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Original Research

Association between Pre-Pregnancy Body Mass Index, Gestational Weight Gain, and Birth Defects, a Retrospective Study

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Abstract

Background: To explore the correlation of pre-pregnancy body mass index (BMI) and gestational weight gain (GWG) with the occurrence of birth defects. **Methods**: Clinical data of pregnant women were collected in Zhuzhou Central Hospital from January 2019 to December 2021. A total of 10,086 newborns, including 175 newborns with birth defects. Birth defect cases were identified, and 350 cases of pregnant women without birth defects were randomly selected as the control group by control case matching (1:2). Clinical baseline data were compared between the two groups, and logistic single-factor analysis was performed to examine the correlation between pre-pregnancy BMI, GWG, and birth defects. **Results**: The study consisted of a total of 175 cases of birth defects, including circulatory system 114 (65.14%) cases, musculoskeletal system 34 (19.43%) cases, urinary system 15 (8.57%) cases, and 12 (6.86%) cases of other birth defects. There were no statistical differences in parity between the two groups ($p > 0.05$). However, statistically significant differences were observed in maternal age, pre-pregnancy medication history, and the perinatal TORCH (Toxoplass, Other (Syphilis, Hepatitis B), Rubivirus, Cytomegalovirus, Herpesvirus) ($p < 0.05$). Logistic single-factor analysis revealed that the proportion of birth defects in obese women was significantly higher than that in the control group (5.14% *vs*. 1.14%, $p = 0.013$). In the birth defect group, the distribution of inadequate, appropriate, and excessive GWG was 9.71%, 34.86%, and 55.43%, respectively. However, no statistical differences were found in the types of birth defects based on maternal BMI and GWG. **Conclusion**: The primary focus on addressing birth defects should center around the prevention and control of congenital heart disease. Abnormal pre-pregnancy BMI is a risk factor for birth defects. Effective control of GWG contributes to preventing adverse outcomes in newborns. Therefore, both women of childbearing age and pregnant women need to pay attention to weight management.

Keywords: body mass index; gestational weight gain; birth defects; pregnancy; newborn

1. Introduction

Birth defects refer to structural, functional, or metabolic abnormalities that occur before birth due to genetic or environmental factors, or a combination of both [1]. The factors leading to birth defects are complex, with more than 80,000 known types [2]. Globally, approximately 8 million newborns are born with birth defects every year [3]. In the United States, about 1 in 33 infants is born with a birth defect [4]. According to estimates in 2018, China adds about 900,000 cases of newborns with birth defects each year, accounting for 5.6% [2]. Birth defects are the main causes of early miscarriages, stillbirths, neonatal and infant deaths, and congenital disabilities [5]. They significantly affect the survival and quality of life of children, causing considerable suffering and imposing substantial economic burdens on the affected children and their families. Therefore, preventing birth defects is a major public health concern to improve child survival and enhance their quality of life.

The currently recognized independent high-risk factors for birth defects include maternal age, medication history, and genetic and environmental factors. With economic development and improved living standards, the incidence of obesity and associated chronic metabolic diseases has been continuously rising [6]. Moreover, obesity can be transmitted across generations [7,8]. Maternal obesity may affect the overall health of the offspring through mechanisms such as chronic inflammatory responses, dysfunctional adipose tissue, dysfunction of the hypothalamic–pituitary–adipose axis, epigenetic changes, genetic factors, and disruptions in gut microbiota [9,10], although the specific mechanisms remain unclear. Monitoring gestational weight gain (GWG) is part of prenatal care, and both insufficient and excessive GWG can have adverse effects on the developing fetus. However, currently, the relationship between GWG and birth defects is not well understood. Thus, this study aims to explore the correlation between pre-pregnancy body mass index (BMI), GWG, and birth defects by analyzing the clinical data of birth defect cases and normal newborns, aiming to provide a foundation for early-life interventions and ensuring the quality of the birth population.

2. Study Subjects and Methods

2.1 Subjects

Retrospective study the clinical data of pregnant women at Zhuzhou Central Hospital of Zhuzhou from January 2019 to December 2021. A total of 10,086 newborns, including 175 newborns with birth defects. The collected data included various factors such as age, height, pre-pregnancy weight, GWG, parity, pregnancy history, pre-pregnancy and pregnancy medication usage, and adverse habits such as smoking and alcohol consumption.

The inclusion criteria were as follows: (1) having undergone a normal pre-pregnancy health checkup, with no pre-pregnancy medication usage or adverse habits; (2) availability of complete prenatal examination data; (3) no family history of psychiatric illness, dementia, birth defects, hypertension, diabetes, or other hereditary diseases; (4) no history of illnesses such as heart disease, tuberculosis, liver disease, kidney disease, chronic hypertension, anemia, blood disorders, psychiatric illness, diabetes, or thyroid dysfunction; (5) residing in the city for more than a year; and (6) willingness to cooperate with clinical data collection.

