Maternal and Perinatal Outcome of Hypertensive Disorders of Pregnancy: A Prospective Study, Al-Hasaa, KSA.

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Abstract:

Background: Hypertension in pregnancy is a major health problem responsible for significant maternal and perinatal morbidity and mortality. Early detection and appropriate monitoring may improve outcome. **Objective:** To determine outcome of hypertensive disorders of pregnancy (HDP) and the associated factors. **Method:** A prospective study was conducted during June 2015 to March 2016. Target population was Saudi hypertensive and normotensive gravidas attending the Maternity and Children Hospital, Al-Hasaa, Saudi Arabia. Data were collected through a scheduled questionnaire, clinical examination, laboratory investigations, sonographic examinations as well record reviewing. **Results:** The study included 132 hypertensive and similar normotensive pregnant women matched by age. Pre-eclampsia was the most prevailing subtype (47.7%). HDP increased the risk of maternal (17.4%, RR=5.4) and perinatal (52.3%, RR=4.7) complications. Hypertensive women were more prone to, preterm labour (RR=5.5), Cesarean section (RR=5), labour induction (RR=5), and pregnancy termination (RR=2). Fetal complications included small for gestational age (RR=15.9), intrauterine growth restriction (RR=15.2), prematurity (RR=4.8), and fetal distress (RR=2.2). Neonates were at risk of admission to neonatal intensive care unit (RR=14.2) and low Apgar score at one (RR=14.4) and five minutes (RR=2.2). No deaths were recorded in the study. Pre-eclampsia was the most risky. Incidence of post HDP chronic hypertension was 18.5%. **Conclusion:** HDP carry a risk for both mothers and babies. Adverse outcome of HDP could be predicted by absent antenatal care, lower maternal age, elevated serum bilirubin, preterm delivery, poor education, uncontrolled blood pressure and primigravida. Proper follow up and timely management may HELLP reduction of unfavourable outcome.

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Introduction

Hypertension is the most common serious medical problem complicating pregnancy with a global prevalence amounting to 10%**.**[1] It includes a group of disorders namely; chronic hypertension, gestational hypertension and preeclampsia (PE). PE may arise de novo during pregnancy or complicate or super impose chronic or gestational hypertension. In all situations it may be complicated by seizures developing into eclampsia, a more severe form. PE is the main and the most common disorder of the group with unclear causes,

diagnosis and etiological treatment. However, it is described that PE is accompanied by abnormal placentation that triggers generalized endothelial cell activation leading to multisystem manifestations; cardiorespiratory, neuro-logical, renal, hepatic, hematological, and feto-placental. Arterial vasoconstriction occurring in hypertension also reduces blood flow to body organs including placenta.[2-4] Poorly controlled hypertensive disorders of pregnancy (HDP) are a leading cause for maternal and perinatal morbidity and mortality worldwide.[1,2] Almost 10% to 15% of maternal deaths are attributed to HDP[5] which are largely avoidable via close materno-fetal monitoring for early recognition and timely management of complications.[2,3]

Few data are available on HDP in Saudi Arabia (KSA). Information on outcome of these disorders and the related factors could be of interest for health policy makers. Hence this study was conducted to determine maternal and perinatal outcomes among Saudi pregnant women with hypertensive disorders and its associated risk factors and predictors.

Methodology:

The present prospective cohort study was conducted during June 2015 to March 2016.

Target population* and *settings: The target population was all Saudi women with hypertensive disorders of pregnancy (HDP) attending Maternity and Children Hospital (MCH), Al-Hasaa, KSA during the study period. It is the only maternal and child referral health facility in Al-Hasaa governorate (Eastern region) and the surrounding catchment area with 300 beds and over 15,000 deliveries annually. During the first three months of the study, all newly diagnosed target women, whatever gestational age, who were referred by the Hospital obstetrician to the medical department (obstetric internist) were involved (132 women). All types of HDP according to the recommended definitions were included; chronic hypertension (pre-existing), gestational hypertension, PE/eclampsia, and pre-eclampsia superimposed on chronic hypertension (PSCH).[2-4] A similar number (132 women) of Saudi normotensive pregnant women were selected for control matched by age and gestational trimester.

