and at 5th min (RR 2.2; OR; 2.36; $P = 0.2$ and 0.2; respectively). In addition, PE/superimposed PE group had significantly high RR and OR for NICU admission (RR 1.6; OR 2.2; $P < 0.0002$ and $P < 0.0001$, respectively) and IUFD (RR 2.9; OR 3.1; $P = 0.01$ and 0.01, respectively). **Conclusion:** women with PE/superimposed PE have high RR and OR for PTD, LBW, and low Apgar score at 1st and 5th min, NICU, and IUFD compared to the gestational and chronic hypertension with pregnancy.

Keywords: Hypertensive, outcome, pregnancy

Introduction

Hypertensive disorders (HTDs) with pregnancy remain a major health problem because of the associated adverse maternal and perinatal adverse outcomes.[1-3]

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Received: 23-11-2019 **Revised:** 11-02-2020
Accepted: 14-02-2020 **Published:** 26-03-2020

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_1054_19

Preeclampsia (PE) have significant avoidable adverse maternal and fetal outcomes[4] and the recorded number of severe PE related annual deaths worldwide is about 50,000–100,000.[5]

The reported incidence of severe PE is 1.3% in Africa and 0.5% in Europe and United Kingdom.[4,5] Ngwenya reported 1.7% (2/121) incidence of maternal mortality and 49.6% incidence of perinatal mortality in severe PE.[4]

Placental insufficiency and/or prematurity are the causes of adverse neonatal outcome associated with HTDs with pregnancy.[2,3]

How to cite this article: Abdelazim IA, Bekmukhambetov Y, Aringazina R, Shikanova S, Amer OO, Zhurabekova G, *et al*. The outcome of hypertensive disorders with pregnancy. J Family Med Prim Care 2020;9:1678-83.

The adverse perinatal outcomes associated with HTDs with pregnancy are obvious in cases of severe PE/eclampsia.[6,7]

Perinatal mortality is an indicator of the maternal care available.[8] Therefore, this study is designed to evaluate the outcome of HTDs with pregnancy.

Patients and Methods

This retrospective multicenter study was conducted in Ain Shams University, Egypt and West Kazakhstan Marat Ospanov Medical University, Kazakhstan; data of women admitted with HTDs with pregnancy and delivered from January 2017 till January 2018 were reviewed and collected after approval of the Ethical Committee of both hospitals.

Women between 18 and 40 years old, ≥24 weeks' gestation, singleton pregnancy, admitted due to HTDs with pregnancy, and delivered from January 2017 till January 2018 were included in this retrospective study after informed consent.

Women with multiple gestation and/or women refused to participate in this study were excluded. Data collected include maternal age, parity, and gestational age at delivery.

Gestational age was calculated according to the first day of the last menstrual period (LMP) and early ultrasound scan (≤20 weeks) according to the hospitals' protocol.[9]

Pregnancy outcome data include preterm delivery (PTD) (<37 weeks) or full-term delivery, birth weight, Apgar scores, admission to the neonatal care unit (NICU), intrauterine fetal deaths (IUFD), and intrapartum and/or early neonatal deaths (NNDs) were also collected.

HTDs with pregnancy in this study classified as PE, gestational hypertension (GH), chronic hypertension (CH), and superimposed PE on top chronic hypertension.[10-12]

The International Society for the Study of Hypertension (ISSH) defined PE as hypertension and proteinuria developed for the first time after 20 weeks and regressed after delivery.[13,14] Hypertension is defined as blood pressure (BP) ≥140/90 mmHg on ≥2 consecutive occasions at least 4 h apart.[13,14]

Proteinuria is defined as ≥+1 on dipstick test on 2 mid-stream urine collections >4 h apart or 24-h urinary protein ≥300 mg.[13,14]

Severe PE is defined as blood pressure >160/110 mmHg on ≥2 occasions at least 6 h apart, proteinuria >5 gm/24 h urine, oliguria (urine output <500 ml/24 h), thrombocytopenia (platelet <100.000/ml), visual disturbances, epigastric pain, vomiting, disturbed liver function, or occurrence of complications (accidental hemorrhage and/or pulmonary edema).[13,14]

GH [pregnancy-induced hypertension (PIH)] is defined as hypertension of new onset of hypertension after 20 weeks, with previously normal blood pressure, without proteinuria or manifestations of PE or eclampsia.[15]

