

Gülseren Yücesoy · Sebiha Özkan · Harika Bodur
Temel Tan · Eray Çalışkan · Birol Vural
Aydın Çorakçı

Maternal and perinatal outcome in pregnancies complicated with hypertensive disorder of pregnancy: a seven year experience of a tertiary care center

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Abstract Objective: The aim of the study was to determine the risk factors, prevalence, epidemiological parameters and maternal-perinatal outcome in pregnant women with hypertensive disorder. **Materials and methods:** A retrospective analysis was undertaken on 255 consecutive cases of hypertensive disorder in pregnancy who were managed at Kocaeli University, School of Medicine, Department of Obstetrics and Gynecology from June 1997 to November 2004. Demographic data involving age, parity, gestational week, clinical and laboratory findings were recorded from the medical files. Additionally delivery route, indications of cesarean section, fetal and maternal complications were determined. Statistical analysis was performed by SPSS programme using Kruskal Wallis nonparametric test, ANOVA (Analysis of variance) and chi-square tests. **Results:** Of 5,155 deliveries in our clinic during the defined period, 438 cases (8.49%) were managed as hypertensive disorder of pregnancy. Medical records of 255 cases could be available. Of 255 cases, 138 patients (54.11%) were found to have severe preeclampsia while 88 cases (34.50%) were diagnosed as mild preeclampsia. Twenty-nine patients (11.37%) were suffering from chronic hypertension. Of 138 severely preeclamptic cases, 28 cases (11%) had eclamptic convulsion and another 28 patients (11%) were demonstrated to have HELLP syndrome. Intrauterine growth restriction, oligohydramnios, placental ablation were the obstetric complications in 75 (29.4%), 49 (19.2%), 19 (7.5%)

cases, respectively. Additionally multiple pregnancy and gestational diabetes mellitus were noted in 5.9% ($n:15$) and 3.9% ($n:10$) of the patients. Delivery route was vaginal in 105 patients (41.2%) while 150 patients (58.8%) underwent cesarean section with the most frequent indication to be fetal distress in 69 cases (46%). Cesarean section rate seemed to be the lowest (48.3%) in chronic hypertensive women while the highest (63.8%) in severe preeclamptic patients. Maternal mortality occurred in 3 cases (1.2%) and all of those cases were complicated with HELLP syndrome. Intracranial bleeding was the cause of maternal death in one case while the other two cases were lost due to acute renal failure and disseminated intravascular coagulation, respectively. Intrauterine fetal demise was recorded in 24 cases on admission. Ten fetuses died during the intrapartum period. Mean gestational age and birth weight were 28 ± 3.5 and 1000 ± 416 g, respectively in this group. In these ten women, five cases were diagnosed as HELLP syndrome, two were severely preeclamptic and three were eclamptic. Perinatal mortality rate was found to be 144/1,000 births. **Conclusion:** Hypertensive disorder of pregnancy is associated with increased risk of maternal-perinatal adverse outcome. The complications of severe preeclampsia and eclampsia could be prevented by more widespread use of prenatal care, education of primary medical care personnel, prompt diagnosis of high-risk patients and timely referral to tertiary medical centers.

Keywords Pregnancy · Hypertension · Maternal · Perinatal · Outcome

G. Yücesoy · S. Özkan · H. Bodur · T. Tan
E. Çalışkan · B. Vural · A. Çorakçı
Department of Obstetrics and Gynecology,
School of Medicine, University of Kocaeli,
Kocaeli, Turkey

G. Yücesoy (✉)
Mazhar Osman Sok, 10/8, Feneryolu-Istanbul, Turkey
E-mail: gulserene@superonline.com
Tel.: +90-532-2627929
Fax: +90-212-3277049

Introduction

Hypertensive disorder of pregnancy seems to be one of the major causes of maternal morbidity-mortality leading to 10–15% of maternal deaths especially in the

developing areas of the world [29]. It occurs in around 12–22% of pregnancies depending on the population and the definitions used [32]. Five classes of hypertensive disorders were identified according to the latest classification system described by the National High Blood Pressure Education Working Group (2000) including preeclampsia, eclampsia, transient hypertension of pregnancy, chronic hypertension and preeclampsia superimposed on chronic hypertension [22]. Differentiating between these groups is mandatory regarding the determination of best management strategies.

Approximately 30% of hypertensive disorders of pregnancy were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/preeclampsia [20].

