Neonatal morbidity and mortality associated with maternal HELLP syndrome

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SUMMARY: Aliefendioğlu D, Yurdakök M, Oran O, Erdem G, Tekinalp G, Önderoğlu L. Neonatal morbidity and mortality associated with maternal HELLP syndrome. Turk J Pediatr 2000; 42: 308-311.

The syndrome of hemolysis, elevated liver enzymes and low platelet count (HELLP syndrome) is a severe form of preeclampsia and eclampsia. To compare the impact of HELLP syndrome and hypertension in pregnancy (HIP) on neonatal morbidity and mortality, 11 infants born to mothers with HELLP syndrome were recruited between 1993 and 1997 from neonatal records. They were compared to 11 infants born to mothers with HIP and 11 control infants born to healthy mothers matched for gestational age, postnatal age and gender. Cesarean section rate was higher in the HELLP group than in the controls ($p < 0.05$). HELLP group infants had lower Apgar scores (54.5% < 1 at 5th min), than controls (9.1%) ($p < 0.05$). Both HELLP and HIP group infants showed a higher incidence of intrauterine growth retardation (63.6% and 54.5%, respectively) than the controls (9.1%) ($p < 0.05$). The incidence of respiratory distress syndrome (RDS) was similar in HELLP and HIP groups and was greater than that in controls (p = NS). Additionally, the neonatal death rate was the highest in the HELLP group (p = NS).

Key words: HELLP syndrome, infant, premature.

The syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP syndrome) is a severe form of preeclampsia and eclampsia. It is a major cause of maternal and perinatal morbidity and mortality. Maternal mortality ranges from 0 to 24 percent and perinatal mortality from 6.6 to 60 percent in the literature[1-3]. The pathogenesis of this syndrome is still unclear. Deterioration of the mother's condition is a major determinant of the management of these pregnancies and often leads to premature delivery. Detailed information on the neonatal manifestations of maternal HELLP syndrome is scarce even though an increased morbidity and mortality has been observed[1,2]. This retrospective study was aimed to compare the outcomes of infants born to mothers with HELLP syndrome and hypertension in pregnancy (HIP).

Material and Methods

We recruited 33 infants born from 1 November 1993 to 30 October 1997 from Hacettepe University Hospital medical records. Infants were grouped (each group included 11 infants) as born to mothers with HELLP syndrome, born to mothers with HIP, and born to healthy mothers. For each HELLP infant, a neonate of a hypertensive mother and a control infant with similar gestational age and, if possible, sex were selected by checking accumulated obstetric records. The selected infant had the birth date closest to the HELLP neonate. Infants of diabetic mothers, infants born to multiple pregnancies, and infants with intrauterine infections and congenital anomalies were excluded. The diagnosis of HELLP syndrome required the presence of thrombocytopenia (< 150000/μl), hepatic dysfunction (increased SGOT, SGPT) and hemolysis (hyperbilirubinemia, and anemia)[3].

Gestational age was determined on the basis of maternal history, early pregnancy ultrasound data and on the Ballard maturity score of the neonate[4]. Small for gestational age (SGA) was

defined as any infant whose birth weight was at the 10th percentile or less for gestational age[5]. The ponderal index was used to detect asymmetric or symmetric SGA. Asymmetric SGA was defined in a newborn whose ponderal index

$$\left(\frac{\text{weight}}{\text{length}^3} \times 100 \left[\frac{\text{gr}}{\text{cm}^3}\right]\right)$$

was below the 3rd percentile[6]. Sepsis was diagnosed based on a positive blood culture and clinical findings, while respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and retinopathy of prematurity (ROP) were diagnosed based on clinical and/or radiological findings. Periventricular-intraventricular hemorrhage (PV-IVH) was diagnosed by cranial ultrasonography.

Results

Maternal and neonatal data are summarized in Tables I and II. Cesarean section rate was the highest in the HELLP group, and the difference between this group and controls was statistically significant; otherwise, the difference between the HELLP and HIP groups was statistically insignificant.

The figures related with the incidence of HELLP syndrome (n = 11) in toxemia (n = 224) and in all pregnancies (n = 9276) was obtained from obstetric records of our hospital from 1 November 1993 to 30 October 1997. Their percentages were 4.9 and 0.12, respectively.

All three groups were similar with respect to gestational age and gender. The control group had the highest birthweight among the other groups. Percentages of SGA infants in the HELLP and HIP groups were close to each other and higher than in controls, and the difference was statistically significant. Apgar scores were less than seven at the 5th minute in six infants in the HELLP group, while the control group had only one infant with a lower Apgar score; the difference was statistically significant.

In the HELLP group two infants (18.2%) died on the 2nd day from RDS, one infant (9.1%) died on the 6th day from sepsis and one infant died on the 15th day from NEC. In the HIP group one infant (9.1%) died on the 2nd day from RDS and one infant died on the 6th day from sepsis. In the control group, only one infant died on the 11th day from sepsis.