Data collection: Data was collected through a scheduled questionnaire (entailing demographic data, habits and family, medical and obstetric history), clinical examination, laboratory investigations, sonographic examination as well record reviewing. Levels of biochemical markers were judged based on the upper and lower limit of the reference normal range for pregnant women according to the used kits. Also, weight and height were measured and body mass index (BMI) was calculated as weight (kg) to height (m2) ratio, and then categorized according to the WHO classification.[6]

Management and Follow up: Hypertension and medical problems were assessed and managed by the medical investigator adopting the recommended Saudi Ministry of Health (MOH) protocols. Hypertensive women were offered private weekly follow up visits (more frequent if necessary) for clinical and laboratory assessment of the condition, evaluation of management plan and to decide any required extra intervention. Blood pressure (BP) was measured manually using a mercury sphygmomanometer.[2,4] Relevant data registered by the obstetricians and neonatologists as well laboratory results were extracted from patients' records.

Table (1): Characteristics of the studied cases and controls, Al-Hasaa, KSA.

Women Characteristics	Hypertensive gravidas n %	Normotensive gravidas n %	Significance Test (p)
Age (years**):(**Mean ± S)	31.5 ± 7.4 (18-48)	31.1±6.4 (19-46)	*t = 0.6 (0.580)*
18-<20	5 3.8	6 4.5	
20-<35	64 48.5	67 50.8	χ^2 = 0.3 (0.865)
35 - 48	63 47.7	59 44.7	
Education:			
Illiterate/ read and write	22 16.7	13 9.9	
Primary school	12 9.1	7 5.3	χ^2 = 5.7 (0.217)
Middle school	25 18.9	22 16.7	
High school	34 25.8	39 29.5	
University or higher	39 29.5	51 38.6	
Work:			
working	21 15.9	30 22.7	χ^2 = 2.0 (0.161)
Not working [a]	111 84.1	102 77.3	
Smoking:			
Smoker	4 3.0	0 0.0	**P=** (0.044) [b]
Non Smoker [a]	128 97.0	132 100	
Arabic Coffee Drinking:			
Yes	81 61.4	79 59.8	χ^2 = 0.1 (0.801)
NO [a]	51 38.6	53 40.2	
BMI (kg/m^2) : (Mean ± S)	30.9 ±7.8	27.7±5.6	*t = 3.8 (<0.001)**
Under weight	6 4.5	2 1.5	
Normal weight	20 15.2	53 40.2	**p=** (<0.001)* [b]
Over weight	46 34.8	32 24.2	
Obese	60 45.5	45 34.1	
Obstetric profile:			
Gestational Age (w)**:** (Mean ± S)	29.1± 9.8 (4-40)	28.0 ± 6.0 (6-38)	*1.1 (0.266)*
Gravidity: (Mean ± S)	4.6±3.4 (1-15)	4.4±2.7 (1-13)	*t = 0.6 (0.574)*
Primigravida	36 27.3	16 12.1	
2-3	19 14.4	41 31.1	χ^2 = 17.4 (0.001)*
4-5	31 23.5	38 28.8	
>5-15	46 34.8	37 28.0	
Parity: : (Mean ± S)	3.1 ± 3.2 (0-13)	2.7± 2.4 (0-11)	*t = 1.2(0.251)*
Nullipara	43 32.6	24 18.2	
1-3	38 28.8	64 48.5	χ^2 = 19.4 (<0.001)*
4-5	21 15.9	30 22.7	
>5-13	30 22.7	14 10.6	
Type of Pregnancy:			
Multiple	7 5.3	2 1.5	**P=** (0.090) [b]
Single [a]	125 94.7	130 98.5	
Antenatal Care:			
NO	21 15.9	14 10.6	χ^2 = 1.6 (0.204)
Yes [a]	111 84.1	118 89.4	
Obstetric History:			
Abortion:			
Yes	35 26.5	48 36.4	χ^2 = 3.0 (0.085)
NO [a]	97 73.5	84 63.6	
Pre-/eclampsia:			
Yes	18 13.6	6 4.5	χ^2 = 6.6 (0.010)*
NO [a]	114 86.4	126 95.5	
Multiple Pregnancy:			
Yes	4 3.0	8 6.1	**P=** (0.237) [b]
NO [a]	128 97.0	124 93.9	

Table (1) cont': Characteristics of the studied cases and controls, Al-Hasaa, KSA.

Women Characteristics	Hypertensive gravidas n %	Normotensive gravidas n %	Significance Test (p)
Premature Labour:			
Yes	20 15.2	14 10.6	χ^2 = 1.2 (0.270)
NO [a]	112 84.8	118 89.4	
Small for Age:			
Ye	17 12.9	10 7.6	χ^2 = 2.0 (0.155)
NO [a]	115 87.1	122 92.4	
Early Neonatal Death:			
Yes	7 5.3	12 9.1	χ^2 = 1.4 (0.234)
NO [a]	125 94.7	120 90.9	
Family History (HDP):			
Yes	37 28.0	16 12.1	χ^2 = 10.4 (0.001
NO [a]	95 72.0	116 87.9	
Total	132 100	132 100	

[a] Reference group * Statistically significant [b] Fisher's Exact Test

Table (2): Adverse maternal outcome among control, hypertensive disorders of pregnancy (HDP) and its subtypes, Al-Hasaa, KSA.

