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Influence of the wars in Croatia and Bosnia and Herzegovina on the incidence and outcome of singleton premature births in the Split University Hospital

Research Article

Ivana Pavlinac, Ana Marin, Maja Valić[1], Jelena Marušić[2], Damir Roje[2], Renata Pecotić[1], Ivica Tadin[2], Zoran Đogaš[1*]

[1] *Department of Neuroscience and Department of Scientific Methodology, Split University School of Medicine, Split, Croatia*

[2] *Department of Gynecology and Obstetrics, Split University Hospital, Split, Croatia*

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Abstract: To investigate the influence of the wars in Croatia and Bosnia and Herzegovina on incidence and perinatal outcome of singleton preterm births at the Department of Gynecology and Obstetrics in the Split University Hospital. Data were collected by reviewing patients' files at the Department of Gynecology and Obstetrics from three periods: the three years before the war (1988-1990), during the war (1992-1994), and after the war (1996-1998). A total of 2,358 patients' files of singleton preterm delivery were analyzed. Singleton preterm delivery rate decreased during the war (5.02%) and post-war period (4.74%) compared to the pre-war period (6.19%). Stillbirth and early neonatal mortality rates of singleton premature babies significantly increased during the war to 226‰, compared to 193‰ before the war and 134‰ after the war. Early neonatal mortality rate was 215‰ during the war, 209‰ in the pre-war period, and 156‰ after the war. Despite the continuous decrease in singleton preterm birth rate throughout the observed periods, the increase in stillbirth rate and early neonatal mortality rate during the war might have been caused by the war. This may be due to primary gynecological care being inadequate for many pregnant women.

Keywords: *Premature birth • War • Perinatal mortality • Cesarean section • Pregnancy outcome*

1. Introduction

Different stressful events, including war, may cause changes in some segments of perinatal outcome; increased abortion rate, low birth weight babies, increase in the number of stillbirths and pregnancy-induced hypertension and pre-eclampsia in war affected areas [1-4]. However, the influence of life stress on premature labor is controversial [5]. Epidemiological studies have identified several risk factors, including psychosocial stress during pregnancy and objective major life events during the third trimester [6], to be associated with the greater incidence of premature delivery. On the other hand, the state of anxiety during pregnancy was not found to be significantly associated with preterm delivery nor with low birth weight [7]. Furthermore, even though war can be considered as a major cause of the long-term stress, the rate of premature deliveries during the Gulf War was not significantly higher [8], or was even reduced during the Yom Kippur War [5].

Increases in the premature birth rate during war have been reported in several areas in Croatia, including the region of the cities Zadar [9] and Zagreb [10].

Rates of complications during pregnancy and labor are shown to be higher in a war-affected area with increased percentage of instrumental deliveries using forceps or vacuum [8].

War in Croatia and in Bosnia and Herzegovina (BH) started in 1991. After March 1994, the war in BH was

* *E-mail: zdogas@bsb.mefst.hr*

Table 1. Frequency and outcome of births in Split University Hospital during the three-year periods before (1988-1990), during (1992-1994), and after (1996-1998) the war in Croatia and Bosnia and Herzegovina.

	Total	Before the war				During the war				After the war				χ^2	p
		1988	1989	1990	Total	1992	1993	1994	Total	1996	1997	1998	Total		
Births, total (n)	45,885	4,782	4,452	4,759	13,993	6,199	6,017	5,201	17,417	4,886	4,828	4,761	14,475	449.20	<0.001
Singleton births (n)	44,573	4,654	4,330	4,607	13,591	6,078	5,857	5,044	16,979	4,762	4,647	4,594	14,003	460.03	<0.001
Stillbirths (n)	589	59	78	76	213	83	77	81	241	60	33	42	135	21.26	<0.001
Stillbirth rate (‰)	13.2	12.7	18.0	16.5	15.7	13.6	13.1	16.1	14.2	12.6	7.1	9.1	9.6	21.26	<0.001
Early neonatal death (n)	455	61	58	51	170	77	62	39	178	29	38	40	107	16.79	<0.001
Early neonatal mortality rate (‰)	10.3	13.3	13.6	11.2	12.7	12.8	10.7	7.9	10.6	6.2	8.2	8.8	7.7	16.79	<0.001
Perinatal mortality (‰)	20.8	23.2	24.7	20.4	22.8	23.1	20.3	22.1	21.8	20.2	15.5	18.9	18.2	5.19	0.075
Cesarean sections; n(%)	3,485 (7.6)	367 (7.7)	347 (7.8)	357 (7.5)	1,071 (7.6)	322 (5.2)	343 (5.7)	376 (7.2)	1,041 (6.0)	404 (8.3)	466 (9.6)	503 (10.6)	1,373 (9.5)	138.74	<0.001

restricted to several cities – for example Sarajevo [11,12] – and finally ended in November 1995. During the war period of 1991-1995 Split University Hospital took on the large burden of managing BH citizens, with increased workloads in the departments of General Surgery, Traumatology, Pulmology and Dermatovenerology [13]. There is no data reported from the Department of Gynecology and Obstetrics in Split University Hospital regarding the number and outcome of pregnancies during the war in Croatia and BH.

