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Does Maternal Underweight Prior to Conception Influence Pregnancy Risks and Outcome?

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Abstract. *Aim: Data analyzing risks during pregnancy and neonatal outcome in Caucasian women with pre-conceptional underweight are scarce. Patients and Methods: We conducted a retrospective cohort study in Northern Germany comparing pregnancy risks and neonatal outcomes in nulliparous women with either pre-conceptional underweight or normal weight. Results: The data of 3,854 nulliparous women with either underweight (n=243; BMI ≤18.5 kg/m^2) or normal weight (n=3611; BMI 18.5-24.9 kg/m^2) were screened. The risks for preterm birth (23.3 vs. 18.6%; p=0.004) and neonatal underweight were significantly higher in women with underweight prior to conception (p<0.0001). The risk for secondary caesarean sections was significantly lower in underweight patients. Conclusion: To our knowledge, the present retrospective cohort study constitutes the largest sub-group analysis on delivery and maternal and neonatal outcome in pre-conceptionally underweight mothers. There are significantly more preterm deliveries in underweight mothers, while maternal outcome and birth-associated trauma (lacerations, caesarean section) is not disadvantageously influenced by maternal underweight. Further investigations are required in order to specify nutritional deficits in underweight pregnant women and to optimize medication in cases where nutritional balance cannot be achieved in order to improve the neonatal status at birth.*

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While obesity in pregnancy and pregnancy outcome in obese women are subjects of diverse research in recent publications, it is remarkable that the data for pregnancy outcome in pre-conceptional underweight mothers is extremely limited. Apart from an increasing prevalence of obesity, however, the prevalence for underweight in distinct sub-groups of mothers is also increasing.

In contrary to obesity, less people are affected by underweight in Europe.

The World Health Organization (WHO) classifies human weight into different categories (1). A body mass index (BMI) less than 18.5 kg/m^2 is defined as underweight. In Germany, the incidence of underweight in women is low with a nationwide prevalence of 3% (2). Especially in young women in certain social groups, an anorectic model-like weight is the ideal of beauty and a lot of cases of underweight in women of childbearing age are due to eating disorders (3). The lifetime incidence of eating disorders in young women of childbearing age is 5.2-6.5 % (4). While obesity is a frequently encountered problem in pregnant women with multiple complications during pregnancy and delivery (5-16), data on pregnant women with underweight or anorexia are scarce (17-19).

Because of hormonal disorders due to anorexia, underweight women often have menstrual irregularities leading to amenorrhea and infertility. Disorders in hypothalamic-hypophysis functions result in hypogonadotrope anovulatory cycles (20). Consequently, studies of underweight pregnant Caucasian patients are limited due to the low quantity of underweight Caucasians in general and diminution of pregnancies in underweight women. Therefore, the aim of the present study was to elucidate whether the constitution of underweight women, which has been demonstrated to influence the hormonal balance (20), as well as suspected nutritional deficits in underweight women, show any adverse effects on the prevalence of pregnancy complications, mode of delivery and neonatal outcome, such as birth weight and gestational age at delivery.

Patients and Methods

This study is a retrospective cohort analysis of all deliveries at the University Clinic of Schleswig-Holstein, Campus Luebeck from January 1st 2000 to December 31st, 2009. Our hospital is the referral Centre for the Northern German coastal region with more than 4 million inhabitants. The region is characterized by a predominantly Caucasian population. We included all single pregnancies of that period that met the following inclusion criteria: Based on maternal BMI calculated from the pregnant women's reported height and pre-pregnancy weight, all pregnant women were divided into two groups: underweight pregnant women with a BMI less than 18.5 kg/m^2 at the time of conception formed group A, women with a normal weight at conception (BMI between 18.5 and ≤24.9 kg/m^2) formed group B. Pregnant women with a preconceptional BMI higher than 25 kg/m^2 were excluded. Only nulliparous women were included in the study. Exclusion criteria were defined as preterm delivery before 24 completed weeks of gestation post-menstruation, confirmed multiple pregnancy and incomplete data sets (Figure 1). Primary outcome was defined as the mode of delivery. Additional maternal data and the neonatal outcome were reported (patient clinical record files as primary data source). Neonatal outcome was determined by either a specially trained obstetrician or paediatrician of the neonatal intensive care unit of the University hospital. Every delivery was accompanied by a midwife and an obstetrician who took responsibility for the course and outcome of labour. We categorized the mode of delivery in spontaneous, vaginal operative and caesarean deliveries. Vaginal operative delivery included forceps and vacuum extraction. Caesarean section was differentiated in primary and secondary caesarean delivery. Emergency delivery was added to secondary caesarean section. Primary caesarean section was defined as elective, whereas secondary Caesarean delivery was defined as non-elective operation. High-grade lacerations were defined as third and fourth degree lacerations.

