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Maternal pre-pregnancy BMI and gestational weight gain as risk factors of jaundice in healthy newborns ≥ 37 weeks of gestation

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ABSTRACT

Introduction: One of the reasons for the delayed hospital discharge of newborns is jaundice. The aim of this study was to analyze the mother's gestational weight gain (GWG) as a factor contributing to jaundice in healthy, breastfed newborns, ≥ 37 weeks of gestation.

Material and methods: The medical documentation of 3594 mother-newborn pairs was analyzed. The newborns' gestational age, birth weight, birth weight loss (BWL) and the total serum bilirubin (TsB) on the 3rd or 4th day of life, as well as the mothers' pre-pregnancy body mass index (BMI), and GWG were analyzed. The newborns were divided into three groups. Group I was composed of those without jaundice (n = 1258), group II with jaundice (TsB between 5 and 11.9 mg/dl; n = 1302), and group III with TsB ≥ 12 mg/dl (n = 1034).

Results: The newborns from group I were more mature (p = 0.000) and had higher birth weight than newborns from groups II and III (p = 0.01). There was no difference in birth weight between groups II and III but newborns from group III were less mature (p = 0.03). There were no differences in BWL between the groups. Pre-pregnancy mean BMI of mothers from group III was higher; they more often were overweight (p = 0.000), but not obese. During pregnancy, they had a greater mean GWG (p = 0.000), and more often had excessive weight gain (p = 0.000), but also gestational diabetes (GDM) and hypertension. On admission to the maternity ward, mothers from group III had higher mean BMI and more often were obese than mothers from groups II and I.

Conclusions: Our study suggests that in addition to the known risk factors of early markedly elevated bilirubin concentration in healthy newborns ≥ 37 weeks of gestation such as lower birth weight and lower gestational maturity, the mother's excessive weight gain during pregnancy and complications of pregnancy such as gestational diabetes and hypertension should be taken into consideration.

KEY WORDS: BMI, gestational weight gain, newborn, jaundice, mother.

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INTRODUCTION

The task of the doctor working in the neonatal unit is to ensure that the newborn's adaptation to the extrauterine life is correct, a bond between the mother and the child has been established, and that the child is successfully breastfed and can be safely discharged home. One of the reasons for delayed discharge and generating additional diagnostic tests is markedly elevated bilirubin concentration in an otherwise healthy newborn, and the risk of a further increase in bilirubin after the discharge. In healthy full-term newborns, physiologic jaundice appears after the first day of life; the average total serum bilirubin (TsB) concentration usually peaks at 5 mg/dl on the third to the fourth day of life and then declines. In some newborns, TsB can be higher. When children are exposed to certain factors, they may develop an exaggerated form of

even physiologic jaundice with TsB as high as 17 mg/dl [1, 2]. It is known that, after reaching too high concentrations, unconjugated bilirubin can cross the blood-brain barrier and damage the central nervous system. The damage is known as bilirubin encephalopathy. Initial clinical symptoms may be nonspecific. There might be muscular hypotonia, unwillingness to suck, apathy, and/or vomiting. If the bilirubin concentration is not effectively reduced, bilirubin will be deposited in the subcortical nuclei (kernicterus) and the spinal cord. The changes will become irreversible, and neurological symptoms will intensify, leading to disability or even death [3-5]. Bearing this in mind, concerns arise that an early discharge of a newborn from a neonatal unit will increase the risk of severe hyperbilirubinemia during the child's stay at home. Therefore, efforts are made to minimize this risk. This is achievable through the understanding and identification of the risk factors, whose presence should be assessed individually for each child, taking into account both the fetal age and calendar age of the child. The American Academy of Pediatrics (AAP) and the European pediatric and neonatal societies have developed guidelines for pre-discharge neonatal management to prevent bilirubinopathy [6, 7]. They suggest measuring bilirubin concentration in children with jaundice [transcutaneous bilirubin (TcB) and total serum bilirubin (TsB)] before discharge, referring the results to hour-specific nomograms, and analyzing risk factors. The known high-risk factors for severe hyperbilirubinemia include: visible jaundice on the first day of life, confirmed hemolytic disease, prematurity less than 35 weeks of gestational age, perinatal injuries, prenatal asphyxia, and high bilirubin concentration on the day of discharge. On the maternal side, infection and decompensated gestational diabetes are also burdening factors [6-9].