This retrospective study was performed to evaluate whether the war in Croatia and Bosnia and Herzegovina influenced the frequency and outcome of singleton preterm deliveries in the Split University Hospital.

2. Material and Methods

Data were collected at the Department of Gynecology and Obstetrics in the Split University Hospital, which is a tertiary perinatal center, over a period of nine years: three years before the war in Croatia and BH (January 1st 1988 – December 31st 1990), three war years (January 1st 1992 – December 31st 1994) and three post-war years (January 1st 1996 – December 31st 1998). The years 1991 and 1995 were considered to be transitional and thus were excluded from the study.

Preterm birth was considered to have occurred if gestation terminated spontaneously after 22 and before 37 completed weeks of pregnancy and if infant birth weight was 500 g or more.

A total of 2,358 files of patients with singleton preterm deliveries were examined for the following parameters: year of birth, mother's age, obstetric anamnesis data, gestational age, fetal presentation (vertex vs. non-vertex presentation), birth weight, trophicity, mode of delivery (cesarean section or vaginal), and pregnancy-related complications (pre-eclampsia). The estimation of the gestational age used in this study is based on the time starting at the first day of the last menstrual period corrected with ultrasound estimation where the difference was greater than one week.

The multiple pregnancies were counted in total births, but were excluded from the study of premature births.

Total number of births, singleton births, singleton preterm birth rate, stillbirth rate, early neonatal mortality, perinatal mortality, cesarean section rate, fetal presentations, pregnancy-related complications, fetal hypotrophy, maternal age, and parity between the three periods were compared using Chi-square test with the level of significance set at $p<0.05$. Average maternal age, average gestational age and average birth weight in the three periods were analyzed using one-way analysis of variance (ANOVA).

3. Results

The total number of deliveries in the Split University Hospital increased significantly during the period of war. There were 13,993 deliveries in the three-year pre-war period, a high of 17,417 deliveries during the war, and then a drop to 14,475 deliveries in the post-war period ($\chi^2=449.20$; $p<0.001$; Table 1).

The total number of singleton deliveries also increased significantly during the war when the three-year periods were compared (13,591, 16,979 and 14,003 respectively; $\chi^2=460.03$; $p<0.001$; Table 1).

The total rate of cesarean sections in the Split University Hospital significantly decreased in the period

Table 2. Frequency and outcome of singleton preterm births during the three-year periods before (1988-1990), during (1992-1994), and after (1996-1998) the war in Croatia and Bosnia and Herzegovina in Split University Hospital; n (%).

	Total	Before the war				During the war				After the war				χ^2	p
		1988	1989	1990	Total	1992	1993	1994	Total	1996	1997	1998	Total		
Singleton births (n)	44,573	4,654	4,330	4,607	13,591	6,078	5,857	5,044	16,979	4,762	4,647	4,594	14,003	460.03	<0.001
Preterm births	2,358	317	266	258	841	369	258	226	853	242	207	215	664	32.67	<0.001
	(5.3)	(6.8)	(6.1)	(5.6)	(6.2)	(6.1)	(4.4)	(4.5)	(5.0)	(5.1)	(4.4)	(4.7)	(4.7)		
Stillbirths (n)	444	44	57	61	162	68	60	65	193	45	19	25	89	20.94	<0.001
Stillbirth rate (‰)	188	139	214	236	193	184	232	288	226	186	91.8	116	134	20.94	<0.001
Early neonatal mortality (n)	374	51	47	44	142	62	50	30	142	24	30	36	90	7.98	0.020
Early neonatal mortality rate (‰)	195	187	225	223	209	206	252	186	215	122	159	189	156	7.98	0.020
Perinatal mortality (‰)	267.7	284.4	303.3	281.5	289.7	315.9	307.2	246.6	289.9	234.9	183.9	237.0	218.6	14.24	<0.001
Cesarean sections	284	31	32	31	94	35	19	25	79	39	33	39	111	20.52	<0.001
	(12.0)	(9.8)	(12.0)	(12.0)	(11.2)	(9.5)	(7.4)	(11.1)	(9.3)	(16.1)	(15.9)	(18.1)	(16.7)		
Non-vertex	364	47	51	35	133	50	46	30	126	42	25	38	105	0.45	0.797
presentations	(15.4)	(14.8)	(19.2)	(13.6)	(15.8)	(13.5)	(17.8)	(13.3)	(14.8)	(17.3)	(12.1)	(17.7)	(15.8)		
Pre-eclampsia	93	18	14	10	42	12	6	6	24	10	10	7	27	5.35	0.070
	(3.9)	(5.7)	(5.3)	(3.9)	(5.0)	(3.2)	(2.3)	(2.6)	(2.8)	(4.1)	(4.8)	(3.2)	(4.1)		
Hypotrophic	246	20	35	18	73	37	23	28	88	22	30	33	85	6.76	0.030
newborns	(10.4)	(6.3)	(13.1)	(7.0)	(8.7)	(10.0)	(8.9)	(12.4)	(10.3)	(9.1)	(14.5)	(15.3)	(12.8)		