Demographic data were abstracted from the prenatal and inpatient records. Gestational age was determined from prenatal records and calculated from last menstrual period or best obstetric estimate based on early prenatal ultrasound and obstetric examination. Data were extracted from the electronic database of our hospital, PIA Fetal DatabaseTM (GE; City, County, USA). All statistical analyses were performed with Prism 5.0 for Windows (GraphPad Software, 2007, San Diego, CA, USA). Analysis included the Mann–Whitney test for continuous data, Chi-square test and Fisher's exact test for categorical data. The results were considered statistically significant when two-sided analysis yielded a p-value ≤0.05.

Results

Three thousand eight hundred and fifty-four (27.7%) of the 13,941 pregnant women screened met the inclusion criteria (Figure 1). Two hundred and forty-three pregnant women with a BMI <18.5 kg/m^2 formed group A and 3,611 pregnant women with a BMI between 18.5 and 24.9 formed group B.

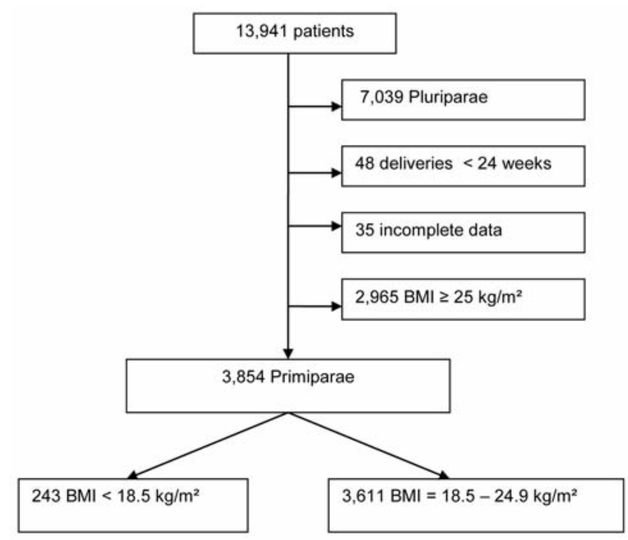

Figure 1. *Data analysis.*

A total of 10,087 (72%) deliveries during the study period were excluded because of multiparity (n=7,039), incomplete data (n=35), delivery before 24 weeks of gestation (n=48) or a pre-conceptional BMI >25 kg/m^2 (n=2,965).

Maternal demographic data showed partially significant differences between the two groups (Table I). The women with lower BMI were significantly younger (26.3 years ±5.8 *vs.* 29.0 years ±5.8; p<0.001). Weight gain during pregnancy did not differ significantly between the two pre-conceptional weight groups (15.03 kg in group A, range, 3 to 31kg *vs.* 15.08 kg in group B; range, 0.5 to 52 kg). Concerning the perinatal data, the average duration of pregnancy was shorter in group A (266.5±21.45 days *vs.* 268.6±23.04 days; p=0.009). Preterm deliveries were significantly more frequent in group A (Figure 2). Sub-group analysis of different gestational age groups demonstrated a significant difference in gestational age at delivery for 32+0 to 36+6 gestational weeks but not for deliveries >37+0 weeks and <32+0 gestational weeks (Table IV). The significant difference in preterm delivery was even more evident in extremely underweight mothers (pre-conceptional BMI <16 kg/m^2) and occurred in 40% of that subgroup (Table V).

A secondary caesarean delivery was significantly less often performed in underweight women (Table II). With regard to the other modes of delivery, there was no statistically significant inter-group difference. Rates for vacuum-assisted vaginal delivery or forceps deliveries did not differ significantly (4.5% *vs.* 5.2%).

