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Hypertensive Disorders in Pregnancy: A 5-year Analysis of the Wartime and Postwar Period in South-Western Region of Bosnia and Herzegovina

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A B S T R A C T

Hypertensive disorders are among the most common complications in pregnancy and a major cause of perinatal morbidity and mortality. The aim of this study was to investigate the risk factors and adverse perinatal outcomes of pregnancies in mothers with hypertensive disorders, as well as the adequacy of prenatal care during the wartime and postwar period in South-Western region of Bosnia and Herzegovina. This study included a total of 542 pregnancies with hypertensive disorders during 5-year study period (1995–1999) and 1559 randomly selected controls. Data on risk factors, adverse perinatal outcomes (for singleton pregnancies only) and prenatal care on pregnant women were extracted from the medical records and compared with controls. Chi-square test and crude odds ratio (OR) with 95% confidence interval (95% CI) were used in statistical analysis. The average five-year incidence of hypertensive pregnancy disorders was 6.5% and it was significantly higher in 1995, the last year of the war, than in the postwar period (1996–1999) ($p=0.02$). Factors significantly associated with hypertensive pregnancy disorders were maternal age >34, nulliparity, multifetal gestation and male newborn ($p<0.001$; except $p=0.002$ for male newborn). Severe forms of hypertensive disorders were significantly associated with adverse perinatal outcomes: preterm birth (OR 2.6, 95% CI 1.08–6.3), cesarean delivery (OR 9.2, 95% CI 5.4–15.6), fetal growth restriction (OR 63.8, 95% CI 34.8–117.0), and stillbirth (OR 5.5, 95% CI 2.1–14.1). Women with hypertensive pregnancy disorders had significantly lower number of prenatal care visits than controls ($p<0.001$). There was a high proportion of normally formed macerated stillbirths in the study (27 out of 30 or 90%) and in the control group (10 out of 12 or 83%). In conclusion, severity of the disorder and adequacy of prenatal care are strongly associated with adverse perinatal outcome related to hypertensive pregnancy disorders.

Key words: *hypertensive disorders, perinatal outcome, prenatal care, risk factors, war, postwar, Bosnia and Herzegovina*

Introduction

Hypertensive disorders of pregnancy are a major cause of maternal and perinatal morbidity and mortality worldwide[1]. Gestational hypertension-preeclampsia is the most common medical complication of pregnancy with reported incidence of 6% to 10%[2]. Adverse maternal and fetal effects develop simultaneously as a consequence of vasospasm, endothelial dysfunction, and ischemia[3]. Maternal and perinatal outcomes usually depend on gestational age at time of diagnosis, severity of hypertensive disorders of pregnancy and adequacy of perinatal care. Delivery remains the only effective treatment of this disease[4]. Despite advances in perinatal care, the incidence of hypertensive disorders of pregnancy has increased because of changes in demographics of women who are getting pregnant (increased nuliparity, increased percentage of women who are getting pregnant at later age, increased rate of obesity, changes in paternity, and increased rate of multifetal gestation)[1]. However, advances in perinatal care have resulted in reduced rates of adverse maternal and perinatal outcomes related to hypertensive disorders complicating pregnancy.

Considering specific living conditions and health care system disorders during the war/postwar period, the aim

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of this research was to investigate potential risk factors, and adverse perinatal outcomes related to hypertensive pregnancy disorders and adequacy of perinatal care during that specific time in one region of Bosnia and Herzegovina.

Patients and Methods

A retrospective case-control study encompassed the 5–year period between January 1995 and December 1999 and was conducted at the Obstetric/Gynaecological and Pediatric Departments of Mostar Hospital, Bosnia and Herzegovina. The observed 5-year period included 1995, the last year of the war in Bosnia and Herzegovina and next 4-year of postwar period. Mostar Hospital was the largest perinatal care center in Southern-Western region of Bosnia and Herzegovina, with approximately 1,600–1,700 deliveries annually. In 1993, the main antenatal clinic in Mostar was destroyed by shelling. During the selected time period, 542 cases of hypertensive pregnacy disorders were identified at our Department. From those, 500 were singleton pregnancies and 42 were twins.