Adverse Outcome	Control n=132	HDP n=132	Chronic Hypertension n=23	Gestational Hypertension n=22	PSCH n=17	Pre-eclampsia/ Eclampsia n=70
	n (%)	n (%) RR (CI), p [1]	n (%) RR (CI), p [1] *RR (CI),* p [2]	n (%) RR (CI), p [1]	n (%) RR (CI), p [1]	n (%) RR (CI), p [1] *RR (CI),* p [2]
Maternal Complications	5 (3.8)	23 (17.4) 5.4 (2.0-14.6), p<0.001*	2 (8.7)	2 (9.1)	1 (5.9)	18 (25.8) 8.8(3.1-24.9), p<0.001* *3.9(1.4-11.4),* p=*0.008* *
Preterm Labour	10 (7.6)	41 (31.1) 5.5 (2.6-11.6), p<0.001*	5 (21.7) 3.4 (1.0-11.1), p=0.034*	2 (9.1)	6 (35.3) 6.7(2.0-21.8), p=0.004*	28 (40.0) 8.1 (3.6-18.2), p<0.001* *2. 5 (1.2-5.5),* p=*0.018* *
Caesarean Section	28 (21.2)	76 (57.6) 5.0 (2.9-8.7), p<0.001*	13 (56.5) 4.8 (1.9-12.2), p <0.001*	8 (36.4)	8 (41.2)	48 (68.6) 8.1 (4.2-15.6), p=0.001* *2.6 (1.3- 5.4),* p=*0.007* *
Induction of Labour	20 (15.2)	62 (47.0) 5.0 (2.8-8.9), p <0.001*	15 (65.2) 10.5 (3.9-28.0), p<0.001*	2 (9.1)	8 (47.1) 4.4(1.5-13.0), p=0.005*	37 (52.9) 6.3 (3.2-12.3), p<0.001*
Termination of Pregnancy	0 (0.0)	5 (3.8) 2.0 (1.8-2.3), p=0.060 * [a]	0 (0.0)	0 (0.0)	1 (5.9)	4 (5.7) 3.0 (2.5-3.7), p=0.014* [a]
Placental Abruption	0 (0.0)	2 (1.5) 2.0 (1.8-2.3), p=0.498 [a]	2 (8.7) 7.3 (4.9-10.8), p=0.02* [a] *6.2 (4.2-9.2),* p=*0.029* * [a]	0 (0.0)	0 (0.0)	0 (0.0)
HELLP Syndrome	0 (0.0)	5 (3.8) 2.0 (1.8-2.3), p=0.060 [a]	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.1) 3.0 (2.5-3.7), p=0.005 * [a]

Post natal follow up visits continued on weekly basis for monitoring of blood pressure and laboratory abnormalities until normalization, then for extra two weeks to ensure stability. Control women were followed during their scheduled prenatal visits then for one week post natal.

Outcome Measures:

Adverse maternal outcome included preterm labour, labour induction, Cesarean delivery, termination of pregnancy, antepartum and postpartum hemorrhage, placental abruption, HELLP (hemolysis, elevated liver enzymes, and low platelets) or partial

Table (3): Adverse perinatal outcome among control, hypertensive disorders of pregnancy (HDP) and its subtypes, Al-Hasaa, KSA.