There were less inductions of labour in underweight pregnant women. Induction of labour tended to be less performed in group A compared to normal weight women (13.6% *vs.* 18.55%; p=0.06).

Table I. *Maternal outcome*.

	BMI <18.5 kg/m^2	BMI 18.5-24.9 kg/m^2	*p*-Value
Mean age at delivery (years)	26.33±5.76	29.02±5.84	<0.0001*
Range	(14.4-43.3)	(15.0-48.3)	
Mean duration of pregnancy (days)	266.5±21.45	268.6±23.04	0.0105*
Range	(168-299)	(168-305)	
Mean gravidity	1.31±0.69	1.29±0.67	0.6957
Range	(1-6)	(1-10)	
Mean blood loss (ml)	308±114.1	328.5±163.2	0.0628
Range	(100-800)	(30-3500)	
Higher grade laceration (of all lacerations)	4/130	36/1970	0.3246

*Significant.

There was also no significant difference of high-grade laceration, postpartum haemorrhage or other complications between the groups. Median maternal peripartum blood loss measured by obstetric standard visual estimation was 308 mL in group A and 329 mL in group B (p=0.064). Postpartal haemorrhage (PPH) did not differ significantly between both groups (2.5% *vs*. 3.8%; p=0.379).

Neonatal weight and length differed significantly between the groups (Table III). Neonatal weight and length were lower in underweight patients.

Vital neonatal characteristics including APGAR scores, arterial cord pH and base excess showed no inter-group differences. However, in group A, admission on neonatal intensive care unit (ICU) was necessary in significantly more cases than in group B (Figure 2) (n=56). The reasons for admission were preterm delivery in most cases (57.1%), intra-uterine growth restriction (7.1%), extremely low birth weight <1,000g (1.8%), neonatal infections (1.8%), malformations (14.3%), maternal drug abuse (5.4%) and others (17.5%). Ten neonates (17.9%) (n=10) in group A were small for gestational age below the 3rd percentile calculated according to percentile curves by PIA Fetal Database™ (GE).

There was no statistically significant difference in the occurrence of intrauterine fetal death.

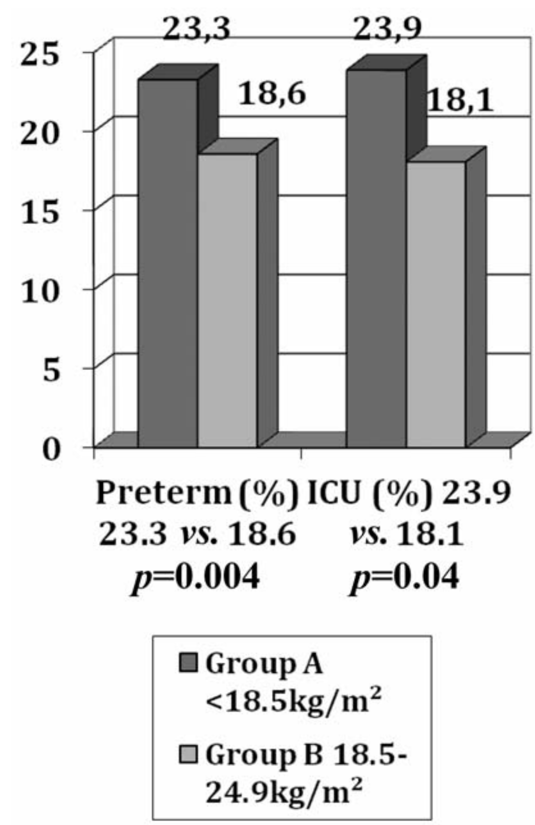

Figure 2. *Preterm delivery and admission to neonatal intensive care unit (ICU).*

Discussion

According to current data, our analysis constitutes the largest retrospective cohort study on delivery and maternal and neonatal birth status in pre-conceptionally underweight primiparous mothers. In particular, the presented sub-group analyses are unique. In a Spanish retrospective cohort study, 168 underweight women showed increased adjusted risk of oligohydramnios and low birth weight babies, while severe or morbidly obese women had an increased adjusted risk of induction of labour, elective and emergency caesarean section, fetal macrosomia, fetal acidosis at birth and perinatal mortality (21).