CH is defined as hypertension that either diagnosed before pregnancy and/or diagnosed before 20 weeks and does not resolve by the 12-week postpartum.[15]

Superimposed PE is defined as CH diagnosed before pregnancy or before 20 weeks and complicated with proteinuria and/or manifestation of severe PE (oliguria, thrombocytopenia, visual disturbances, epigastric pain, vomiting, disturbed liver function, or occurrence of complications).[15]

Low birth weight (LBW) is defined as the first weight recorded hours after birth <2500 g.[16] Early NND is defined as the death of a new-born within the first seven days after birth.[17] Low Apgar score is defined as Apgar score <7 at 1st and 5th min after delivery.[8]

Sample size and statistical analysis

The G Power software version 3.17 (Heinrich Heine Universität; Düsseldorf; Germany) was used for calculation of the required sample size. The effective sample includes >220 women needed to produce a statistically acceptable figure. Data were collected, tabulated, then analyzed using the Statistical Package for Social Science (SPSS) (Chicago, IL, USA). Categorical variables were presented as number and percentage (%) and mean ± SD (standard deviation). Chi-square (X^2) was used to compare qualitative variables and Student *t*-test was used to compare quantitative variables. Logistic regression analysis was used to calculate the relative risk (RR) and Odds ratio (OR) of adverse outcome with different types of HTDs with pregnancy. *P* value < 0.05 was considered significant.

Results

Data of four hundred and five (405) hypertensive women were collected and categorized into 3 groups: preeclampsia (PE)/superimposed PE group (211 women), GH (152 women), and CH (42 women).

Women with PE/superimposed PE were younger than those with CH (23.2 ± 1.2 versus 31.3 ± 0.9 years, respectively; *P2* = 0.01). In addition, women with GH were younger than those with CH (24.7 ± 1.3 versus 31.3 ± 0.9 years; *P3* = 0.003). No difference recorded between the PE/superimposed PE versus the GH group regarding the maternal age (*P1* = 0.9).

Parity of the women with PE/superimposed PE group was significantly low compared to women with CH (1.2 ± 1.7 versus 2.7 ± 1.3, respectively; *P2* = 0.02), whereas there was no difference between PE/superimposed PE versus GH group (*P1* = 0.9) and between GH versus CH group (*P3* = 0.9) regarding the parity.

Gestational age at delivery was less in the PE/superimposed PE compared to CH group (35.2 ± 1.3 versus 37.6 ± 0.9, respectively; *P2* = 0.003), whereas there was no difference between PE/superimposed PE versus GH group (*P1* = 0.9) and between GH group versus CH group (*P3* = 0.9) regarding the gestational age. Table 1.

The adverse outcome was compared for the preeclampsia (PE)/superimposed PE group (211 women) versus GH and CH group (152 and 42 women, respectively).

PTD and low birth weight (LBW) rates were significantly high in PE/superimposed PE group (49.8 and 53.1%, respectively) versus GH/CH group (22.7 and 26.3%, respectively), (*P* = 0.001 and 0.0002, respectively). Low Apgar score at 1st and 5th min rates were significantly high in PE/superimposed PE group (21.8 and 11.4%, respectively) versus GH/CH group (12.4 and 5.2%, respectively), (*P* = 0.03 and 0.03, respectively). In addition, NICU and IUFD rates were significantly high in PE/superimposed PE group (51.7 and 9%, respectively) versus GH/CH group (32.5 and 3.1%, respectively), (*P* = 0.01 and 0.02, respectively). Table 2.

The relative risk (RR) of PTD [RR 2.1 (95%CI: 1.6–2.9) *P* = 0.0001], LBW [RR 2.01 (95%CI: 1.5–2.6) *P* = 0.0001], and low Apgar score at 1st min [RR 1.7 (95%CI: 1.1–2.8) *P* = 0.01] and 5th min [RR 2.2 (95%CI: 1.08–4.5) *P* = 0.02] was significantly high in PE/superimposed PE group versus GH/CH group.

In addition, the RR of NICU admission [RR 1.6 (95%CI: 1.2–2.02) *P* < 0.0002] and IUFD [RR 2.9 (95%CI: 1.18–7.1) *P* = 0.01] was significantly high in PE/superimposed PE group versus GH/CH group. Table 3.