Study sample

Study group included 542 pregnancies with hypertensive disorders (HD) of pregnancy.

A classification of hypertensive pregnancy disorders was made according to the criteria of Working Group of the National High Blood Pressure Education Program[5]. Cases with gestational hypertension, mild preeclampsia (minimum criteria[5]) and chronic hypertension were defined as mild form of disorders and formed mild hypertensive pregnancy disorders subgroup. Severe hypertensive disorders subgroup consisted of pregnant women with severe preeclampsia or preeclampsia defined according to increased certainty of preeclampsia[5] criteria (blood pressure ≥160/110 mmHg, proteinuria 2.0 g/24 hours or ≥2+ dipstick, serum creatinine >1.2 mg/dl, platelets <100,000/mm^3, increased LDH, elevated ALT or AST, persistent headache or other cerebral or visual disturbance, persistent epigastric pain), eclampsia and superimposed preeclampsia[5]. Data needed for definition and classification of cases were derived from medical records. Cases with incomplete outcome data (n=22) as also mutiple gestation were excluded from analysis of perinatal outcomes. The most of them were transferred to clinical centers in Croatia. Finally, the total number of 480 women were categorized according to severity of disorders. There were 117 (24%) pregnant women in severe hypertensive disorders subgroup, from those 10 with eclampsia, one with superimposed preeclampsia and 106 with severe preeclampsia. In the mild hypertensive subgroup there were 363 (76%) women, seven of them were diagnosed chronic hypertension. Control group consisted of 1559 simple randomly selected pregnancies of women either delivered vaginally or by cesarean section in the 5-year study period recruited from perinatal birth registry from a total number of 8,397 deliveries. For each case, 3 randomly selected unmatched controls were chosen. Exclusion criteria were hypertensive disorders in pregnancy and incomplete data (n=1).

Outcome measures

For all women with hypertensive disorders of pregnancy and their controls, medical records were carefully reviewed and available parameters regarding potential risk factors, perinatal care and adverse perinatal outcomes were extracted and compared. The maiority of data regarding potential risk factors were missed, so the only few were obtained in satisfactory proportion: age of pregnant women, previous parity, multiple gestation and newborn's sex. Data of prenatal care were missed in more than third participants in the control (39%) and in the study group (33%), so the only overview of this data was present. Prenatal care for each woman was evaluated by using Kessner Index[6]. Care during pregnancy was adequate if it began during the first trimester of pregnancy and the total number of visits was nine or more, and inadequate if it began during the third trimester and the total number of visits was less than five, and intermediate for all other combinations.

The following data of adverse outcomes were obtained for singleton pregnancies: placental abruption, caesarean section rate, preterm birth <37 weeks' gestation (spontaneous and iatrogenic), fetal growth restriction, stillbirth at or more than 24 weeks' gestation or birth weight ≥500 g, neonatal intensive care admission >24 hours and early neonatal death by 7 days after birth. Gestational age was diagnosed by last menstrual period and/or ultrasound examination. Fetal growth restriction was defined, when birth weight was below the 10th percentile of that anticipated for gestational age, and according to fetal growth chart established by Dražančić et al.[7] Since autopsies were not performed, the causes of death were based on clinical assesment and categorized according to Wigglesworth's classification[8].

Statistical analysis

Pearson's χ^2 was used to assess an association between observed data and expected data represented by frequencies. Multinomial logistic regression has been used for regressing a categorical dependent variable with more than two categories on a set of independent variables. Statistical significant difference was at $p<0.05$, and confidence interval (CI) higher than 95%. For statistical analysis of the obtained data was used software system SPSS for Windows (13.0, SPSS Inc, Chicago, Illinois, SAD).