In our patient collective, there were less inductions of labour in underweight patients in comparison to normal-weight mothers. The difference did not reach statistical significance (p=0.059); however, there was a tendency reflecting current data (22). One reason might be that the rates of pregnancies beyond term, as well as gestational diabetes, are lower in underweight patients and

Table II. *Mode of delivery.*

	BMI <18.5	BMI 18.5-24.9	p-Value
Spontaneous delivery	154/243 63.4%	2088/3611 57.8%	0.0933
Vaginal operative delivery	11/243 4.5%	189/3611 5.2%	0.765
Primary caesarean section	40/243 16.5%	567/3611 15.7%	0.7168
Secondary caesarean section	38/243 15.6%	766/3611 21.2%	0.0412*
Breech delivery	0/243 0.0%	1/3611 <0.1%	1.0000

*Significant.

Table III. *Neonatal outcome.*

Neonatal length (cm)	49.31±4.339	50.27±4.475	<0.0001*
Range	(28-56)	(21-61)	
Neonatal weight (g)	2961±662.6	3115±724.2	<0.0001*
Range	(480-5040)	(490-5420)	
Gender	104f/139m	1749f/1862m	0.0972
APGAR after 5 min.	9.49±1.04	9.50±1.12	0.4486
Range	1-10	1-10	
APGAR after 10 min	9.78±0.85	9.76±0.97	0.9766
Range	1-10	1-10	
pH umbilical artery	7.302±0.08118	7.305±0.07048	0.7115
Range	(6.630-7.460)	(6.720-7.500)	
Base excess	–4.035±3.739	–4.032±3.205	0.3730
Range	(–38.0-4.3)	(–26.2-15.0)	

f: Female, m: male. *Significant.

Table IV. *Preterm delivery according to gestational week.*

	Group A <18.5 kg/m^2	Group B 18.5-24.9 kg/m^2	p-Value
>42+0 weeks	1/243 0.41%	45/3611 1.25%	0.36
40+0 to 42+0 weeks	65/243 26.74%	1266/3611 35.05%	0.01*
37+0 to 40+0 weeks	113/243 46.50%	1627/3611 45.05%	0.69
32+0 to 36+6 weeks	53/243 21.81%	513/3611 14.21%	0.002*
28+0 to 31+6 weeks	9/243 3.70%	93/3611 2.57%	0.29
<28+0 SSW weeks	2/243 0.82%	67/3611 1.82%	0.32

*Significant.

Table V. *Preterm deliveries according to grade of underweight in Group A.*

Grade of underweight	Preterm (n)	Term (n)	Total
Light 17.1-18.5 (kg/m^2)	39 (26%)	108	147
Moderate 16.1-17 (kg/m^2)	13 (20%)	53	66
Severe ≤16 (kg/m^2)	12 (40%)	18	30

consequently fetal macrosomia is less common (23). Bhattacharya *et al*. support the hypothesis that non-preterm pregnancies in underweight women do not present with more risks than pregnancies in normal-weight patients resulting in lower rates of labour induction. This hypothesis is corroborated by equal APGAR scores and umbilical arterial pH values in neonates in underweight and normal weight patients according to current literature and to our present data (24).

Regarding the mode of delivery in this defined cohort, a secondary caesarean delivery was significantly less often performed in the underweight group than in patients with normal weight (Table II). This observation is in line with current data. Cesarean section is significantly less often performed in pre-conceptionally underweight patients in comparison to normal weight patients (25-26). Again, the reason might be that the rates of pregnancies beyond term, as well as gestational diabetes, are lower in underweight patients and consequently fetal macrosomia associated with prolonged delivery is less common (23).

The lower rate of vacuum assisted deliveries and forceps deliveries in underweight patients, though not significant, might be traced back to the same reasons, as operative assisted births are often performed in prolonged deliveries, *e.g*. in macrosome neonates.

The rate for lacerations in our collective was comparatively low in both groups. On the one hand, underweight patients were significantly younger and young nulliparous women have been demonstrated to experience fewer lacerations in comparison to older women (27).

Maternal peripartum blood loss was 308 mL in group A and 329 mL in group B; however, the difference did not reach statistical significance (p=0.064). Again, regarding the association of maternal weight and post partum haemorrhage, obese patients experience severe postpartum haemorrhage more often (22). Underweight is not a risk factor for postpartum haemorrhage.