of war to 5.98% (n=1,041) versus 7.65% (n=1,071) in the pre-war period (χ^2=34.79; p<0.001; Table 1). In the post-war period it increased to 9.48% (n=1,373).

3.1. Singleton births

The stillbirth rate of total singleton labors significantly decreased during the three periods. It was 15.7‰ (n=213) in the pre-war period, 14.2‰ (n=241) during the war, and 9.64‰ (n=135) in the post-war years (χ^2=21.26; p<0.001; Table 1).

Similarly, the rate of early neonatal mortality decreased during the time course of the three periods. In the pre-war years it was 12.7‰ (n=170), during the war it decreased to 10.6‰ (n=178), and in the post-war period it dropped to 7.71‰ (n=107) (χ^2=16.79; p<0.001; Table 1).

3.2. Singleton preterm births

The rate of singleton preterm deliveries decreased in the war (5.02%, n=853), and post-war (4.74%, n=664) periods versus the pre-war period (6.19%, n=841) (χ^2=32.67; p<0.001; Table 2).

However, the stillbirth rate of singleton premature labors significantly increased in the war period (226‰, n=193) when compared to the pre-war (193‰, n=162) and the post-war period values (134‰, n=89) (χ^2=20.94; p<0.001; Table 2).

The early neonatal mortality rate of singleton preterm deliveries significantly increased during the period of war (215‰, n=142) when compared with the pre-war (209‰, n=142) and the post-war period (156‰, n=90) (χ^2=7.98; p=0.020; Table 2).

The cesarean section rate of singleton preterm deliveries significantly increased during the post-war period to 16.7% (n=111), from 11.2% (n=94) during the pre-war period and 9.3% (n=79) in the war period, (χ^2=20.52; p<0.001; Table 2).

There was no significant difference in the number of singleton preterm deliveries with non-vertex presentations in three periods (χ^2=0.45; p=0.797; Table 2).

The incidence of pre-eclampsia among singleton preterm deliveries did not significantly change during the war (2.81%, n=24), compared to the pre-war period (4.99%, n=42) and the post-war period (4.07%, n=27) (χ^2=5.35, p=0.069; Table 2).

Before the war there occurred rates of 8.7% (n=73) hypotrophic newborns and 80.3% (n=675) eutrophic newborns, and after the war the rate of hypotrophic newborns rose to 12.8% (n=85) and the rate of eutrophic babies decreased to 74.1% (n=492) (χ^2=6.71, p=0.010, and χ^2=8.10, p=0.004 respectively; Table 2).

Average maternal age in singleton preterm deliveries showed a slight increase during the three periods. It was 27.1±5.5 during the pre-war years, 28.3±6.0 during the

Table 3. Maternal age and parity of singleton preterm births during the three-year periods before (1988-1990), during (1992-1994), and after (1996-1998) the war in Croatia and Bosnia and Herzegovina in Split University Hospital.