The aim of the study was to determine whether pre-pregnancy maternal body mass index (BMI) and total weight gain during pregnancy contribute to the jaundice in healthy, exclusively breastfed newborns ≥ 37 weeks of gestation.

MATERIAL AND METHODS

The study is retrospective. Medical documentation of 5058 mother-child pairs hospitalized at St. John's Hospital in Lublin between January 2014 and June 2016 was screened; for further analysis, 3594 healthy newborns (1962 female, 1632 male) were qualified. Children were from single pregnancies, born between 37 and 42 weeks of gestation, in good general condition, with a birth weight between the 10th and 90th percentile, correctly adapting to the extra-uterine life. Out of the newborns enrolled, 2682 (74.63%) were born naturally, and 912 (25.37%) were delivered by a cesarean section. Newborns with jaundice on the first day of life, premature (< 37 weeks of gestation), small for gestational age, with genetic and developmental defects, with congenital and perinatal infections, injuries, serological conflict, and hemolytic anemia were excluded. Newborns of mothers with clinical features of infection and/or fever in the period preceding the delivery, with diabetes prior to pregnancy and uncontrolled course of pregnancy, as well as newborns hospitalized again for severe jaundice in the first month of life were also excluded.

In neonates, the fetal age, delivery type, vitality (Apgar score), birth weight, and the percentage of birth weight loss (BWL) were taken into account. Gestational age was estimated by maternal last menstrual period, fetal ultrasound, and Ballard assessment. The newborns were weighed with a digital electronic weighing scale with an accuracy of 5 g. The Fenton growth charts for assessment of birth weight vs. gestational age were used. Body length and head circumferences were taken with a non-stretchable plastic measuring tape.

Due to the visible yellowing of the skin in 2336 newborns, the total serum bilirubin (TsB) concentration was determined. In all these children TsB concentrations were measured on the 3rd or 4th day of life using standard laboratory methods (high-pressure liquid chromatography, HPLC-B). When the measurements were made twice (on the 3rd and 4th day), the higher bilirubin concentration was taken into account.

The characteristics of the newborns investigated are given in Table 1.

Maternal height and weight were measured on the day of the mothers' admission to the maternity ward. Data on pre-pregnancy body weight and the mothers' health condition were obtained from medical interviews

TABLE 1. Characteristics of the investigated newborns (*N* = 3594)

Factor	Statistics				
	Mean	SD	Median	Min.	Max.
Gestational age (weeks)	39.39	1.03	40	37	42
Birth weight (g)	3436.33	443.62	3420	2450	4330
Body length (cm)	54.34	1.75	54	51	60
Head circumference (cm)	33.83	1.07	34	33	37
Apgar score (points in first min.)	9.91	0.49	10	7	10
Apgar score (points in fifth min.)	9.95	0.30	10	8	10
Birth weight loss (%)	8.50	1.20	8.72	3.24	12.25
Days of hospitalization	4.45	0.68	4	3	9

and pregnancy records. Pre-pregnancy maternal body mass index (BMI) and total weight gain during pregnancy were assessed. The regularity of weight gain during pregnancy was determined with reference to the BMI before pregnancy [10].

The characteristics of the mothers of the examined newborns are given in Table 2. The highest pre-pregnancy BMI was 36.43 kg/m^2. On the day of admission to the maternity ward the highest BMI was 40.53 kg/m^2. There was only one mother who had a BMI of 40 or above.

Among mothers, 533 (14.8%) were overweight (BMI 25-29.9) and 250 (7.0%) were obese (BMI between 30 and 36.43, mean 32.2, median 32.3) before pregnancy. None had class III obesity (BMI of 40 or greater). Only two mothers had too low BMI before pregnancy (Table 3). When assessing the amount of weight gain during pregnancy, it was found that 52% of all respondents had normal weight gain in relation to the BMI before pregnancy, 29% too low, and 19% too high. Excessive weight gain was noted in 11.22% of women with a normal BMI, in 63.41% of overweight, and in 12% of obese women (Table 3).