Preeclampsia is a multisystem disorder of unknown etiology, unique to pregnancy [3, 7]. Preeclampsia can present as HELLP syndrome (hemolysis, elevated liver enzymes and low platelet count) or eclampsia that is occurrence of convulsions that can not be attributed to other etiologic factors. Eclampsia is reported to be associated with a maternal mortality rate of 0.5–10% usually requiring high quality intensive care [1]. Additionally, preeclampsia predisposes toward potentially lethal complications involving placental ablation, disseminated intravascular coagulation, intracranial hemorrhage, hepatic failure, acute renal failure and cardiovascular collapse. Intrauterine fetal growth restriction (IUGR), intrauterine fetal demise and prematurity appear to be the other related obstetric problems [27]. All these clinical situations mandate prompt diagnosis and aggressive management in order to reverse adverse maternal-perinatal outcome.

The aim of our study was to evaluate the prevalence, sociodemographic parameters, maternal and fetal complications of this potentially devastating disorder of pregnancy in a developing region of the world.

Materials and methods

A descriptive, cross-sectional, retrospective study was undertaken reviewing the medical records of all gravid women with hypertensive disorder of pregnancy who were managed at Kocaeli University, School of Medicine, Department of Obstetrics and Gynecology between June 1997 and June 2004. The present study was approved by Local Ethics Committee. The diagnosis of hypertension in pregnancy was based on the criteria defined by National High Blood Pressure Education Programme Working Group on High Blood Pressure in Pregnancy [22]. Preeclampsia was defined as a blood pressure $\geq 140/90$ mmHg together with albuminuria of at least 300 mg/24 h after 20 weeks of gestation. Severe preeclampsia was diagnosed with one or more of the following criteria: blood pressure $\geq 160/110$, proteinuria of at least 5 g/24 h, oliguria (< 600 ml/24 h or < 30 –50 ml/h), intrauterine fetal growth restriction, oligohydramnios (amniotic fluid index ≤ 50 mm), symptoms

suggesting end organ failure such as headache, visual disturbances, epigastric pain, medical complications involving pulmonary edema, cerebral edema, acute renal insufficiency, hepatic hematoma, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count). Generalized seizures in a preeclamptic pregnant woman not associated with other etiologic factors are considered to be due to eclampsia. The pregnant women with previous hypertension or hypertensive women without proteinuria early in pregnancy before 20 weeks of gestation are suggested to be chronically hypertensive. Chronic hypertensive cases with new onset of proteinuria are diagnosed as superimposed preeclampsia. The patients in whom we diagnosed hypertensive disorder of pregnancy were grouped as chronically hypertensive cases (Group I), mildly preeclamptic cases (Group II) and severely preeclamptic cases (Group III) involving eclamptic women and the cases with HELLP syndrome according the clinical and laboratory criteria described above.

Patients were hospitalized in great majority of the cases once the diagnosis was made. In selected cases (gestational hypertension, mild preeclampsia, chronic hypertension with regular blood pressure measurements) at request of the patients ambulatory control was allowed. On admission blood samples were collected for laboratory evaluation. Blood pressure measurements were done, 24 h urinary albumin excretion was determined. Blood samplings were repeated every 3 days depending on the severity of the disease. Fetal status was assessed with nonstress test each day and ultrasonographic evaluation twice a week. Maternal complications such as eclampsia, HELLP syndrome, acute renal insufficiency, disseminated intravascular coagulation, placental abruption and oliguria were recorded. Fetal complications including intrauterine fetal growth restriction, oligohydramnios, fetal distress, low APGAR scores, acidotic pH values after birth and requirement of neonatal intensive care unit (NICU) determined.

In patients with severe preeclampsia, antepartum management included bed rest, MgSO₄ infusion to prevent eclamptic convulsions (4.5 g intravenous loading dose followed by 1–3 g intravenous per hour until 24 h after delivery). Nifedipine was administered sublingually to control high blood pressure values $\geq 160/110$ mmHg and Ringer's lactate was given intravenously at a rate of 60–120 ml/h for expansion of plasma volume. Betamethasone, two doses of 12 mg, was administered intramuscularly 24 h apart to accelerate the fetal lung maturity in cases with gestational age of 28–34 weeks. Prostaglandin analogue or oxytocin infusion were preferred to induce or augment labour according to Bishop score in cases which were decided to be delivered.