Adverse Outcome	Control n=132	HDP n=132	Chronic Hypertension n=23	Gestational Hypertension n=22	PSCH n=17	Pre-eclampsia/ Eclampsia n=70
	n (%)	n (%) RR (CI), p [1]	n (%) RR (CI), p [1] *RR (CI),* p [2]	n (%) RR (CI), p [1]	n (%) RR (CI), p [1]	n (%) RR (CI), p [1] *RR (CI),* p [2]
Perinatal Complications	25 (18.9)	69 (52.3) 4.7 (2.7-8.2), p=0.019*	12 (52.2) 4.7 (1.8-11.8), p=0.001*	8 (36.4)	6 (35.3)	43 (61.4) 6.8 (3.6-13.0), p=0.001* *2.2 (1.1-4.4),* p=*0.025* *
Intrauterine Growth Restriction (IUGR)	2 (1.5)	25 (18.9) 15.2(3.5-65.6), p<0.001*[a]	2 (8.7)	0 (0.0)	2 (11.8)	21 (30.0) 27.9 (6.3-123.3), p<0.001* [a] *6.2 (2.0-19.3),* p=*0.001** [a]
Fetal Distress	12 (9.1)	23 (18.1) 2.2 (1.0-4.7), p=0.034*	2 (8.7)	2 (9.1)	0 (0.0)	19 (28.8) 4.0 (1.8-9.0), p<0.001* *5.8 (1.8-18.1),* p=*0.001** [a]
Small for Gestational Age (SGA) [b]	2 (1.5)	25 (19.7) 15.9(3.7-68.8), p<0.001*[a]	2 (8.7)	0 (0.0)	2 (12.5)	21 (31.8) 30.3 (6.8-134.5), p<0.001*[a] *6.6 (2.1-20.8),* p<*0.001** [a]
Prematurity b	10 (7.6)	36 (28.3) 4.8 (2.3-10.2), p<0.001*	5 (21.7) 3.4 (1.03-11.1), p=0.034*	2 (9.1)	5 (31.2) 5.5 (1.6-19.1), p=0.003*	24 (36.4) 7.0 (3.1-15.8), p<0.001* *2.3(1.0-5.2),* p=*0.037* *
Admission to Neonatal Intensive Care Unit (NICU) [b]	4 (3.0)	39 (30.7) 14.2(4.9-41.1), p<0.001*[a]	3 (13.0)	2 (9.1)	5 (31.2) 14.5 (3.4-62.1), p=0.001*[a]	29 (43.9) 25.1 (8.3-75.9), p<0.001 [a] *4.0 (1.7-9.2),* p=*0.001**
Low Apgar score 1 [b] (<7)	5 (3.8)	46 (36.2) 14.4 (5.5-37.8), p<0.001*	7 (30.4) 11.1 (3.2-39.2), p<0.001*	2 (9.1)	6 (37.5) 11.5 (2.9-46.1), p<0.001*	31 (47.0) 22.5 (8.1-62.1), p<0.001* *2.7 (1.3-5.8),* p=*0.009* *
Low Apgar score 5 [b] (<7)	0 (0.0)	18 (14.2) 2.2 (1.9-2.5), p<0.001*[a]	3 (13.0) 7.6 (5.1-11.4), p=0.003*[a]	0 (0.0)	2 (12.5) 10.4(6.3-17.2), p<0.011*[a]	13 (19.7) 3.5 (2.8-4.4), p<0.001*[a]

*PSCH: preeclampsia superimposed on chronic hypertension, RR: relative risk, CI: Confidence Interval p: p-value of χ^2-test, [1]Versus control, [2]Versus Other Types, *Statistically significant, [a] Fisher's Exact Test, [b] Calculated for live births (n=127)*

HELLP syndrome, oliguria, renal or hepatic dysfunction or failure, intracranial hemorrhage, pulmonary oedema, hypertensive encephalopathy, admission to intensive care unit (ICU), and maternal death in hospital.

Adverse fetal outcome included intrauterine growth restriction (IUGR), prematurity, small for gestational age (SGA), fetal distress, intra uterine fetal death (IUFD), oligohydramnios, neonatal ICU admission (NICU), low Apgar score (<7), still birth and neonatal death. WHO definition and sub-categories of prematurity were adopted in the study.[7]

Statistical analysis:

Statistical analysis was conducted using SPSS program version 16 (SPSS Inc. Chicago, IL, USA). Frequency, mean and standard deviation, the student t-tests, chi- square, Fissure Exact Test, relative risk (RR, with 95% confidence interval, CI), and logistic regression (forward Wald) were performed. Significance of the obtained results was judged at the 5% level.

Table (4): Predictors of adverse outcomes among women with HDP, Al-Hasaa, KSA.

Predictor	Odds ratio	Adjusted odds ratio (95% CI)	P value
Maternal Complications:			
Absent antenatal care	5.5	45.2 (25.9-132.4)	<0.001
Maternal age below 35 years	2.7	14.5 (1.7-28.0)	0.016
Elevated serum bilirubin	2.4	10.6 (1.4-38.0)	0.024
Constant	-5.3	0.005	0.001
R^2 = 0.41, Adjusted R^2 = 0.68, X^2 (p value) = 69.7 (<0.001), Model sensitivity = 92.4%			
Fetal Complications:			
Preterm delivery	4.0	52.2(9.2-297.3)	<0.000
Elevated serum bilirubin	2.5	12.1(1.8-80.2)	0.010
Poor education	2.0	7.1(2.1-23.8)	0.002
Uncontrolled BP	1.9	6.5(1.6-26.2)	0.008
Primi gravida	1.5	4.5(1.3-15.9)	0.018
Constant	-13.4	<0.000	<0.000
R^2 = 0.46, Adjusted R^2 = 0.61, X^2 (p value) = 80.1 (p<0.001), Model sensitivity = 83.3%			

Ethical considerations:

The study proposal was reviewed and approved by the Research Ethics Committee of Alexandria Faculty of Medicine. The official authorities' permissions were obtained from the MCH, Al-Hasaa. Purposes of the research and the expected benefits were explained to the selected women and a written consent to participate was obtained. The privacy of mothers was kept confidential.