Table I. Maternal Characteristics

	HELLP syndrome n = 11	Hypertension in pregnancy (HIP) n = 11	Control n = 11
Maternal age*	26.1 ± 4.1	28.8 ± 4.9	28.9 ± 6.7
Multiparity	7	9	8
Cesarean section**	11	8	5
Antenatal steroid	6	5	5
Mortality	0	0	0

* (Mean ± SD).
** $p < 0.05$ HELLP syndrome versus control.
$p > 0.05$ in all comparison groups by chi square test.

Table II. Demographic Characteristics, Neonatal Morbidity and Mortality

	HELLP syndrome n = 11	Hypertension in pregnancy (HIP) n = 11	Control n = 11
Gestational age (w)*	31 ± 3.7	31.4 ± 3.8	31.0 ± 3.4
Birth weight (g)*	1217 ± 512.7	1285 ± 584	1526 ± 646
Male/Female	4/7	4/7	4/7
Apgar score < 7 at 5th min.**	6	3	1
Neonatal mortality			
Early (< 1 week)	3	2	–
Late (≥ 1 week)	1	–	1
Total	4	2	1
SGA***	7	6	1
Symmetric	4	3	–
Asymmetric	3	3	1
Hypoglycemia	4	2	–
RDS	5	4	1
Sepsis	3	5	2
NEC	1	–	1
Pulmonary hemorrhage	1	–	1
PV-IVH	1	2	1
ROP	1	–	1
BPD	1	–	1

SGA : small for gestational age.
RDS : respiratory distress syndrome.
NEC : necrotizing enterocolitis.
PV-IVH: periventricular-intraventricular hemorrhage.
ROP : retinopathy of prematurity. BPD: bronchopulmonary dysplasia.

* Mean ± SD.
** $p < 0.05$ (HELLP group versus control).
*** $p < 0.05$ (HELLP and HIP group versus control).
$p > 0.05$ in all comparison groups by chi-square test.

Discussion

Although described by several investigators for a number of years[7,8], this variant of preeclampsia was described by the acronym HELLP by Weinstein[3]. The disorder is characterized primarily by microangiopathic hemolytic anemia that progresses to low grade disseminated intravascular coagulation in proportion to the primary process[9]. The pathogenesis of HIP and

HELLP syndrome is attributed to vasoactive agents causing endothelial damage and platelet activation. It is still unknown whether these agents may affect the fetus[10].

Deterioration of the mother's condition is a major determinant in the management of these pregnancies. The termination of the pregnancy results in an increase of the number of thrombocytes and a normalization of the liver enzymes within a few days[11]; therefore, an immediate delivery has been recommended after the diagnosis is made. In our study, cesarean section was the primary mode of delivery in accordance with other reports[1,12].

HELLP syndrome may occur in five to 15 percent of patients with toxemia and the overall incidence is 0.12-0.85 percent for all pregnancies[13,14]. These figures were 4.9 percent and 0.12 percent, respectively, in our study. Pregnancies complicated by the HELLP syndrome have been associated with both poor maternal and neonatal outcome in several publications. While maternal mortality has been reported as between 0-24 percent in literature[1-3], there was no maternal death in our series.

Most of the cases of this study were multipara, as reported by Barlas et al.[15] The gestational ages of infants ranged from 27 to 37 weeks, with a mean of 31.2 (Table II), while it is around 32 to 34 weeks in literature[1,2].

The use of antenatal steroid was not different among the groups. The incidence of RDS was greater in HELLP and HIP groups (36.3%) than in the controls (9.1%), but the difference was not statistically significant. The role of hypertension in pregnancy as a risk factor for neonatal respiratory morbidity is well known. The increased incidence of RDS in babies of hypertensive mothers may be due to the absence of labor before delivery because of the greater likelihood of cesarean section[16]. However, in another study it was observed that after adjustment for labor and mode of delivery, hypertensive disease remained associated with an increase in RDS incidence. The authors concluded that, if the hypertensive disease had not resulted in abnormal antepartum tests, the protective effect would not have developed, and furthermore, the risk of RDS would have increased[17]. In a recent comparative study it was reported that incidence of severe RDS is higher in the HELLP group than in the HIP and control groups[18].

As seen from Table II, SGA proportions for HELLP and HIP groups were close to each other and were significantly higher than those of the control group. Intrauterine growth retardation is a well known consequence of placental insufficiency in babies of mothers with hypertension in pregnancy. Insignificant differences in the HELLP and HIP groups led us to suggest that the growth retardation is basically related to hypertension which begins at earlier or later periods of gestation and that it is not aggravated with maternal HELLP syndrome.

Furthermore, the percentage of lower Apgar scores at the 5th minute was significantly higher in the HELLP group than in the control group, in accordance with other studies[14,19]. Finally, the incidence of neonatal death was greater in the HELLP group but the difference was not statistically significant.

In summary, considering the limitations of its retrospective character, our study suggests an increased morbidity and mortality in infants born to mothers with HELLP syndrome that can be basically related to maternal hypertension.

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