The exclusion criteria were: (1) residing in the city for less than a year; (2) abnormal results of pre-pregnancy health checkup, pre-pregnancy medication usage, or adverse habits; (3) incomplete prenatal examination data; (4) presence of relevant family history and/or past medical history; and (5) availability of convenient and safe non-invasive methods for monitoring gestational weight gain. This study was approved by the ethics committee of the hospital.

2.2 Methods

The clinical data of the pregnant women were collected. The collected information included the following:

(1) Basic information of pregnant women: this included their age, height, pre-pregnancy weight, GWG, premarital examination results, adherence to a healthy diet, maintenance of a regular lifestyle, and parity.

(2) Maternal health conditions: details about the women's health were recorded, including their pre-pregnancy and pregnancy medication history, instances of pregnancy-related complications, any adverse pregnancy history, and a history of psychiatric and neurological abnormalities.

(3) Maternal adverse habits: information regarding habits such as smoking, alcohol consumption, and drug use.

(4) Basic information about pregnant women before delivery: information regarding weight, uterine height, and abdominal circumference.

(5) Labor process and newborn information: comprehensive information about the labor process and the newborns.

The criteria for inclusion in the control group were as follows: when diagnosing a newborn with a birth defect during childbirth, two healthy infants were randomly selected as controls. These control infants had to meet the following conditions: pregnant women with age difference of no more than 2 years, and they should be from the same geographical area and have the same gender, and delivery time of no more than 3 moths compare with matched birth defect cases. Moreover, the selected controls had to have no obvious adverse pregnancy outcomes. During the study period, a total of 175 cases of birth defects were identified, and throng control case matching (1:2) selected as controls. 350 cases of pregnant women without birth defects were randomly selected as the control group by control case matching (1:2). Matching factors include maternal age, pre-pregnancy BMI, delivery time of pregnant women and birth weight of newborn.

The diagnostic criteria for identifying birth defects involved a comprehensive approach. Clinical monitoring was conducted according to the requirements of the "China Birth Defects Monitoring Program" and the 23 categories of birth defect diagnostic criteria outlined in the "China Birth Defect Working Manual" published by the National Defects Monitoring Center.

Pre-Pregnancy BMI and Gestational Weight Gain Groups

The BMI was calculated using the formula: weight (kg) $\div$ (height (m))^2. The method for calculating GWG involved subtracting the weight before delivery from the pre-pregnancy weight. Measurements were taken in the morning, on an empty stomach, after bowel movement, and at approximately 25 °C. The GWG of the pregnant women was categorized according to the "Guidelines for Monitoring and Evaluation of Maternal Weight Gain During Pregnancy in China" [11] published by the China Nutrition Society in 2021 (Table 1).

Table 1. Weight gain during pregnancy and recommended weekly weight gain in the middle and late stages of pregnancy based on pre-pregnancy BMI classification.

Pre-pregnancy BMI classification (kg/m^2)	Total gain range (kg)
Underweight (<18.5)	11.0–16.0
Normal (18.5–23.9)	8.0–14.0
Overweight (24.0–27.9)	7.0–11.0
Obese (≥28.0)	5.0–9.0

BMI, body mass index.

2.3 Statistical Analysis

The control group were selected by case control matching (1:2) [12,13]. Data analysis was conducted using SPSS 26.0 software (IBM, Armonk, NY, USA). Normally distributed continuous data were represented as the mean $\pm$ standard deviation ($\bar{x} \pm$ s). Categorical data were presented as frequencies (n), and data comparisons were conducted using chi-squared tests or the Monte Carlo method.

A p-value < 0.05 was considered statistically significant. Two-sided tests were performed, with a significance level set at $\alpha = 0.05$.

3. Results

3.1 General Characteristics of the Maternal Population

A total of 525 parturients were included in the study. Their mean age was 30.3 $\pm$ 4.16 years, with 478 (91.05%) participants being younger than 35 years and 47 (8.95%) being 35 years or older. Among the participants, 83 had low pre-pregnancy weight, 352 had normal weight, 77 were classified as overweight, and 13 were categorized as obese. Regarding GWG, 48 participants had gained inadequate weight, 205 had gained appropriate weight, and 272 had gained excessive weight. The distribution of primiparous, second-parous, and multiparous women was 165, 188, and 172 cases, respectively. There were 224 cases of primiparity, 276 cases of second parity, and 25 cases of third or higher parity. Additionally, 167 patients had experienced pregnancy-related complications, whereas 358 did not experience any complications. Among the participants, 464 did not use any medication during pregnancy, while 61 did. Postpartum checkups revealed that 157 participants showed normal results, whereas 346 participants showed abnormal findings (Table 2).