Among 3594 mothers there were 152 mothers with gestational diabetes controlled by diet, 54 mothers with gestational diabetes controlled by insulin, 131 mothers with hypertension during pregnancy and 38 with both diabetes and hypertension. All these mothers had regular check-ups and complied with medical recommendation; hence glucose and blood pressure during pregnancy remained within the normal range.

The newborns were divided into three groups. The first group (I) consisted of newborns without visible yellowness of the skin (TsB was not assessed) and newborns with TsB < 5 mg/dl (n = 1258; 35%), the second group (II) consisted of newborns with TsB between 5 and 11.9 mg/dl (n = 1302; 36.23%), and the third group (III) consisted of newborns with TsB ≥12 mg/dl (n = 1034; 28.77%).

STATISTICAL ANALYSIS

The distribution of the studied variables was assessed using the Kolmogorov-Smirnov test. The one-way ANOVA or non-parametric Kruskal-Wallis test and post-hoc test were used to evaluate differences between groups

TABLE 2. Characteristics of mothers of the examined newborns (N = 3594)

Factor	Statistics				
	Mean	SD	Median	Min.	Max.
Age (years)	27.7	5.17	28	16	45
Pre-pregnancy body weight (kg)	65.95	7.26	64	51	98
Body height (cm)	164.92	0.02	165	157	179
Pre-pregnancy BMI (kg/m^2)	24.26	2.75	23.50	17.23	36.43
Pregnancy weight gain (kg)	12.42	2.94	12	5	29
BMI before delivery (kg/m^2)	28.83	2.67	28.22	20.96	40.53

TABLE 3. Number and percentage (%) of mothers with too low, normal, and too high pre-pregnancy body mass index (BMI) and pregnancy weight gain

Pre-pregnancy BMI	Number (%) of mothers		Pregnancy weight gain		
			Too low	Normal	Too high
< 18.5 (underweight)	2 (0.05)	Gain (kg)	< 12.5	12.5-18.0	> 18.0
		n	2	0	0
		(%)	100	0	0
18.5-24.9 (normal weight)	2809 (78.16)	Gain (kg)	< 11.5	11.5-16.0	> 16.0
		n	1038	1456	315
		(%)	36.95	51.83	11.22
25.0-29.9 (overweight)	533 (14.83)	Gain (kg)	< 7	7.0-11.5	> 11.5
		n	2	193	338
		(%)	0.38	36.21	63.41
≥ 30 (obese)	250 (6.96)	Gain (kg)	< 5	5-9	> 9
		n	0	220	30
		(%)	0	88.00	12.00
Total	3594 (100)	Total	1042 (29%)	1869 (52%)	683 (19%)

for quantitative features. Correlations between quantitative features were calculated using the Pearson correlation coefficient test. The non-parametric Pearson χ^2 test was used to assess the differences between the groups for qualitative features. A 5% inference error and the related significance level $p < 0.05$ were assumed. The database was built and statistical analyses were carried out using the Statistica 13.0 computer software (StatSoft, Poland).

RESULTS

Mean TsB in newborns from the second group (II) was 9.42 ± 1.73 mg/dl, and from the third group (III) 14.56 ± 1.59 mg/dl (min – 12 mg/dl, max –22 mg/dl). Newborns from group I (TsB < 5 mg/dl) were more mature and weighed more than those from groups II and III, but the mean birth weight of newborns from groups II and III was similar. Considering the gestational age, it was also found that children from the third group were less mature than those from the second group. There were no statistically significant differences in the mean percentage of the decrease in birth weight between the groups (ANOVA; F = 2.04; $p = 0.13$) (Table 4). When analyzing the vitality of newborns based on the Apgar scores, it was found that the number of points obtained in each group, both in the first and in the fifth minute, was similar (Kruskal-Wallis test: H = 0.63; $p = 0.73$ and H = 0.96; $p = 0.62$).

No statistically significant correlations were found between the bilirubin concentration and the birth weight of the newborns or the percentage of its decrease after birth.