The Odds ratio (OR) of PTD [OR 3.3 (95%CI: 2.19–5.1) *P* = 0.0001], LBW [OR 3.17 (95%CI: 2.08–4.82) *P* = 0.0001], and low Apgar score at 1st min [OR 1.9 (95%CI: 1.15–3.38) *P* = 0.01] and 5th min [OR 2.36 (95%CI: 1.09–5.07) *P* = 0.02] was significantly high in PE/superimposed PE group versus GH/CH group.

In addition, the OR of NICU admission [OR 2.2 (95%CI: 1.48–3.32) *P* < 0.0001] and IUFD [OR 3.1 (95%CI: 1.2–7.9) *P* = 0.01] was significantly high in PE/superimposed PE group versus GH/CH group. Table 4.

Discussion

HTDs in pregnancy associated with significant perinatal morbidity[8] and are the second leading cause of maternal death worldwide responsible for 30,000–50,000 maternal deaths annually.[18,19]

In addition, the development of albuminuria on top of HTDs with pregnancy increases the risk of complications.[20]

Ngwenya reported 1.3% incidence of PE/eclampsia with 1.7% incidence of maternal mortality and 49.6% incidence of perinatal mortality following PE/eclampsia.[4]

Table 1: Demographic data of the three studied groups

Variable	Preeclampsia (PE) + Superimposed PE group	Gestational hypertension (GH) group	Chronic hypertension (CH) group	*P*
	Number 211 (%)	Number 152 (%)	Number 42 (%)	95% CI
Maternal age Mean±SD	23.2±1.2	24.7±1.3	31.3±0.9	*P1*=0.9 (-1.7, -1.2) *P2*=0.01 (-8.4, -7.7) * *P3*=0.003 (-6.9, -6.3) *
Parity Mean±SD	1.2±1.7	1.5±1.9	2.7±1.3	*P1*=0.9 (-0.6, 0.08) *P2*=0.02 (-1.9, -1.03) * *P3*=0.9 (0.7, 1.7)
Gestational age at delivery Mean±SD	35.2±1.3	36.1±1.5	37.6±0.9	*P1*=0.9 (-1.2, -0.6) *P2*=0.003 (-2.7, -2.07)* *P3*=0.9 (1.13, 1.9)

*:Significant difference. Data presented as mean±SD, P1: *P* value when comparing the PE/superimposed PE group to the gestational hypertension group, P2: *P* value when comparing the PE/superimposed PE group to the chronic hypertension group, P3: *P* value when comparing gestational hypertension to the chronic hypertension group, PE: Preeclampsia. Student t-test used for statistical analysis

Table 2: Adverse outcome in the PE/superimposed PE group compared to gestational and chronic hypertension group

Variable	Preeclampsia (PE) + Superimposed PE	Gestational (GH) + Chronic (CH) hypertension	*P*
	Number=211 (%)	Number=194 (%)	
PTD (<37 Weeks)	105 (49.8)	44 (22.7)	0.0001*
Low birth weight (LBW)	112 (53.1)	51 (26.3)	0.0002*
Apgar score <7 at 1 min	46 (21.8)	24 (12.4)	0.03*
Apgar score <7 at 5 min	24 (11.4)	10 (5.2)	0.03*
NICU admission	109 (51.7)	63 (32.5)	0.01*
IUFD	19 (9)	6 (3.1)	0.02*
Intrapartum death	3 (1.4)	2 (1.03)	0.7
Early neonatal death	4 (1.9)	2 (1.03)	0.4

*: Significant difference. Data presented as number and percentage (%). Chi-square (χ^2) used for statistical analysis. IUFD: Intrauterine fetal death. NICU: Neonatal intensive care unit. PTD: Preterm delivery

Table 3: Relative risk (RR) of adverse outcome in the PE/superimposed PE group compared to gestational and chronic hypertension group