Data regarding the demographic parameters, gestational age (determined by known last menstrual period or first trimester ultrasonography), associated medical problems such as hypertension, diabetes mellitus and smoking, presenting signs and symptoms, blood pressure measurements on admission, laboratory evaluation

of blood samples collected on admission (complete blood count, liver enzymes, urea, creatinine, uric acid, coagulation profile), 24 h urinary albumin excretion were recorded. Delivery route, indications of cesarean delivery, obstetric problems involving preterm labour and premature rupture of membranes, maternal and fetal complications during the hospital stay, maternal deaths and fetal deaths, neonatal birth weight, APGAR scores were also gathered from the available data on medical recording files. Perinatal mortality rate was defined as the number of all fetal (after 22 weeks of gestation) and neonatal (during the first 29 days after birth) deaths /1,000 births.

Statistical analysis was performed using SPSS 11.5 programme. Data were defined as means \pm standard deviation. Kruskal Wallis nonparametric test, ANOVA and chi-square tests were used where appropriate. *P* values < 0.05 were considered to be statistically significant.

Results

In this retrospective survey, 5155 deliveries were studied. Of 5155 deliveries 438 (8.49%) patients were found to be complicated with hypertensive disorder of pregnancy. Medical recordings of 255 cases were available. Chronic hypertension was diagnosed in 29 cases (11.37%), 88 patients (34.50%) appeared to be mildly preeclamptic and severe preeclampsia complicated 138 cases (54.11%) involving both eclamptic (*n*:28, 11%) and HELLP syndrome patients (*n*:28, 11%). Underlying medical disease was noted in 38 cases (14.9%).

Twin pregnancy was diagnosed in 15 cases (5.9%), three of them were in chronic hypertension group, seven cases and five cases were in mild and severe preeclampsia groups, respectively. Gestational diabetes mellitus was found to be in ten cases (3.9%).

Demographic and clinical data of three groups are demonstrated in Table 1.

Maternal age, gravida and parity were found to be the highest in chronic hypertension group ($P < 0.001$,

$P < 0.001$, $P < 0.001$, respectively) while maternal age was the lowest in severe preeclampsia group, gravida and parity seemed to be the lowest in mild preeclampsia group. Gestational age and neonatal birth weight were demonstrated to be the lowest in severely preeclamptic cases ($P < 0.001$, $P < 0.001$). Analysis of laboratory data revealed higher hematocrit and leukocyte counts while the pathology was worsened. Aspartate transaminase (AST) and alanine transaminase (ALT) values were the highest in severe preeclampsia ($P = 0.009$, $P = 0.004$). Accompanying medical problems were present in 58.6% of the chronic hypertension patients while mild and severe preeclampsia cases were complicated with medical diseases in 9.1% and 9.8% of the cases respectively. Antihypertensive medication was required in 31% of the chronic hypertension group while only 9.1% and 8.7% of the other two groups needed antihypertensive therapy, respectively. Twenty-seven of all cases (10.6%) were determined to be smokers. Most of them were of severely eclamptic cases (*n*:16), seven cases were mildly preeclamptic and only four patients were chronically hypertensive but smoking did not appear to be significantly different between groups ($P = 0.637$).

Delivery route was vaginal in 105 cases (41.2%) and abdominal in 150 cases (58.8%). "Fetal distress" was the most frequent indication in 69 patients (46%) followed by "previous cesarean section" of 16 cases (10.66%). The other cesarean section indications appeared as malpresentation in 14 (9.33%), nonprogressive labour in 13 (8.66%), placental ablation in 12 (8%), multiple pregnancy in 6 (4%), abnormal Doppler examination findings in 6 (4%), cephalopelvic disproportion in 5 (3.33%), maternal medical complication in 3 (2%), elective in 3 (2%) and placenta previa in 2 (1.33%) cases. Majority of the patients who were delivered abdominally due to fetal distress consisted of severely preeclamptic 40 and mildly preeclamptic 20 patients. Delivery route and indications of cesarean section did not differ significantly between the groups ($P = 0.184$, $P = 0.872$) but abdominal delivery rates seemed to be the highest in severely preeclamptic cases while the lowest in chronic hypertensive group (63.8% and 48.3%, respectively).