In group I, 271/1258 (21.54%) children were born by cesarean section, 348/1302 (26.73%) in group II, and 293/1034 (28.34%) in group III. Children from groups III and II were born significantly more often by cesarean section than those from group I (Pearson's c^2 test = 15.81; df = 2; $p = 0.0004$), but neither in group II nor in group III was the mean TsB higher than in children born via vaginal delivery.

A statistically significant difference was found between the mean age of the women from the analyzed groups (one-way ANOVA F = 3.37; $p = 0.03$). Based on the post-hoc test for unequal numbers in the groups, it was found that mothers from group I were statistically significantly older than mothers from group II, but at a similar age as mothers from group III (Table 4). There was a statistically significant difference between their mean pre-pregnancy BMI (ANOVA; F = 20.60; $p = 0.000001$). Mothers from group III had a significantly higher mean BMI than mothers from group II or I. Also, during pregnancy, the mean weight gain of women from group III was significantly larger than that of women from groups I and II (ANOVA; F = 305.61; $p = 0.001$). Comparing the average BMI of mothers on admission to the maternity ward, it was found that while the BMI values of mothers from groups I and II were similar, the BMI of mothers from group III was significantly higher than the others (Table 4).

The mothers of the newborns with the highest bilirubin concentration ≥ 12 mg/dl (group III) were significantly more likely to experience excessive weight gain during pregnancy (Pearson's $\chi^2 = 506.18$; $p = 0.00001$). Before pregnancy they were overweight (BMI 25-29.9) significantly more often than the other mothers (Pearson

TABLE 4. Gestational age, birth weight, weight loss of newborns and age, body mass index (BMI), and pregnancy weight gain of mothers in group I (TsB < 5 mg/dl) in group II (TsB 5-11.9 mg/dl) and in group III (TsB ≥ 12 mg/dl)

Factor	Group I ($n = 1258$), mean ± SD	Group II ($n = 1302$), mean ± SD	Group III, ($n = 1034$), mean ± SD	Post-hoc test		
				I vs. II	I vs. III	II vs. III
Newborns						
Gestational age (weeks)	39.51 ± 1.02	39.36 ± 1.03	39.27 ± 1.02	$p = 0.000$	$p = 0.000$	$p = 0.03$
Birth weight (g)	3460.33 ± 429.19	3409.22 ± 444.67	3404.72 ± 433.72	$p = 0.009$	$p = 0.01$	ns
Birth weight loss (%)	8.54 ± 1.16	8.53 ± 1.13	8.44 ± 1.33	ns	ns	ns
Apgar score (in first min.)	9.91 ± 0.47	9.91 ± 0.5	9.90 ± 0.49	ns	ns	ns
Apgar score (in fifth min.)	9.96 ± 0.24	9.96 ± 0.26	9.94 ± 0.39	ns	ns	ns
TsB (mg/dl)	Was not calculated	9.42 ± 1.73	14.56 ± 1.59	–	–	$p = 0.000$
Mothers						
Age (years)	27.92 ± 5.26	27.41 ± 5.19	27.79 ± 5.02	$p = 0.043$	ns	ns
BMI-1 (kg/m^2)	23.94 ± 2.79	24.25 ± 2.76	24.67 ± 2.78	$p = 0.01$	$p = 0.000$	$p = 0.001$
Weight gain (kg)	11.9 ± 2.52	11.53 ± 2.47	14.17 ± 3.19	$p = 0.002$	$p = 0.000$	$p = 0.000$
BMI-2 (kg/m^2)	28.31 ± 2.82	28.50 ± 2.79	29.89 ± 2.92	$p = 0.17$	$p = 0.000$	$p = 0.000$

BMI-1 – pre-pregnancy. BMI-2 – on day of admission to maternity ward

χ^2 test = 128.64; p = 0.00001) but obesity (BMI > 30) was more often observed among mothers from groups II and I than from group III (7.75 and 7.07% vs. 5.81%, respectively) (Table 5). Before delivery, obesity was more often observed among mothers from group III than among other groups (Pearson χ^2 test =221.64; p = 0.00001). There was a positive correlation between maternal weight gain and bilirubin concentration in neonates from group III (r = 0.29; p = 0.000).