A higher rate of neonatal admissions to ICU was observed, which was in most cases due to preterm delivery (57.1%).

In our cohort, the rate of preterm deliveries was significantly higher in the underweight group (23.3 *vs*. 18.6%). Moreover, the preterm delivery rate of normal-weight patients was remarkably high (18.6%) in comparison to national average, which goes in line with a high risk population in our tertiary prenatal referral Centre. According to current data, the general national rate of preterm deliveries in Germany is 9% (28). The higher rate of preterm deliveries was even more significant in extremely underweight patients with 40% of preterm deliveries in the severe underweight group (BMI <16 kg/m^2). One reason might be pre-existent maternal malnutrition (29). In our cohort, average neonatal weight was lower in the maternal underweight group. Apart from malnutrition, this observation might be interpreted as a fetal adjustment reaction. Belogolovkin *et al*. demonstrated a higher rate of intrauterine fetal death in normal to macrosome fetuses in underweight mothers (30). The rates of intra-uterine growth retardation are highest in preconceptionally underweight women with inadequate weight gain during pregnancy (31). Interestingly, in our patient population a significantly higher rate of preterm deliveries was observed between 32+0 and 36+6 weeks in underweight patients. In the group of extremely and very preterm deliveries (<32+0 weeks), preterm deliveries did not differ between underweight and normal-weight mothers. This observation is consolidated by the current literature (32). An increase in intra-uterine growth retardation (IUGR) in underweight mothers, in comparison to normal weight mothers, can only be observed after 30 gestational weeks (33). Iatrogenic pre-term delivery due to IUGR is, thus, no more frequent in underweight women <30 gestational weeks.

In 17.85% of all neonates admitted to ICU, intrauterine malnutrition with a birth weight below the 3rd percentile was declared the main reason. It remains unclear whether IUGR is due to pre-conceptional maternal underweight and malnutrition or undernourishment continued during pregnancy for eating disorders (34). However, underweight is not always associated with malnutrition. In our retrospective approach we did not analyze the reason for maternal underweight (malnutrition, gastrointestinal chronic disease accounting for malabsorption, eating disorders *etc*.). According to the literature, fetal weight gain correlates with maternal weight gain. For example, in a Nigerian study, adolescents' weight gain during pregnancy was significantly lower compared to adult pregnant women. The authors demonstrated a correlation between low maternal weight gain and low birth weight in the newborns (35, 36). In our cohort, median weight gain during pregnancy was equal in both groups (15.03 kg in group A *vs*. 15.08 kg in group B). The institute of medicine recommends a weight gain of 28 to 40 lbs (12.7 to 18.14 kg) in underweight patients and 25 to 35 lbs (11.34 to 15.88 kg) in normal weight patients (37). Thus, average weight gain in both groups was adequate according to recommended weight gain. Recommendations for maternal weight gain during pregnancy are higher for underweight patients; this was not fulfilled in our patient collective (38).

There were no cases of intrauterine or early postpartum death in the underweight group. In the normal-weight group, intra-uterine fetal death extra muros was reported in 0.33%, neonatal death occurred in 0.13%; these data go in line with current epidemiologic data (39). Precedent studies analyzing the correlation of maternal weight and rate of intrauterine fetal death found a correlation with preconceptional maternal obesity (39).

In contrast to maternal outcome in underweight patients, which is not adversely influenced by underweight, our data suggest that neonatal outcome is deteriorated by maternal underweight due to preterm delivery and intrauterine growth retardation.

Our data generate a hypothesis rather than being conclusive due to the retrospective design of the study. As a consequence of the present data, advising underweight pregnant patients on adequate nutrition and considering eating disorders during pregnancy is indispensable. A cohort study of women with anorexia nervosa, bulimia nervosa, or both, found that women with bulimia nervosa were significantly more likely to experience miscarriages and those with anorexia nervosa were significantly more likely to have smaller babies compared with the general population (40). It remains unclear whether intrauterine growth retardation and preterm deliveries in underweight patients are mainly due to reduced calorie intake or to a deficiency in vitamin and micronutrients intake. Analysis of placenta and maternal serum components could elucidate this question (41, 42).

In the present study, we focused on the neonatal status at birth. Long-term follow-up of children of underweight mothers is still missing and should be the aim of future studies.

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