Table 1 Demographic and clinical data of pregnant women with hypertensive disorder of pregnancy

	Chronic hypertension <i>n</i> = 29	Mild preeclampsia <i>n</i> = 88	Severe preeclampsia <i>n</i> = 138	<i>P</i> value
Age (years)	32.79 \pm 6.21	27.75 \pm 6.20	27.49 \pm 6.390	< 0.001
Gravida	4.14 \pm 2.82	2.34 \pm 1.86	2.72 \pm 1.89	< 0.001
Parity	2.52 \pm 2.38	0.98 \pm 1.44	1.35 \pm 1.61	< 0.001
Gestational age (weeks)	34.48 \pm 4.88	36.2 \pm 3.59	33.72 \pm 4.34	< 0.001
Birth weight (g)	2200 \pm 894.23	2582.50 \pm 853.80	1994.56 \pm 913.78	< 0.001
Hemoglobin (mg/dl)	11.79 \pm 1.92	11.71 \pm 1.85	12.07 \pm 2.03	0.369
Haematocrit (%)	34.61 \pm 5.07	34.55 \pm 5.06	35.67 \pm 5.61	0.258
Leukocyte (cell/mm ³)	11488 \pm 3884	11287 \pm 3487	12438 \pm 4340	0.092
Platelet count (cell/mm ³)	211672 \pm 83874	221567 \pm 69058	185345 \pm 93863	0.006
AST (U/l)	27.59 \pm 15.35	29.05 \pm 35.42	131.43 \pm 352.50	0.009
ALT (U/l)	18.07 \pm 11.31	20.53 \pm 29.66	80.61 \pm 193.31	0.004
LDH (U/l)	239.10 \pm 116.45	278.26 \pm 318.95	622.35 \pm 1085.82	0.004
BUN (mg/dl)	14.10 \pm 8.01	11.86 \pm 4.10	14.49 \pm 7.04	0.01
Creatinine (mg/dl)	0.92 \pm 0.76	0.76 \pm 0.17	0.85 \pm 0.28	0.077

Data are expressed as mean \pm standard deviation

Maternal complications were presented in Table 2. The most frequently encountered one was defined to be placental ablation followed by acute renal failure and disseminated intravascular coagulation. Placental ablation was diagnosed in severely preeclamptic, mildly preeclamptic and chronically hypertensive groups with incidences of 10.1%; 14 cases, 4.5%; 4 cases and 3.4%; 1 case, respectively, with a statistically nonsignificant difference ($P=0.202$).

Maternal mortality occurred in 3 cases (1.2%) of whom all were diagnosed as HELLP syndrome. Table 3 presented the clinical characteristics of those maternal death cases.

Table 4 demonstrated fetal complications. Intrauterine fetal growth restriction was noted most frequently in severely preeclamptic cases ($P=0.032$) while oligohydramnios did not appear to be significantly different between the groups ($P=0.917$). Antepartum evaluation revealed fetal tachycardia (fetal heart rate >160 /min) more frequently in severely preeclamptic group ($P=0.048$). APGAR scores at 1 min and 5 min were determined to be low more frequently in severely preeclamptic women ($P=0.002$, $P=0.006$). Admission to neonatal intensive care unit was more frequently required in severely preeclamptic cases ($P=0.014$). Premature rupture of membranes (PROM) was recorded in 21 patients. PROM complicated the mild preeclamptics more frequently (13 cases, 61.90%) while only 5 (21.80%) severely preeclamptic and three (14.28%) chronically hypertensive women had PROM ($P=0.011$). On the other hand 25 cases (9.8%) experienced premature labour, of whom 12 cases (48%) were severely preeclamptic, 10 (40%) were mildly preeclamptic and only three cases (12%) had chronic hypertension. Premature labour did not seem to differ significantly between the groups ($P=0.81$).

Two hundred thirty six of 270 fetuses were born alive. In 24 cases intrauterine fetal demise was noticed on admission. Ten fetuses were lost during the intrapartum period. Mean gestational age and birth weights were found to be 28 ± 3.5 and $1,000 \pm 416$ g, respectively, in those cases. Of those ten cases, two mothers were severely preeclamptic, three cases were eclamptic and five cases were diagnosed as HELLP syndrome. In four severely preeclamptic women and one mildly preeclamptic case fetuses were lost in the neonatal period. These

neonates were all under 800 g and were dead secondary to complications such as sepsis, respiratory distress syndrome, intraventricular hemorrhage. Perinatal mortality rate was found to be 144/1,000 births.