	Total	Before the war				During the war				After the war				χ^2	p
		1988	1989	1990	Total	1992	1993	1994	Total	1996	1997	1998	Total		
Average maternal	28.1±	26.8±	27.1±	27.5±	27.1±	28.0±	28.6±	28.3±	28.3±	29.2±	28.9±	28.9±	29.0±	-	<0.001
age± SD†	5.9	5.7	5.4	5.4	5.5	5.8	6.1	6.1	6.0	6.2	6.0	6.2	6.1		
Age of mothers	390	37	29	31	97	63	54	40	157	51	40	45	136	24.69	<0.001
≥35; n (%)*	(16.6)	(11.8)	(11.0)	(12.0)	(11.6)	(17.1)	(20.9)	(17.9)	(18.5)	(21.1)	(19.4)	(21.0)	(20.5)		
Age of mothers	20	3	3	3	9	5	2	3	10	1	0	0	1	5.42	0.070
<18; n (%)*	(0.8)	(1.0)	(1.1)	(1.2)	(1.1)	(1.4)	(0.8)	(1.3)	(1.2)	(0.4)	(0.0)	(0.0)	(0.1)		
Mothersparity>2;	571	58	44	55	157	94	62	60	216	74	63	61	198	24.94	<0.001
n (%)	(24.9)	(18.9)	(17.1)	(22.5)	(19.4)	(25.7)	(24.2)	(27.1)	(25.6)	(31.6)	(30.7)	(29.8)	(30.7)		

** % of singleton preterm births with data available*
† ANOVA, F=19.79

Table 4. Average birth weight (g) according to gestational age in preterm singleton births during the three-year periods before (1988-1990), during (1992-1994), and after (1996-1998) the war in Croatia and Bosnia and Herzegovina in Split University Hospital.

Gestational age*	Total; n (%)	Before the war				During the war				After the war			
(weeks)		N	%	mean±	SD	N	%	mean±	SD	N	%	mean±	SD
22-28	283 (12.0)	105	12.5	874±	290.1	111	13.0	870±	339.2	67	10.1	863±	278.4
29-32	340 (14.4)	122	14.5	1,741±	502.9	126	14.8	1,653±	480.8	92	13.9	1,650±	459.8
33-37	1,682 (71.3)	587	69.8	2,672±	1,390.0	600	70.3	2,582±	532.7	495	74.5	2,605±	556.5
Missing data	53 (2.2)	27	3.2	-		16	1.9	-		10	1.5	-	-
Total†	2,358 (100.0)	841	100.0	2,248.4±	1,369.9	853	100.0	2,187.1±	817.3	664	100.0	2,269.6±	798.4

**Chi-square test of the difference among three periods in the number of births in each gestational age group:*
(22-28) - χ^2=3.31, p=0.191
(29-32) - χ^2=0.26, p=0.877
(33-37) - χ^2=4.74, p=0.094
† ANOVA test of the difference in birth weight in the three periods: F=1,33, p=0,266

war, and 29.0±6.1 years in the post-war period (F=19.79, p<0.001). However, during and after the war, the number of mothers who had singleton preterm deliveries and were 35 years and older increased significantly (χ^2=24.69; p<0.001; Table 3). In the pre-war period 11.6% (n=97) of all singleton preterm deliveries were by mothers older than 35, whereas in the war and after-war periods that number increased to 18.5% (n=157) and 20.5% (n=136) respectively. Similarly, more mothers who already had two or more children had singleton preterm deliveries during and after the war (25.6%, n=216 and 30.7%, n=198, respectively) versus the pre-war period (19.4%, n=157) (χ^2=24.94, p<0.001). The number of mothers younger than 18 who had singleton preterm deliveries did not significantly change during the war compared to the pre-war period, but decreased after the war to only 1 case in three years (Table 3).

Primiparity was equally represented among the women with preterm labor between the three periods. Average gestational age of preterm babies was similar in all observed periods, 33.2±3.6 weeks before the war, 33.3±3.6 weeks during the war, and 33.5±3.7 weeks after the war.

The rate of very early singleton preterm deliveries (22-28 weeks of gestation) did not show a significant difference over the three periods. It was 12.5% (n=105) in the pre-war period, 13.0% (n=111) during the war, and 10.1% (n=67) in the post-war period (χ^2=3.31; p=0.191; Table 4).

Birth weight of premature newborns did not significantly change during the war as shown in Table 4.

4. Discussion

The total number of deliveries in the Split University Hospital significantly increased during the war and dropped to pre-war frequencies after the war.

On the other hand, the singleton preterm delivery rate decreased during the war. However, both stillbirth and early neonatal mortality rates increased during the three-year war period.

The incidence rate of pre-eclampsia was surprisingly reduced during the war, and the number of C-sections in this group of deliveries did not follow the trend of increase

that was obvious after the war. These findings indicate the strong influence of war on the OB-GYN practice.

In 1992, with the beginning of an open armed conflict in BH, increased inflow of patients was detected at many departments in the Split University Hospital [13], including the Department of Obstetrics and Gynecology as shown in the present study. The peak of admissions at the Department of Obstetrics and Gynecology was recorded in 1992 and 1993, similar to other departments during the war [13].