Results:

I- Women characteristics:

The present study included 132 women with hypertensive disorders of pregnancy (HDP) and 132 normotensive pregnant women with 100% response rate. Table (1) shows that personal characteristics of both groups were comparable except starting body weight which was significantly higher among hypertensive women (p<0.001). Women with HDP were mostly obese (45.5%) while controls were mostly of normal weight (40.2%), p<0.001.

Table (1) displays a mean gestational age of 29.1± 9.8 and 28.0 ± 6.0 weeks among hypertensive and normotensive women respectively. The table also reveals that the rank of first and >fifth pregnancy were significantly more common in HDP than in controls (27.3% versus 12.1%) and (34.8% versus 28.0%) respectively, p=0.001. Nulliparity and parity exceeding five were significantly more presented in HDP than controls (32.6% versus 18.2%) and (22.7% versus10.6%) respectively, p=0.001. Hypertensive women were more likely to have history of pre-/eclampsia (p=0.001) and family history of HDP (p=0.001) than normotensive. No significant differences were observed among other parameters of obstetric profile or history.

II- Medical profile:

Among HDP, the most prevailing subtype was PE (47.7%) followed by chronic (17.4%) and gestational (16.7%) hypertension. PSCH constituted 12.9% and eclampsia 5.3%. The mean systolic BP was 159.7±19.3 mmHg and the mean diastolic BP was 99.2±13.9 mmHg. Onset of hypertension predated pregnancy/<

20 gestational week in 30.3%, at ≥ 20 weeks of gestation in 62.1% and intra labour in 6.1% Of HDP. Severe cases (PB≥110/160) constituted 55.3%. After management, acceptable BP control was achieved in most cases (71.2%). Laboratory results of HDP showed positive albuminuria in 65.9% of cases (1+ in 19.7%, 2+ in 18.9% and 3+ in 27.3%). low RBCs and low platelet counts were observed among 23.5% and 15.9% respectively. Elevated serum levels of liver enzymes (11.4%), bilirubin (8.3%) and uric acid (11.4%) were also recorded. Serum levels of creatinine, electrolytes and BUN (blood urea nitrogen) were normal in all cases. As to controls, BP was normal (113.2±11.5 and 69.1±7.8 mmHg for systolic and diastolic BP respectively). Their laboratory results were also normal except low RBCs count among 15.9%. Inhalational cortisone was reported by 3.8% of HDP and 9.8% of controls, while 8.3% of controls were on oral cortisone therapy. None of the studied women had a history of diabetes mellitus, gestational diabetes or renal disease.

III. Outcome:

- **Maternal Outcome:**

Compared to controls, women with HDP had significantly higher weight gain in pregnancy (12.9±6.3 versus 10.3±5.7 kg, p=0.001) and lower gestational age at ending of pregnancy (36.6±3.8 versus 39.3±1.5 weeks, p<0.001). Pregnancy of hypertensive women was ended extremely preterm (<28 weeks) in 3.8%, very preterm (28-<32) in 12.1% and moderate to late preterm (32-<37 weeks) in 15.2% (data not shown). Table (2) compares maternal outcome among controls and cases. It shows that women with HDP were more prone to complications (RR=5.4), preterm labour (RR=5.5), Cesarean section (CS) (RR=5), and labour induction (RR=5). HDP was also significantly associated with pregnancy termination (RR=2). All terminations were before 28 weeks' gestation and were indicated due to IUFD (40%), uncontrolled condition (20%), or combination of both (40%) (data not shown).

No significant case-control differences were observed among partial HELLP, HELLP syndrome, placental abruption, antepartum hemorrhage, oliguria, and other complications. No postpartum hemorrhage was reported in HDP. No cases of pulmonary oedema, renal or hepatic failure, intracranial haemorrhage, hypertensive encephalopathy, admission to ICU, or maternal deaths were seen among cases or control. No cases of PE proceeded to eclampsia. No eclamptic seizures were observed during follow up. Versus control, table (2) shows also that PE/eclampsia was the most serious type carrying a greater risk of developing most of the observed maternal complications followed by chronic hypertension. While PSCH was less risky, gestational hypertension showed no risk.