Variable	Preeclampsia (PE) + Superimposed PE Number=211 (%)	Gestational (GH) + Chronic hypertension (CH) Number=194 (%)	Relative Risk (95% CI) *P*
PTD (<37 Weeks)	105 (49.8)	44 (22.7)	2.1 (1.6-2.9)
Delivery>37 Weeks	106 (50.2)	150 (77.3)	*P*<0.0001*
Low birth weight (LBW)	112 (53.1)	51 (26.3)	2.01 (1.5-2.6)
Average birth weight	99 (49.9)	143 (73.7)	*P*<0.0001*
Apgar score <7 at 1 min	46 (21.8)	24 (12.4)	1.7 (1.1-2.8)
Apgar Score >7 at 1 min	165 (78.2)	170 (87.6)	*P*=0.01*
Apgar score <7 at 5 min	24 (11.4)	10 (5.2)	2.2 (1.08-4.5)
Apgar Score >7 at 5 min	187 (88.6)	184 (94.2)	*P*=0.02*
NICU admission	109 (51.7)	63 (32.5)	1.6 (1.2-2.02)
No NICU admission	102 (48.3)	131 (67.5)	*P*<0.0002*
IUFD	19 (9)	6 (3.1)	2.9 (1.18-7.1)
No IUFD	192 (91)	188 (96.9)	*P*=0.01*
Intrapartum death	3 (1.4)	2 (1.03)	1.3 (0.23-8.16)
No Intrapartum death	208 (98.6)	192 (98.97)	*P*=0.7
Early neonatal death	4 (1.9)	2 (1.03)	1.8 (0.34-9.92)
No early neonatal death	207 (98.1)	192 (98.97)	*P*=0.4

*Significant difference. CI: Confidence interval. Data presented as number and percentage (%). IUFD: Intrauterine fetal death. NICU: Neonatal intensive care unit. PE: Preeclampsia. PTD: Preterm delivery

Table 4: Odds ratio (OR) of adverse outcome in the PE/superimposed PE group compared to gestational and chronic hypertension group

Variable	Preeclampsia (PE) + Superimposed PE Number=211 (%)	Gestational (GH) + Chronic hypertension (CH) Number=194 (%)	Relative Risk (95% CI) *P*
PTD (<37 Weeks)	105 (49.8)	44 (22.7)	3.3 (2.19-5.1)
Delivery>37 Weeks	106 (50.2)	150 (77.3)	*P*<0.0001*
Low birth weight (LBW)	112 (53.1)	51 (26.3)	3.17 (2.08-4.82)
Average birth weight	99 (49.9)	143 (73.7)	*P*<0.0001*
Apgar score <7 at 1 min	46 (21.8)	24 (12.4)	1.9 (1.15-3.38)
Apgar Score >7 at 1 min	165 (78.2)	170 (87.6)	*P*=0.01*
Apgar score <7 at 5 min	24 (11.4)	10 (5.2)	2.36 (1.09-5.07)
Apgar Score >7 at 5 min	187 (88.6)	184 (94.2)	*P*=0.02*
NICU admission	109 (51.7)	63 (32.5)	2.2 (1.48-3.32)
No NICU admission	102 (48.3)	131 (67.5)	*P*<0.0001*
IUFD	19 (9)	6 (3.1)	3.1 (1.2-7.9)
No IUFD	192 (91)	188 (96.9)	*P*=0.01*
Intrapartum death	3 (1.4)	2 (1.03)	1.3 (0.22-8.4)
No Intrapartum death	208 (98.6)	192 (98.97)	*P*=0.7
Early neonatal death	4 (1.9)	2 (1.03)	1.85 (0.33-10.4)
No early neonatal death	207 (98.1)	192 (98.97)	*P*=0.4

*: Significant difference. CI: Confidence interval. Data presented as number and percentage (%). IUFD: Intrauterine fetal death. NICU: Neonatal intensive care unit. PE: Preeclampsia. PTD: Preterm delivery

Women with PE/superimposed PE in this study were younger with low parity compared to those with chronic hypertension.

von Dadelszen and Magee found that the risk of PE/eclampsia is increased in women with young maternal age and higher body mass index.[18]

Ghimire recorded 112 cases of severe PE/eclampsia; the majority (41%) of them were <19 years and 63.4% were primiparas.[7]

PTD rate in this study was significantly high in the PE/superimposed PE group ($P = 0.001$), and the PE/superimposed PE group had higher RR and OR for PTD (RR 2.1; OR; 3.3; $P = 0.0001$ and $P = 0.0001$, respectively).