The total preterm delivery rate increased from 1990 to 1992 in the University Medical School of Zagreb, and expatriated women had preterm deliveries twice as often as non-displaced women [10]. Emotional reactions during pregnancy have been associated with the wide variety of pathological conditions that arise during pregnancy, such as prolonged labor, breech births, miscarriages, and preterm births [13]. Previous studies show that despite all the calamity and anxieties, wars in which the civilian population was far from the front line have not been associated with the increase in the rate of preterm deliveries [5]. Similar findings were reported in a study on a population who was subjected to extensive long-term stress in the Gulf War [1,8], where no significant change in preterm delivery rate during the War was reported. During the Yom-Kippur War significant decrease in preterm delivery rate was reported compared to the after-war period [5]. Acute fright is often reported by pregnant women as causing immediate and prolonged uterine contractions, yet not enough to initiate labor [14]. However, a study in Manchester showed that the level of psychosocial stress in pregnancy was particularly high in mothers whose babies were born preterm [6]. In this study, we observed continuous decrease in the preterm labor rates throughout the examined periods, with the highest rates pre-war and the lowest ones post-war. Therefore, the war period did not interfere with the preterm labor rates. Studies in Zadar and Zagreb during the war in Croatia showed an increase in preterm delivery rates in 1991 and 1992 compared to 1990 [9,10], but preterm delivery rate in expatriated women decreased from 1990 to 1992 [10]. Acute stress with the abrupt change in usual activities seems to influence preterm delivery rates only over a short period of time, with no change in preterm delivery rates if the level of stress and anxiety does not acutely change.

The increased stillbirth and early neonatal mortality rates during the three-year war period are similar to the findings of the war-associated increased perinatal mortality in Bosnia and Herzegovina [15,16].

The cesarean section rate in both total and singleton preterm deliveries decreased during the war in Croatia and increased in the post-war period. There is a worldwide trend of increasing the rate of C-sections [17,18], which means the war may have interrupted this trend.

The incidence rate of pregnancy complications, such as pre-eclampsia, among singleton preterm deliveries in this study was significantly lower during the war compared to the both pre- and the post-war periods. The possible lack of effective primary gynecological care programs directed at high-risk populations of women during the war, especially those coming from BH and the refugees from occupied parts of Croatia, may be an important additional factor that influenced this finding and may indicate under-diagnosed pregnancy complications [10]. As presented earlier [10], more than half of the refugees were not examined by perinatologist, and their laboratory and ultrasound estimations were not available for the perinatologist after they came to free regions of Croatia. Finally, better primary healthcare and increased number of OB-GYN staff or reduced workload, due to smaller numbers of total labors in the period after the war, may have improved diagnostics and contributed to the higher number of diagnosed complications.

There was an increasing trend of average maternal age between the observed periods. The number of mothers who had singleton preterm deliveries and were 35 years or older increased significantly during and after the war. There was a larger number of mothers who already had two or more children in the total singleton preterm deliveries during and after the war. In the wartime and immediate after-war period, the Croatian government pursued the so-called “Population politics” where certain benefits were provided for mothers and families with 3 or more children. Numerous families have decided to have another child, and this might explain the increased number of mothers who already had two or more children or were at the age of 35 or older among those having a preterm labor.

The factors contributing toward the low birth weight of newborn babies can be summarized as maternal, obstetric, and fetal risk factors [19,20]. Maternal stress was reported to be associated with low birth weight [21]. Maternal age is one of the risk factors of low birth weight if the mother is under 18 or over 35 years of age [19,20]. The results of our study indicate there was a continuous increase in the number of hypotrophic babies throughout the observed periods, which correlates with increased maternal age. Although low maternal caloric and protein intake might influence fetal growth as well [19], the war in Croatia and thus in Split was not characterized by any significant shortage of food.

In conclusion, during the three periods from the beginning of 1988 to the end of 1998, the number of

singleton preterm deliveries was continuously decreasing, but the stillbirth rate and early neonatal mortality rate of preterm singleton deliveries increased during the war and then strongly decreased during the post-war period. This may be due to primary gynecological care being out of reach or inadequate for many pregnant women in the war-affected areas or those who unwillingly left their homes during the actual pregnancy and were admitted in the Split University Hospital for the labor.

The results of this study of preterm singleton deliveries suggest that the wars in Croatia and Bosnia and Herzegovina may have hidden, rather than slowed down, the process of significant improvement in perinatal care in the area gravitating to the Split University Hospital during the observed periods.

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