Compared to other types, PE/eclampsia showed association with maternal complications, CS, and preterm labour, whilst chronic hypertension was linked to placental abruption. Gestational hypertension and PSCH showed no risk versus other subtypes.

Women with uncontrolled BP (≥140/90 mmHg) or severe hypertension (BP≥ 160/110 mmHg) were more prone to develop maternal complications, where RR=3.5 (CI=1.4-8.8, p=0.006) and RR= 2.8 (CI=1.0-7.3, p=0.048) respectively (data not shown)

- **Fetal Outcome:**

Perinatal complications among hypertensive and normotensive women are compared in table (3). Fetuses of hypertensive mothers showed increased risk for perinatal complications (RR=4.7),

SGA (RR=15.9), IUGR (RR=15.2), prematurity (RR=4.8), and fetal distress (RR=2.2), More, neonates among HDP group were more prone to have low Apgar score at one minute (RR=14.4) and at five minutes (RR=2.2), and to be admitted to NICU (RR=14.2), table (3). Oligohydramnios showed no significant differences among the studied women. No stillbirths or neonatal deaths were recorded in the study (data not shown).

It is clear from table (3) that versus control, PE/eclampsia was the most risky subtype showing association with all of the observed perinatal complications. Adding, whereas HDP exhibited no significance among IUFD, PE/eclampsia did [RR=3.0, CI=(2.5-3.7), p=0.014, not shown]. Gestational hypertension carried no significant risk for babies, whilst chronic hypertension and PSCH displayed intermediate risk, table (3).

In subtype analysis, only PE/eclampsia manifested significant link to almost all perinatal complications. No risk was involved in all other subtypes.

Perinatal complications significantly increased with uncontrolled state (RR=8.4, CI=3.4-20.6, p<0.001) than controlled. Severity of hypertension had no effect on perinatal complications (data not shown).

Chronic hypertension:

Among de novo HDP (92 out of 132), recovery rate was 45.7% immediately after birth and increased to 81.5% by 12 weeks post term. Beyond this point, the remaining 18.5% (17 women) were still hypertensive and continued therapy (five women controlled and 12 uncontrolled). By 16 weeks, another nine women became controlled on medication. Beyond 18 weeks follow up the remaining three women (3.3%) were still resisting treatment. The incidence of chronic hypertension among types was 28.6% in eclampsia, 20.6% in PE, and 9.1% in gestational type.

Predictors of adverse outcome:

Risk factors of adverse outcome in univariate analysis were entered into regression models. Maternal age below 35 years (compared to≥35 years), poor education (≤primary school compared to higher education), nullipara, absent antenatal care (ANC), low platelet count, elevated serum bilirubin, elevated liver enzymes, uncontrolled BP, and PE/eclampsia were associated with both maternal and perinatal complications. Further, family history of HDP, elevated serum uric acid and severity were associated with maternal while primigravida was associated with perinatal unfavourable outcome (data not shown). Table (4) shows the predictors of adverse outcome among HDP. It reveals that absent ANC (AOR=45.2), maternal age below 35 years (AOR=14.5) and elevated serum bilirubin (AOR=10.6) are the predictors of adverse maternal outcome. This model correctly classifies 92.4% of causes. Predictors of perinatal complications are preterm delivery (AOR=52.2), elevated serum bilirubin (AOR=12.1), poor education (AOR=7.1), uncontrolled BP (AOR=6.5) and primigravida (AOR=4.5). These factors correctly classify 83.3% of causes.

Discussion:

HDP continue as a major health problem responsible for significant maternal and perinatal morbidity and mortality worldwide. [8] The present study enrolled 132 pregnant women with HDP, where pre-eclampsia was the most prevailing subtype, in consistence with multicountry observations.[8-14] In our controlled prospective study 17.4% of mothers with HDP experienced complications (table 2). A lower rate was detected in Western KSA (9.4%)[9], while higher rates were recorded in other

countries.[13,15]

CS was the most common (57.6%) maternal complication of HDP in this study. Lower figures were previously obtained in Eastern KSA[16] as in other countries[12,17,18], whereas higher rates were observed in larger studies.[14,19] An extremely high rate of CS (98.5%) was seen among hypertensive mothers whose neonates were admitted to NICU.[20] The great variations in the rate of CS may be attributed to the nature of the cases, differences in evaluation technology or differences in considering HDP an indication for CS.[14,20] In harmony with prior reports[9,12,14,16,17], our increased risk of CS was mainly encountered in PE /eclampsia.