Asseffa and Demissie reported PTD rate of 28.1% (43/153) in PE/superimposed PE.[21] Premkumar *et al.* found that the risk of spontaneous and medically indicated PTD (<32 weeks) is increased in women with superimposed PE.[22]

LBW rate in this study was significantly high in the PE/superimposed PE group ($P = 0.0002$), and the PE/superimposed PE group had higher RR and OR for LBW (RR 2.01; OR; 3.17; $P = 0.0001$ and $P = 0.0001$, respectively).

Asseffa and Demissie reported 9.8% incidence of LBW following PE/superimposed PE[21] and Adu-Bonsaffoh *et al.* found the LBW rate was the highest among the PE compared to other HTDs with pregnancy.[8]

Browne *et el.* studied the outcome of HTDs with pregnancy and found that women with PE had high RR for LBW (Adjust RR 7.95) compared to PIH and/or CH.[23]

Xiong *et al.* found the differences in mean birth weight between the PE and normotensive controls ranged from –547.5 g to 239.5 g and the differences in mean birth weight between the gestational hypertension and normotensive controls ranged from –434.2 g to 55.1 g. Xiong *et al.* concluded that for women delivering at ≤37 weeks, birth weights were significantly lower among women with PE and among women with gestational hypertension compared to the normotensive controls.[24]

PE/superimposed PE studied group had higher RR and OR for low Apgar score at 1st min (RR 1.7; OR 1.9; $P = 0.01$ and 0.01, respectively) and at 5th min (RR 2.2; OR; 2.36; $P = 0.2$ and 0.2, respectively).

Adu-Bonsaffoh *et al.* found higher proportion of low Apgar scores in the women with PE.[8] In addition, Ayaz *et al.* concluded that PE associated with adverse neonatal outcome including low Apgar score, LBW, and increased NICU admission.[25]

Susilo *et al.* concluded that early-onset PE, severe PE, and PTD are independent risks factors for low Apgar score at 1st min in PE.[26]

NICU rate in this study was significantly high in PE/superimposed PE compared to those with GH and CH ($P = 0.01$) and the PE/superimposed PE group had significantly high RR and OR for NICU admission (RR 1.6; OR 2.2; $P < 0.0002$ and $P < 0.0001$, respectively).

Asseffa and Demissie reported 11.1% incidence of NICU admission following PE/eclampsia[21] and Adu-Bonsaffoh *et al.* reported a high rate of NICU admission in PE compared with other HTDs with pregnancy.[8]

Sibai found that most of the NICU admission in pregnancy complicated with GH and PE occurs for those who deliver ≥37 weeks.[27]

PE/superimposed PE studied group had significantly high RR and OR for IUFD (RR 2.9; OR 3.1; $P = 0.01$ and 0.01, respectively).

Adu-Bonsaffoh *et al.* reported 6.8% stillbirths and 3.8% early neonatal deaths following HTDs with pregnancy, especially PE.[8]

Asseffa and Demissie reported 11.1% incidence of perinatal death following PE/eclampsia[21] and Ghimire reported 9% incidence of perinatal death following PE/eclampsia.[7]

Lawn *et al.* reported that 16% of the estimated 2.6 million stillbirths annually occurs due to HTDs with pregnancy.[28]

von Dadelszen and Magee found that the HTDs with pregnancy precede 10% of early NNDs[18] and Browne *et al.* found that women with PE had high RR for NND (Adjust RR 18.41) compared to PIH and/or CH.[23]

HTDs in pregnancy are a major health problem associated with avoidable adverse maternal and fetal outcomes. In addition, we are in need of an international program to increase the awareness of the population toward the adverse outcomes of the HTDs with pregnancy.

This study was the first multicenter study conducted to evaluate the outcome of HTDs with pregnancy.

The limited number of cases in the chronic hypertension group and the retrospective nature of this study were the limitation faced during this study.

Future prospective multicenter studies are needed to compare the neonatal outcome in PE/superimposed PE to other HTDs with pregnancy (gestational and chronic hypertension) and normal pregnant controls.

Conclusion

Women with PE/superimposed PE have high RR and OR for PTD, LBW, and low Apgar score at 1st and 5th min, NICU, and IUFD compared to the gestational and chronic hypertension with pregnancy.

Ethical approval

Ethical Committee approval of both Ain Shams University and West Kazakhstan Medical University hospitals obtained before this study.

Declaration of patient consent

Informed written consent from each studied woman obtained before conducting this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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