It was found that in group I mothers with gestational diabetes controlled by diet comprised 3.73%, in group II 2.99%, and in group III 6.3%. Gestational diabetes controlled by insulin was found in 1.51% of mothers from group I, 1.38% of mothers from group II, and 1.6% of mothers from group III (Table 5). Mothers of newborns with TsB ≥ 12 mg/dl (group III) had diet-controlled gestational diabetes significantly more often than mothers from the other groups (Pearson's χ^2 test = 15.846; p = 0.00007), but not insulin-controlled diabetes. Mothers from the third group also significantly more often had hypertension (Pearson's χ^2 = 3.928; p = 0.0475) and hypertension during pregnancy (Pearson's χ^2 =18.69; p = 0.00009) than mothers from the other groups (Table 5).

It is worth mentioning that the mother who had a BMI of 40.53 had also gestational diabetes and hypertension but the newborn was born on time, without macrosomia or any other complication. On the 4th day of life he had a bilirubin level of 15.75 mg/dl.

DISCUSSION

Our study concerned healthy newborns ≥ 37 weeks of gestation, appropriate for gestational age, exclusively breastfed, with a normal course of adaptation to the extra-uterine life. Among them, nearly 30% (1034/3594), at the 3rd or 4th day of life, had markedly elevated bilirubin concentration (TsB ≥ 12 mg/dl) as an isolated symptom. According to an hour-specific TsB nomogram proposed by APP, there was an intermediate and high risk of them developing clinically significant hyperbilirubinemia. Due to the fear of such a complication, the length of their hospitalization was longer than in the case of newborns with a lower bilirubin concentration. Causes such as congenital and perinatal infections, injuries, or serological conflict were excluded. The method of delivery was not found to influence the bilirubin concentration. However, Lain *et al.* found that vaginal delivery and exclusive breastfeeding are risk factors for readmission to hospital due to jaundice [11]. On the other hand, Bhutani and the Committee on Fetus and Newborn, American Academy of Pediatrics, found that jaundice tended to worsen in a larger number of infants born by cesarean section [12]. In our study, newborns with bilirubin concentration

TABLE 5. Mothers with normal body mass index (BMI), underweight, overweight, and obesity before pregnancy and with too little, normal and excessive weight gain as well as with GDM and hypertension during pregnancy, in group I (TsB < 5 mg/dl; n = 1258), group II (TsB 5-11.9 mg/dl; n = 1302), and group III (TsB ≥ 12 mg/dl; n =1034)

Factor	Group I, *n* (%)	Group II, *n* (%)	Group III, *n* (%)	Total, *n* (%)
BMI < 18.5				
I	2 (0.16)	0	0	2 (0.05)
II	0	0	0	0
BMI 18.5-24.9				
I	1050 (83.47)	1045 (80.20)	714 (69.12)	2809 (78.16)
II	38 (3.02)	28 (2.15)	5 (0.48)	71 (1.98)
BMI 25.0-29.9				
I	117 (0.30)	157 (2.05)	259 (5.07)	533 (14.83)
II	1011 (80.37)	1011 (77.59)	600 (58.08)	2622 (72.95)
BMI > 30w				
I	89 (7.07)	101 (7.75)	60 (5.81)	250 (6.96)
II	209 (16.61)	264 (20.26)	428 (41.43)	901 (25.07)
Weight gain too little	415 (32.99)	509 (39.06)	118 (11.42)	1042 (30)
Weight gain normal	720 (57.23)	646 (49.58)	503 (48.69)	1869 (52)
Weight gain excessive	123 (9.78)	148 (11.36)	412 (39.88)	683 (19)
Hypertension	40 (3.18)	43 (3.3)	48 (4.64)	131 (3.64)
GDM controlled diet	47 (3.73)	39 (2.99)	66 (6.3)	152 (4.22)
GDM controlled by insulin	19 (1.51)	18 (1.38)	17 (1.6)	54 (1.50)
GDM and hypertension	7 (0.56)	10 (0.77)	21 (2.03)	38 (1.06)