Efficient therapeutic measures for HDP are lacking and treatment is largely symptomatic with close observation of mother and fetus for optimal timing of delivery to improve outcome. In many cases preterm delivery is mandatory regardless gestational age.[1-3] Preterm delivery amounted to 31.1% in our study which is comparable with the previous rates from KSA and other regions (28.1-30.2%)[12,14,16] and higher than that reported in Ghana (21.7%).[18] Almost 28.3% of our live births were premature. Consistent (31.4%)[12], and higher (52%)[20] figures were also observed. Contradicting Kheir et al[20], prematurity was not associated with gestational hypertension in our study but with all other types of HDP (tables 2,3). In agreement with previous studies[12,13,16], preterm delivery in this report was a main predictor for perinatal complications. Sometimes mother's condition cannot be controlled, mainly in PE/ eclampsia, and termination of pregnancy becomes the only solution to save mothers via eliminating placenta, the root cause of PE. Yet, timing may be on the expense of fetal survival.[1-3,14] Our results were confirmatory where all pregnancy terminations were combined with extremely preterm deliveries, largely due to uncontrolled condition and associated PE/eclampsia. In line, Seyom et al recorded all study terminations within PE.[12] In this study, labour induction (47.0%) was significant in almost all types of HDP versus control without differences among types. Seyom et al obtained an identical figure (47.9%) with more distribution in PE.[12] A lower rate (30.8%) was observed among eclampsia.[19]

A strong association between placental abruption and hypertension in pregnancy was documented.[21] In contrast, the incidence of placental abruption in this work was low (1.5%) and insignificant. Consistent low rates were observed by others.[12,14,19] While higher figures of abruption were reported in PE/eclampsia inside[16] and outside KSA[17], abruption was only encountered in chronic hypertension in our analysis (8.7%, RR=7.3), table 2. This may be an effect of chronicity. Similarly, HELLP (3.8%) was insignificant complication in the present study. Our rate varies from the old zero level in KSA[10] and the 12.4 % in Ethiopia.[12] Among types, our cases were only significant in PE (7.9%, RR= 3.0, table 2). Lower[17] and higher[19] rates in PE/eclampsia were observed by other authors. However, due to the differences in diagnostic criteria, the true incidence of this syndrome is unknown.[17]

In consistence with our low incidence of some maternal complications (table 2) and absence of others including deaths, previous Saudi studies reported similar observations of low and zero levels.[9,10] Zero maternal mortality was also observed in Saudi and non-Saudi studies.[10,12,13,20] On the other hand, various reports recorded higher figures of

complications.[12-14,16,17,19] and variable rates of mortality (0.1% to 2.8%).[8,9,11,14,17] Higher maternal mortality in some studies may reflect missing or misdiagnosis of the disorder, inadequate or delayed management of the condition or associated complications or co-morbidities. Mortality was also associated to deprived or low rate of ANC.[8] In the current work, absent maternal deaths and serious complications may be attributed to improved antenatal care, appropriate monitoring and timely appropriate interventions. Also, hospital deliveries under medical supervision could contribute to improved outcome.[8,12,17,20]

Persistent hypertension beyond three months post term represents chronic hypertension.[4] Almost 18.5% of our cases showed persistent hypertension opposite 33.5% reported by Gansevoort et al.[13] Our rates in eclampsia and PE were much higher than prior Indian rates.[17]

In the present study, perinatal complications amounted to 52.3%, which was much lower than the 89.3% observed in Ethiopia[12] and higher than other European rates.[13,15] The study analysis significantly linked IUGR, fetal distress and SGA to HDP and to PE/eclampsia (tables 3). These complications could be attributed to disturbed placental vascularity of PE, poor placental perfusion with secondary fetal insufficiency.[2,3] While consistent association of SGA with PE was reported[20], a Saudi study failed to confirm an association.[9] There is also a proof that the rate of SGA increases with increasing degree of hypertension and ceases with controlling BP.[22] In accordance, our low rate of SGA (17.9%) may be attributed to the achieved level of BP control (71.9%). Other studies observed higher rates of SGA (57%) and of low birth weight (24.7% to 66.7%).[12,14,17,18]

Our significant low Apgar score at one minute (36.2%) was associated with PE, whereas at five minutes (14.2%) was not associated with any type. Very similar observations were recorded in a previous study with 34.0% and 14.7% rates at one and five minutes respectively. Further, association with PE was significant at one but not at five minutes.[18] Other studies reported comparable rates at five minutes but in association with gestational type and eclampsia.[12,17] On the other hand, a Saudi report couldn't associate Apgar scores with subtypes of HDP.[9] The detected improvement in Apgar scores at five minutes might be due to effective neonatal care.[18]

Our NICU admissions (30.7%) showed significant association with all forms of PE (table 3). Lower admission rates in association with PE/eclampsia were previously described.[17-19]

While still births and perinatal deaths disappeared from the present study, perinatal mortalities between 3.4% and 4.7% and still births of 2.3% were previously described in KSA in association with deprived ANC, prematurity, birth weight, and severity.[10,16] In other countries, perinatal deaths from 2.7% to 12.0% and still births from 6.8 % to 16.9% were reported.[8,12-14,17-19] Adding to regular maternal care and proper case management, our zero perinatal mortality might be attributed to effective natal and neonatal services.