Discussion

Hypertensive disorder of pregnancy is considered to be a major worldwide health problem running an increased risk of perinatal and maternal morbidity and mortality [23]. There seems to be a confusion about the terminology and classification of these disorders. Not only the etiology and pathophysiology still remain to be unclear, but also effective prevention and treatment modalities are absent [8, 31]. A number of different complex mechanisms involving the lipid and protein oxidation, altered nitric oxide production and adhesion molecules and placental glycoproteins playing role in trophoblastic-endothelial dysfunction may be suggested to be associated with the etiopathogenesis of preeclampsia [6, 12, 25, 26, 30]. The spectrum of the disease ranges from mildly elevated blood pressure measurements with minimal clinical significance to severe hypertension and multiorgan dysfunction.

The prevalence of hypertensive disorder of pregnancy varies according to geographic regions of the world and ranges from 1.5% in Sweden to 7.5% in Brazil [9]. Some studies from Saudi Arabia reported prevalences between 2.6% and 3.7% while Ventura determined a prevalence of 3.8% in USA in 2000 [2, 28]. The incidence of hypertension in pregnancy according to our study was 8.49%. The variations can be attributed to racial differences, socioeconomic status and some other demographic parameters such as parity and age. Somewhat higher numbers may be attributed to the fact that our center serves as a referral medical facility for an extended number of primary care units of the surrounding rural areas.

The exact incidence of preeclampsia is unknown but it has been reported to be affecting approximately 5–8% of pregnant population. Eclampsia is diagnosed in upto 0.03–0.9% of pregnancies. HELLP syndrome is a further complication of preeclampsia/eclampsia and reported to be associated with 0.17–0.85% of pregnancies. On the other hand chronic hypertension occurs in 1–5% of the pregnant women while it is complicated with superimposed preeclampsia in 25–34% of the cases. Our study demonstrated the incidences of preeclampsia, eclampsia, HELLP syndrome and chronic hypertension to be 4.34%, 0.54%, 0.54% and 0.56%, respectively.

Health care providers mostly focus on antenatal and intrapartum management of preeclampsia/eclampsia but the risk of postpartum onset of eclamptic convulsions especially within the first 48 h and less frequently beyond 48 h should not be ignored. Since 5.7% of the preeclamptic cases are diagnosed in the postpartum period and 11.33% of the preeclamptics experience convulsions in this period, postpartum monitorization is

Table 2 Maternal complications of 255 cases with hypertensive disorder of pregnancy

Complication	Number
Placental ablation	19 (7.5%)
Acute renal failure	6 (2.35%)
Disseminated intravascular coagulation	6 (2.35%)
Pulmonary edema	2 (0.78%)
Adult respiratory distress syndrome	1 (0.39%)
Retinal detachment	2 (0.78%)
Intracranial bleeding	3 (1.17%)
Maternal death	3 (1.17%)

Table 3 Clinical characteristics of maternal death cases

Characteristics	Case I	Case II	Case III
Maternal age (year)	26	17	28
Gestational age (week)	26	33	40
Associated pathologies ^a	Eclampsia, intrauterine fetal demise	Severe preeclampsia, cerebral edema, DIC, acute renal failure, pulmonary edema	Severe preeclampsia, intrauterine fetal demise, cerebral edema, DIC, acute renal failure
Delivery route	Vaginal	Abdominal	Abdominal
Birth weight (g)	800	2,540	3,150
Postpartum day of maternal death	21	11	5
Complication leading to death	Intracranial bleeding	Septic shock	Cardiopulmonary arrest

^aAll of the maternal death cases had the clinical criteria of HELLP syndrome

critical in this group of patients [4, 15]. None of our patients experienced postpartum convulsions that was attributed to affective anticonvulsive prophylaxis and sufficient period of hospitalization and observation of the cases in this period.

Primiparous, young women with low socioeconomic status are the most typical characteristics of preeclamptic cases. Our study also revealed clinical and sociodemographic data similar with the patient profile of the present literature. Most of them had no regular antenatal visits, were of low socioeconomic status from rural regions, primiparous and young. They had their first convulsion mostly at home or other medical units from which they were referred to us. Fetal and maternal complications were all related with eclampsia and HELLP syndrome, the more severe forms of the disorder possibly due to lack of community health education.