GDM – gestational diabetes, I – before pregnancy, II – on day of admission

≥ 5 mg/dl were significantly more often born by cesarean section than newborns with a lower bilirubin concentration, but neither in the group with TsB between 5 and 11.9 mg/dl (group II) nor in the group with TsB ≥ 12 mg/dl (group III) did the differences in mean TsB concentration depend on the method of birth. Usually, a cesarean section is performed in a situation where the continuation of natural labor threatens the life of the mother or child, so these newborns may require more intensive care or treatment. Elective cesarean section can prevent the occurrence of severe jaundice [13]. Unfortunately, we did not have precise information on how many of the cesarean sections in the study were elective. We do know, however, that all newborns after birth were considered to be in good health. They scored a 7 or above according to the Apgar scale and their gestational age was ≥ 37 weeks. We found a correlation between gestational age and bilirubin concentration. Newborns with TsB below 5 mg/dl were found be more mature (close to two days) and had a higher mean birth weight than newborns with TsB ≥ 12 mg/dl. It is known that low gestational age, and thus low birth weight, are among the most important factors in determining the risk of worsening jaundice [6,14]. According to the recently published American Academy of Pediatrics (AAP) clinical practice guideline for the management and prevention of hyperbilirubinemia in the newborn infant ≥ 35 weeks' gestation, risk increases with each additional week less than 40 weeks [15].

Some authors have noted a relationship between birth weight loss and hyperbilirubinemia. Chang *et al.*, examining healthy, exclusively breastfed infants, born ≥ 35 weeks, with a birth weight above 2500 g and hyperbilirubinemia, found that the younger the fetal age and greater the percentage of loss of birth weight, the more likely it is that jaundice will worsen [16]. Excessive birth weight loss (BWL) during the first days of life is usually caused by inadequate breastfeeding [17-19]. Zhao *et al.* stated that newborns with BWL over 4.5% on the first day after birth, receiving early intervention milk supplementation, could have their serum bilirubin concentration significantly reduced at 72 h after birth and recommended early and consecutive milk supplementation after birth [19]. Yang *et al.* observed that healthy and term neonates with significant hyperbilirubinemia 72 hours after birth had a mean BWL percentage of 8.4% by day 3 compared to 6.4% in the non-significant hyperbilirubinemia group [17]. Additionally, Blumovich *et al.* stated that substantial weight loss (> 5% difference between birth and discharge) is a risk factor for readmission to hospital for phototherapy and suggested that it should be taken into account in the decision to discharge a neonate with low-risk jaundice [20]. The clinical practice guideline committee recently convened by the AAP also lists suboptimal breast milk (which is frequently associated with excess weight loss) as a risk factor of hyperbilirubinemia. This so-called "breastfeeding jaundice" which is due to decreased stool frequency and increased enterohepatic circulation of bilirubin should be prevented by early, adequate feeding. Importantly, infants who are breastfed and are adequately hydrated should not routinely receive supplementation with commercially available infant formula [15]. In our study, newborns were exclusively breastfed. The mean BWL in each group was relatively large (about 8.5%) and did not differ between groups. Children with the highest TsB did not lose more weight than the others. There was also no correlation between the bilirubin concentration and the percentage of birth weight loss.

Analyzing the maternal factors of markedly elevated bilirubin concentration in newborns, the mothers' age and body weight before pregnancy were taken into consideration. In our study, it was not found that a high bilirubin concentration is related to maternal age. Mothers of newborns with TsB 12 mg/dl and above (group III) were at the same age as mothers from group I. It is worth recalling that maternal age > 25 years is listed as a minor risk factor for the development of severe hyperbilirubinemia in infants of 35 weeks or more [2]. In our study, the mean age of the mothers in each group was greater than 27 years. It is known that pregnant women with obesity are at a higher risk of complications during pregnancy, such as hypertension, gestational diabetes mellitus (GDM), preeclampsia, and cesarean section. Also, the fetuses of obese pregnant women are at higher risk of complications such as preterm and post-term birth, macrosomia, birth injuries, congenital abnormalities, and metabolic disturbances [21-23]. Some authors also point to the relationship between mothers' obesity and hyperbilirubinemia in newborns [13, 21, 22]. In our study mothers from group III were more often overweight before pregnancy (BMI 25.0-29.9) and had a significantly higher mean BMI than mothers from the other groups. However, the percentage of obesity (BMI ≥ 30) was higher in mothers of newborns with lower bilirubin concentrations (from groups I and II). At the day of admission to the maternity ward mothers of newborns from group III were more often obese than mothers from the other groups. On the basis of our observations, we can conclude that an excessive increase in maternal weight during pregnancy may be a risk factor for intensified hyperbilirubinemia in the newborn. Mothers of newborns with bilirubin concentration ≥ 12 mg/dl had statistically significantly greater weight gain during pregnancy than mothers of newborns from other groups. Moreover, in children from this group, a positive correlation was found between the weight gain of mothers and the concentration of bilirubin in newborns. Hedderson *et al.* found that women who gained more weight than recommended were nearly 1.5 times more likely to have an infant with hyperbilirubinemia [21]. Similarly, Özdek *et al.* reported that