In consistence with previous reports[8,11,14,15], our study presented PE/eclampsia as the most serious subtypes responsible for the highest maternal and perinatal morbidity (tables 2-3). A recent Saudi report couldn't significantly associate outcomes with subtypes of

HDP.[9] However, our type differences dropped from regression model, in contrast with Cicero et al.[15]

High serum bilirubin was a main predictor of adverse maternal outcomes and may be a signal of hemolysis suggesting the serious HELLP syndrome.[2,13] Un-controlled BP was linked to our unfavorable outcomes and predicted fetal complications, indicating the importance of BP monitoring for materno- fetal protection. Consistent conclusion was reported by Cicero et al.[15] Our observations associated severity of HDP with maternal but not fetal complications, that agrees with Seyom et al[12] and varies from Al-Mulhim et al who observed association with both in Eastern KSA.[16]

Most cases of HDP are asymptomatic and accidently discovered in perinatal clinics[9,16], eliciting the importance of regular ANC in early recognition and better outcome. In line with several studies[11,12,16], this study associated absent ANC with unfavorable outcomes and further presented it as the most prominent predictor of maternal complications. Whereas the present work significantly associated primigravida with adverse outcome of HDP in both univariate and multivariate analysis, another Saudi study showed no association.[9] The current report linked maternal age below 35 years and poor education with unfavorable materno-fetal outcome in both univariate and multivariate analysis. Maternal age below 30 years predicted maternal and fetal complications in a consistent report.[13] Poorly educated women may be of low health awareness, low medical care attendance and consequently poor prognosis.[11]

However, different study results may be attributed to the variations between characteristics and size of the study population, type, place, time and duration of study, objectives, and methods of researches. Differences in definitions, classifications, criteria of diagnosis, and different management protocols may also play a role. In addition, proportion of risk factors, quality of reporting and recording, state of country development, technology, medication and policy of health care delivery may contribute.[8,14]

Strength & limitations:

The strength of this study is that it is prospective, controlled, included all types of HDP, and involved both perinatal and maternal outcomes including post natal complications. The fact that the study is uni-center and involved a small number limited its results. The limited similar recent researches in the region for comparison are considered a limitation of the study. Presence of cases-control differences among some factors as BMI, gravidity, parity and history of PE might affect differences in the incidence of complications and constitutes another study limitation.

Conclusion:

Pre-eclampsia was the most prevailing type of the hypertensive disorders. HDP carried a risk of adverse outcome for both mothers and babies. PE/eclampsia was the most risky. Incidence of chronic hypertension following pregnancy hypertension was18.5%. Adverse outcome of HDP could be predicted by absent ANC, younger maternal age, elevated serum bilirubin, preterm delivery, poor education, uncontrolled BP and primigravida. Regular follow up, proper timely management and BP control may help reduction of maternal and perinatal morbidity and mortality.

Recommendations:

Continuous medical education and training on early detection of women with HDP, timely referral, continuous monitoring,

and appropriate management.

Early prediction of HDP complications giving attention to women with abnormal laboratory results, uncontrolled BP, deprived of ANC, primi gravida, young age, and poorly educated.

Women and community health education about pregnancy and care of pregnant women to encourage early, regular and more widespread use of ANC.

Further multicenter studies throughout KSA to predict HDP and its outcome.

Advocating women school education.

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Conflicts of interests

The authors declare no competing interests.

Abbreviation:

KSA: Kingdom of Saudi Arabia, PE: Pre-eclampsia, HDP: Hypertensive disorders of pregnancy, PSCH: Pre-eclampsia superimposed on chronic hypertension, BMI: Body mass index, BP: Blood pressure, HELLP: Hemolysis, elevated liver enzymes, and low platelets, ICU: Intensive care unit. IUGR: Intrauterine growth restriction. SGA: Small for gestational age. IUFD: Intra uterine fetal death. NICU: Neonatal intensive care unit. Apgar:Appearance, Pulse, Grimace, Activity, and Respiration. RR: Relative risk. CI: Confidence Interval CS: Cesarean section OR: Odds ratio. AOR: Adjusted odds ratio. RBC: Red blood cells.

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