Hypertensive disorder of pregnancy is responsible of significant maternal/perinatal morbidity and mortality. Maternal deaths associated with preeclampsia/eclampsia assumed further importance since previously more frequently encountered etiologies such as infection and hemorrhage became less common nowadays [24, 30]. In our study, maternal deaths were due to intracranial

bleeding, septic shock and cardiopulmonary arrest. Irregular or absent antenatal visits, late admission to medical facilities, improper anticonvulsive prophylaxis at primary care units were characteristic of the cases that all demonstrated the clinical criteria of HELLP syndrome, the end of the disease spectrum.

Fetal complications associated with preeclampsia/eclampsia are intrauterine growth restriction, oligohydramnios, preterm delivery, nonassuring fetal heart patterns during labour, low APGAR scores at birth and requirement of neonatal intensive care unit. Obviously intrauterine fetal growth restriction with oligohydramnios and fetal distress and preterm birth of a fetus consequently carry a high-risk of early neonatal death due to complications of prematurity in the neonatal intensive care unit. IUGR, fetal tachycardia, low APGAR scores, requirements for intensive care unit and fetal deaths during labour were significantly more frequent in severely preeclamptic women when compared to other groups. Different perinatal mortality rates were presented in literature changing in the range of 47–370/1,000 [10, 13, 14, 16, 18, 21].

Our perinatal mortality rate was found to be 144/1,000 births which can be considered as high in developed countries but as reasonably moderate in developing countries.

Both maternal and fetal complications are increased in chronically hypertensive women. Elder maternal age, obesity, diabetes mellitus and a number of other medical problems are added to the severity of the clinical status. Multiparity, recurrent abortions, previous fetal losses, previous abdominal deliveries, polyhydramnios, malpresentation, postpartum bleeding requiring blood transfusion make the issues more complex [19]. In our study also the maternal age, gravida, parity were significantly higher and associated medical problems were diagnosed more frequently in chronic hypertension group.

The definitive treatment of severe preeclampsia/eclampsia is mainly delivery regardless of the gestational age after anticonvulsive prophylaxis and the patient's clinical condition is stabilized. Steroids are administered

Table 4 Fetal and neonatal complications of 270 fetuses

	Group I (32 fetuses)	Group II n(95 fetuses)	Group III n(143 fetuses)	P value n
Oligohydramnios	5	18	26	0.917
IUGR	7	18	50	0.032
Fetal tachycardia	3	9	30	0.048
Low APGAR ^a score at 1 min	6	17	52	0.002
Low APGAR score at 5 min	1	2	18	0.006
Intrapartum fetal exitus	0	0	10	0.002
Admission to NICU	5	17	45	0.014
Neonatal death ^b	0	1	4	0.424

^aAPGAR scores < 7 were accepted as low APGAR score

^bNeonatal death in the first 29 days after birth

to induce fetal lung maturity in premature cases [17]. In severe preeclampsia before 32 weeks of gestation, expectant management for a short period may be tried [22]. Expectant management in eclamptic cases is present in literature only as case reports [17]. In mild preeclampsia and chronically hypertensive cases with regular blood pressure values, expectant management is recommended until fetal lung maturation is achieved. We preferred aggressive management in the cases involving HELLP syndrome, eclampsia and severe preeclampsia.

Operative delivery is reported to be increased in hypertensive disorder of pregnancy [11]. Vaginal delivery is recommended for the severely preeclamptic cases in the absence of obstetric indication for cesarean section. Elective abdominal delivery may be preferred in cases before 30 weeks of gestation with low Bishop scores or cases before 32 weeks with IUGR and oligohydramnios [26]. Coppage and colleagues concluded that immediate abdominal delivery did not improve maternal and neonatal outcome in severe preeclampsia and induction of vaginal delivery did not lead to increased morbidity and mortality [5]. In our study, delivery route and cesarean indications did not differ significantly between the groups. Fetal distress was the most frequent cesarean section indication as reported in the literature too.

As a conclusion devastating effects of hypertensive disorder associated with pregnancy could be prevented by close antenatal follow up, timely prediction of risk factors and reasonable management strategies. In spite of the recent advances in public health and provision of our primary health care units, much more effort and further skilled care are mandatory for a satisfactory decline in adverse maternal and fetal outcome. Early detection of high-risk individuals and mild cases by well-trained primary medical personnel and timely referral to advanced tertiary centers will lead to improved perinatal and maternal outcomes in this critical group of patients.

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