Results

Out of a total of 8,397 deliveries in the observed five-year period, 542 were cases of hypertensive disorders complicating pregnancies. The calculated average five-year incidence of hypertensive disorders complicating pregnancy was 6.5% in our population of pregnant women. The incidence was significantly higher in 1995, the last year of the war in Bosnia and Herzegovina

TABLE 1
OVERVIEW OF PRENATAL CARE AMONG HYPERTENSIVE DISORDERS (HD) COMPLICATING PREGNANCIES AND CONTROL PARTICIPANTS

	With HD (n=363)	Control (n=946)	p
Adequate	18 (5.0)	65 (6.9)	<0.001
Intermediate	217 (59.8)	684 (72.3)	<0.001
Inadequate	128 (35.3)	197 (20.8)	<0.001

Data are shown as number (%)

(8.7%), than showed a decreasing trend toward 1998–1999 (4.9%–5.2%) (p=0.020, Yates)[9]. We analysed obtained potential risk factors for hypertensive disorders of pregnancy in the study participants and controls. The distribution according to age groups (<19, 19–24, 25–34, >34 years) revealed a significantly higher frequency of pregnant women older than 34 years in the hypertensive disorders group than in the control group (27.7% *vs.* 13.6%, respectively; p<0.001). The frequency of nulliparous women was significantly higher in the hypertensive disorders group than in the control group (48.3% *vs.* 34.4%; p<0.001). Twins were significantly more frequent in the study than in the control group (7.8% *vs.* 1.0%; p<0.001). The number of male infants was significantly higher in the hypertensive disorders group than in the control group (59.0% *vs.* 51.0%; p= 0.002)[13]. A significantly higher number of women with hypertensive pregnancy disorders received inadequate prenatal care than the control participants (p<0.001, Table 1). Women without hypertensive pregnancy disordes received more often intermediate prenatal care than the study participants (p<0.001, Table 1). Small percentage of pregnant women in both group received adequate prenatal care, but significantly higher in the control group. Table 2 presents the multivariate results for the association between severity of the hypertensive pregnancy disoders and adverse perinatal outcome in singleton pregnancies. Placental abruption was diagnosed more than 10-fold in the mild hypertensive disorders (HD) group and more than 3-fold in the severe HD group compared with control participants (Table 2). Severe HD group had a higher rate of preterm birth than the mild HD group, and that of the control group (Table 2). Of preterm births in the severe HD group, 87% were medically indicated; conversely, 76% of preterm in the mild HD group and 70% of those in the control group followed the spontaneous onset of preterm labor (data not shown in the table). The cesarean delivery rate was 9-fold higher in the severe HD group and more than 2-fold in the mild HD group than in the control group (Table 2). Among women with severe HD, there was a higher frequency of fetal growth restriction as also among women with mild HD than in the control participants (Table 2). Severe HD of pregnancy increased 5.5-fold risk of fetal death, but not mild HD versus the control group (Table 2). Both severe HD and mild HD had similar risk for neonatal intensive care unit >24h as a control group (Table 2). Table 3 present categorizing of fetal and early neonatal death in the study and control group according Wigglesworth's classification[8]. The majority of stillbirths (SB) in both HD (27 out of 30) and control group (10 out of 12) were normally formed macerated SB (Table 3). There were two fetal deaths during labour (fresh SB), the same as in the control group and one SB with maior congenital malformations in the HD group (Table 3). The maiority of early neonatal deaths (END) in HD group (5 from 7) were associated with immaturity. In the control group there was one END associated with immaturity and the one associated with congenital malformations. The percentage of cases with eclampsia was 0.1% (1:837). There were no maternal deaths.

TABLE 2
ADVERSE PERINATAL OUTCOMES ACCORDING TO SEVERITY OF HYPERTENSIVE DISORDERS (HD) OF SINGLETON PREGNANCIES IN THE STUDY GROUP COMPARED WITH CONTROL SINGLETON PREGNANCIES

Adverse outcomes	Severe HD (n=117)			Mild HD (n=363)			Control (n=1542)
	%	OR†	(95% CI‡)	%	OR	(95% CI)	%
Placental abruption	5.2	3.3	(0.4–22.4)	2.5	10.7	(1.9–58.3)	0.1
Preterm birth	25.9	2.6	(1.08–6.3)	5.6	0.9	(0.5–2.0)	4.1
Cesarean delivery	45.7	9.2	(5.4–15.6)	18.3	2.4	(1.7–3.4)	7.8
Fetal growth	54.3	63.8	(34.8–117.0)	18.3	13.8	(8.5–22.6)	1.6
Restriction							
Fetal death (≥4 wks*)	18.1	5.5	(2.1–14.1)	1.9	1.1	(0.4–2.9)	0.6
Neonatal intensive care unit >24h	19.0	1.5	(0.4–4.4)	3.3	1.4	(0.5–3.8)	1.6