the concentration of bilirubin in healthy full-term newborns on the 5th and 15th day of life was statistically significantly higher in children of mothers with excessive weight gain during pregnancy than in infants of mothers whose body weight increase was regular or lower than recommended [24]. There are no studies that could fully explain this relationship. However, it has been proven that excessive maternal body weight is a risk factor of gestational diabetes and uncontrolled maternal diabetes can be the reason for severe hyperbilirubinemia [25]. In our study, it was found that mothers of newborns with bilirubin concentration ≥ 12 mg/dl were significantly more likely to experience gestational diabetes and required dietary treatment (but not insulin) than the other mothers. Moreover, these mothers also had hypertension significantly more often. Both gestational diabetes and hypertension lead to increased fetal erythropoiesis and polycythemia, which in turn may increase the bilirubin concentration in newborns [22, 26]. It is worth mentioning that it is not the mother's diabetes itself that causes hyperbilirubinemia, but the fetal macrosomia caused by diabetes [15]. It can be presumed that the increase in the availability of carbohydrates, fats, and proteins to the fetus of an obese mother (or one with too much weight gain in pregnancy) changes its metabolism and endocrine regulation and also contributes to the increase in bilirubin concentration [27].

Our data have some limitations, such as their retrospective character, the lack of assessment of the exact time of blood collection for bilirubin testing, which made it impossible to use the age-specific bilirubin nomogram before discharge, and the lack of follow-up of children after discharge. Finally, we only analyzed a few separate factors that can influence bilirubin concentration, while the mechanism of increasing hyperbilirubinemia is more complex.

CONCLUSIONS

Our study suggests that in addition to the known risk factors of early markedly elevated bilirubin concentration in healthy newborns ≥ 37 weeks of gestation such as lower birth weight and lower gestational maturity, the mother's excessive weight gain during pregnancy and complications of pregnancy such as gestational diabetes and hypertension should also be taken into consideration.

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DISCLOSURE

The authors report no conflict of interest.