Data are shown as percent
† OR: Odds ratio
‡ CI: Confidence interval
* wks: weeks

TABLE 3
STILLBIRTHS (SB) AND EARLY NEONATAL DEATHS (END) IN THE HYPERTENSIVE DISORDERS SINGLETON PREGNANCIES (HD) GROUP AND CONTROL PARTICIPANTS ACCORDING WIGGLESWORTH'S CLASSIFICATION[8]

	HD group (SB/END =30/7)	Control group (SB/END =12/2)
Normally formed macerated SB	27	10
Congenital malformations:		
Stillbirths	1	–
Early neonatal deaths	1	1
Conditions associated with immaturity (END)	5	1
Asphyxial conditions developing in labour(fresh SB)	2	2
Specific conditions other than above:		
Stillbirths	–	–
Early neonatal death	1	–

Discussion

The incidence of hypertensive disorders in pregnancy was within the range observed in other studies[2]. Significantly higher incidence in 1995, the last year of the war in Bosnia and Herzegovina, than in postwar period (1998–1999) could be explained with negative perinatal trends during the war/postwar period which was reported by the other authors[10,11]. In the present study, the incidence of hypertensive disorders of pregnancy was sigificantly higher in pregnant women aged >34, nulliparous, twins gestation and male infant pregnancies which is in concordance with other studies[12–15]. Thus, risk factors associated with hypertensive pregnancy disorders include advanced maternal age >34, nulliparity, multifetal gestation and male infant[12–15]. Pregnancies with hypertensive disorders are a high-risk group of pregnancies and they need appropriate prenatal care with higher number of prenatal care visits than pregnancies without complications. In our study, women with hypertensive pregnancy disorders had siginificantly lower number of prenatal care visits and 35.3% of them received inadequate prenatal care. For comparison, The National Center for Health Statistics reported that 12 percent of American women delivering in 2000 received inadequate prenatal care, according Kessner Index[16]. High proportion of missing data in our study and unknown quality of prenatal care limited analysis and data comparison. Furthermore, only 5.0% of hypertensive disorders pregnant women and 6.9% of controls received adequate prenatal care in our study. Poor prenatal care could be explained by specific situations such as war conditions of living and break down of the perinatal care system as well as health care system at all[10,11]. In 1993, building of main Mostar antenatal clinic was destroyed by shelling, as well as medico-technical support. Lack of medical staff was the next possible reason for poor prenatal care.

Contrary to some previous studies where association between placental abruption and severity of hypertensive pregnancy disorders was observed, our results showed insignificant association with severe forms, but significant association with mild forms of hypertensive pregnancy disorders[17]. On of the possible explanation could be the fact that we had relatively small sample size. Similar to other studies, our results confirm that severity of hypertensive pregnancy disorders were associated with increased rate of preterm birth and cesarean delivery, mostly due to iatrogenic preterm births and elective cesarean sections[18–20]. Fetal growth restriction of diverse causes affects fair number of newborn infants worldwide, mainly in developing countries[21]. Preeclampsia, as it is well known, increases the risk for severe perinatal outcomes, mostly by its effect on reducing birth weight[18]. Our results confirmed that severe forms of hypertensive pregnancy disorders are a major cause of intrauterine growth restriction, and this finding is in agreement with other reports[1,18,22]. A widely quoted study by Friedman and Neff (1976) showed that diastolic hypertension of 95 mm Hg or greater was associated with a threefold increase in the fetal death rate[23]. In our study, severe hypertensive disorders in pregnancy were associated with a 5.5-fold increase in the fetal death rate, but contrary to some studies mild hypertensive disorders were not associated with increase in the fetal death at all[24]. Probably, small sample size could be explained latter result. According to our results, neonatal morbidity present as neonatal intensive care unit admission >24 hours were not associated with hypertensive disorders in pregnancy, and that is in disaggrement with other reports[18,24]. Different defining of neonatal morbidity and inadequate collection of perinatal data in the observed period could be explanation for disaggrement between our results and the other reports. Perinatal mortality analysis was performed without necropsy findings because there was no pathologist in our hospital during observed period. So, we categorized stillbirths and early neonatal deaths according to Wigglesworth's classification[8]. High rate of macerated stillbirths in both groups (90% in the study and 83% in the control) mainly due to lower adequacity and accessibility of prenatal care. Additional impact in the study group is related to background maternal factors or hypertensive disorders. Furthermore, stillbirth ratio is an important indicator of the quality of antenatal and obstetric care[25]. The most of early neonatal deaths in the study group (5 out of 7) were classified as conditions associated with immaturity. First of all, lack of medico-technical support (no one respirator for newborns) was the reason for poor neonatal care. The results of perinatal mortality analyses in the Federation of Bosnia and Herzegovina (1999) showed that EPH gestosis along with premature birth were the most frequent causes of perinatal deaths[26]. In conclusion, the overall results and high proportion of normally formed macerated stillbirths in the study group in particular indicated to lower adequacy and accessibility of prenatal care during the war/postwar period in South-Western region of Bosnia and Herezegovina. Severity of disorders and quality of prena-