References

1. Hammerman C, Kaplan M. Hyperbilirubinemia in the term infant: re-evaluating what we think we know. Clin Perinatol 2021; 48(3): 533-554.
2. Pace EJ, Brown CM, DeGeorge KC. Neonatal hyperbilirubinemia: an evidence-based approach. J Fam Pract 2019; 68(1): E4-E11.
3. Olusanya BO, Kaplan M, Hansen T. Neonatal hyperbilirubinaemia: a global perspective. Lancet Child Adolesc Health 2018; 2(8): 610-620.
4. Das S, van Landeghem F. Clinicopathological spectrum of bilirubin encephalopathy/kernicterus. Diagnostics (Basel) 2019; 9(1): 24.
5. Kaplan M, Maisels MJ. Natural history of early neonatal bilirubinemia: a global perspective. J Perinatol 2021; 41(4): 873-878.
6. Borszewska-Kornacka MK, Tołłoczko J. Żółtaczki okresu noworodkowego. W: Standardy opieki nad noworodkiem w Polsce. Zalecenia Polskiego Towarzystwa Neonatologicznego [Neonatal jaundice. Standards of care for a newborn in Poland. Recommendations of the Polish Neonatal Society]. Medi Press, Warszawa 2017; 86-96.
7. Romagnoli C, Barone G, Pratesi S, et al. Italian guidelines for management and treatment of hyperbilirubinaemia of newborn infants ≥ 35 weeks' gestational age. Ital J Pediatr 2014; 40(1): 11.
8. Boo NY, Sin S, Chee SC, et al. Genetic factors and delayed TSB monitoring and treatment as risk factors associated with severe hyperbilirubinemia in term neonates admitted for phototherapy. J Trop Pediatr 2020; 66(6): 569-582.
9. Maisels MJ, Newman TB, Kaplan M. A new hour-specific serum bilirubin nomogram for neonates ≥35 weeks of gestation. J Pediatr 2021; 237: 317.
10. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines ; Rasmussen KM, Yaktine AL (eds.). Weight Gain During Pregnancy: Reexamining the Guidelines. Washington (DC): National Academies Press; 2009.
11. Lain SJ, Roberts CL, Bowen JR, Nassar N. Early discharge of infants and risk of readmission for jaundice. Pediatrics 2015; 135(2): 314-321.
12. Bhutani VK, Committee on Fetus and Newborn, American Academy of Pediatrics. Phototherapy to prevent severe neonatal hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2011; 128(4): e1046–e1052.
13. Norman M, Åberg K, Holmsten K, et al. Predicting nonhemolytic neonatal Hyperbilirubinemia. Pediatrics 2015; 136(6): 1087-1094.
14. Muchowski KE. Evaluation and treatment of neonatal hyperbilirubinemia. Am Fam Physician 2014; 89(11): 873-878.
15. Kemper AR, Newman TB, Slaughter JL, et al. Clinical practice guideline revision: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2022; 150(3): e2022058859.
16. Chang RJ, Chou HC, Chang YH, et al. Weight loss percentage prediction of subsequent neonatal hyperbilirubinemia in exclusively breastfed neonates. Pediatr Neonatol 2012; 53(1): 41-44.

17. Yang WC, Zhao LL, Li YC, et al. Bodyweight loss in predicting neonatal hyperbilirubinemia 72 hours after birth in term newborn infants. BMC Pediatr 2013; 13: 145.
18. Jang GJ, Ko S. Effects of a breastfeeding coaching program on growth and neonatal jaundice in late preterm infants in South Korea. Child Health Nurs Res 2021; 27(4): 377-384.
19. Zhao LL, Lee EP, Kuo RN, et al. Effect of early supplemental formula intervention on body weight and hyperbilirubinemia in neonates during 72 h after birth. Front Pediatr 2021; 9: 625536.
20. Blumovich A, Mangel L, Yochpaz S, et al. Risk factors for readmission for phototherapy due to jaundice in healthy newborns: a retrospective, observational study. BMC Pediatr 2020; 20(1): 248.
21. Hedderson MM, Weiss NS, Sacks DA, et al. Pregnancy weight gain and risk of neonatal complications: macrosomia, hypoglycemia, and hyperbilirubinemia. Obstet Gynecol 2006; 108(5): 1153-1161.
22. Peters S, Andrews C, Sen S. Care of infants born to women with diabetes. Curr Diab Rep 2020; 20(8): 39.
23. Marchi J, Berg M, Dencker A, et al. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. Obes Rev 2015; 16(8): 621-638.
24. Özdek S, Kul M, Akcan AB, et al. The effect of the pre-pregnancy weight of the mother and the gestational weight gain on the bilirubin level of term newborn. J Matern Fetal Neonatal Med 2016; 29(15): 2434-2437.
25. Riskin A, Itzchaki O, Bader D, et al. Perinatal outcomes in infants of mothers with diabetes in pregnancy. Isr Med Assoc J 2020; 22(9): 569-575.
26. Okoye HC, Nwogoh B, Odetunde OI. Correlation of hematocrit and Apgar scores in newborns of women with hypertensive disorders in pregnancy. J Neonatal Perinatal Med 2017; 10(4): 387-392.
27. Desoye G, Herrera E. Adipose tissue development and lipid metabolism in the human fetus: the 2020 perspective focusing on maternal diabetes and obesity. Prog Lipid Res 2021; 81: 101082.

AUTHORS' CONTRIBUTIONS

JD, BKR prepared the concept of the article, collected and interpreted data, wrote the manuscript. BKR took part in preparing the final version of the publication.