tal care has great impact on adverse perinatal outcome related to hypertensive pregnancy disorders.

The limitations of the study were incomplete data on prenatal care, socio-demographic characteristics, medical conditions of mothers (such as gestational diabetes mellitus), as well as personal behaviors (smoking, alcohol abuse). This is due to the retrospective nature of the study, as well as impossibility of collecting valid health records, particularly perinatal information in the observed war/postwar period.

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HIPERTENZIVNI POREMEĆAJ TRUDNOĆE – ANALIZA PETOGODIŠNJEG RAZDOBLJA I USPOREDBA RATNOG I POSLIJERATNOG RAZDOBLJA U JUGO-ZAPADNOM DIJELU BOSNE I HERCEGOVINE

SAŽETAK

Hipertenzivni poremećaj je jedna od najčešćih komplikacija tijekom trudnoće i glavni uzrok perinatalnog morbiditeta i mortaliteta. Cilj ovog istraživanja bio je istražiti čimbenike rizika i perinatalne komplikacije trudnoća tijekom kojih je zabilježena hipertenzija, kao i prikladnost prenatalne skrbi tijekom ratnog i poslijeratnog razdoblja u jugo-istočnom dijelu Bosne i Hercegovine. U istraživanje je bilo uključeno 542 trudnoće sa zabilježenom hipertnezijom tijekom petogodišnjeg razdoblja (1995–1999) i među 1559 kontrolna odabranih slučajnim odabirom. Podaci su dobiveni iz zdravstvenih zapisa (samo za ne-blizanačke trudnoće) i uspoređeni s zdravim kontrolama. Podaci su analizirani korištenjem χ^2-testa i grubih omjera šansi s 95% rasponom pouzdanosti. Prosječna petogodišnja prevalencija iznosila je 6,5% i bila je statistički značajno veća nego tijekom 1995. godine, u posljednjoj godini rata (p=0,02). Čimbenici povezani s hipertenzivnim poremećajem bile su majčina dob veća od 34 godine, prva trudnoća, blizanačke trudnoće i muški spol novorođenčeta. Teži oblici hipertenzivnog poremećaja bili su povezani s perinatalnim komplikacijama: prijevremenim porodom (OR 2,6; 95% IP 1,08–6,30), carskim rezom (OR 9,2; 5,4–15,6), ograničenjem rasta (OR 63,8; 34,8–117,0) i mrtvorođenčadi (OR 5,5; 2,1–14,1). Žene s hipertenzivnim poremećajima imale su manje pregleda nego kontrole (p<0,001). Zabilježena je i visoka prevalencija normalno oblikovane macerirane novorođenčadi u obje skupine (27 od 30, 90% u hipertenzivnim trudnoćama i 10 od 12, 83% među kontrolama). U zaključku, klinička važnost ovog poremećaja i prikladnost perinatalne zaštite su bili snažno povezani s perinatalnim ishodima vezanim uz hipertenzivni poremećaj trudnoće.