Table 2. Clinical Characteristics of 525 Maternities.

Characteristics	No. (%)
Age (year)	
<35	478 (91.05)
≥35	47 (8.95)
BMI	
Underweight	83 (15.81)
Normal weight	352 (67.05)
Overweight	77 (14.67)
Obesity	13 (2.47)
Weight gain	
Insufficient	48 (9.14)
Appropriate	205 (39.05)
Excessive	272 (51.81)
Parity (No.)	
1	165 (31.43)
2	188 (35.81)
≥3	172 (32.76)
Births (No.)	
1	224 (42.67)
2	276 (52.57)
≥3	25 (4.76)
Pregnancy complications	
Present	167 (31.81)
Absent	358 (68.19)
Medication use during pregnancy	
No	464 (88.38)
Yes	61 (11.62)
Postpartum checkup	
Normal	346 (65.90)
Abnormal	157 (29.90)
Not checked	22 (4.19)

3.2 Distribution of Birth Defects

Among the 175 cases of birth defects, there were 21 different types. The top three types were circulatory system 114 (65.14%) cases, musculoskeletal system 34 (19.43%), urinary system 15 (8.57%). These defects were categorized based on the system involved, as follows: circulatory system defects, including congenital heart disease and vascular malformations; musculoskeletal system defects, including polydactyly/syndactyly, clubfoot, and umbilical hernia; urinary system defects, including congenital inguinal hernia and hypospadias; digestive system defects, including anal atresia, esophageal atresia, and small bowel atresia; and other system defects, including cleft lip/palate, sacral agenesis, and cerebral ventricle malformation. The specific data are presented in Table 3.

Table 3. Distribution of birth defect categories.

Birth defect category	No. (%)
Circulatory system	114 (65.14)
Musculoskeletal system	34 (19.43)
Urinary system	15 (8.57)
Digestive system	6 (3.43)
Other systems	6 (3.43)
Total	175 (100.00)

3.3 Comparison of General Characteristics between the Birth Defect Group and the Control Group

Differences in age, pre-pregnancy BMI, GWG, parity, number of pregnancies, pregnancy-related complications, perinatal examinations, medication during pregnancy, smoking history, and alcohol consumption history were compared between the two groups (Table 4). We found that age (≥35 years), medication use during pregnancy, and perinatal TORCH (Toxoplass, Other (Syphilis, Hepatitis B), Rubivirus, Cytomegalovirus, Herpesvirus) showed statistically significant differences between the two groups ($p < 0.000$, odds ratio (OR) (95% confidence interval (CI)), 3.66 (1.97, 6.81), $p < 0.000$, OR (95% CI), 16.02 (7.67, 33.47), $p < 0.000$, OR (95% CI), 283.74 (128.36, 627.21), respectively), indicating their independent roles as risk factors for causing birth defects. However, no statistically significant differences were observed in terms of weight gain, parity, number of pregnancies, pregnancy-related complications, smoking history, and alcohol consumption history ($p > 0.05$). However, 2 number of births have was significantly difference ($p = 0.002$, OR (95% CI), 0.55 (0.37, 0.80). Notably, in the classification of pre-pregnancy BMI, obesity exhibited statistically significant

abnormalities between the two groups ($p = 0.01$), whereas low body weight and overweight showed no statistically significant abnormalities.

3.4 Proportional Analysis of GWG in Birth Defect Cases

We conducted a correlation analysis of GWG in the 175 cases of birth defects. The distribution of inadequate, appropriate, and excessive GWG cases was 17, 61, and 97, respectively, constituting proportions of 9.71%, 34.86%, and 55.43%, respectively (Table 5). Despite the lack of statistical significance in the comparison of GWG between the control group and the birth defect group ($p < 0.05$, Table 3), based on the proportions of GWG within the birth defect cases, we considered both insufficient and excessive GWG as potential risk factors for birth defects.

3.5 Comparison of Pre-Pregnancy BMI and Gestational Weight Gain in Different Birth Defect Categories

The fetal outcomes were categorized into six groups, and the frequencies of gestational BMI and weight gain groups were compared using the Monte Carlo method. The *p*-values for both the pre-pregnancy BMI group and the GWG group were >0.05, indicating no statistically significant differences (Table 6).

4. Discussion

According to the "National Comprehensive Prevention and Control Program for Birth Defects" issued by the National Health Commission in 2018, the overall incidence rate of birth defects in China is approximately 5.6%. In our study, the birth defect rate accounted for 1.74% (175/10,068), which is lower than the total birth defect rate. This may be related to the region. The main cause of birth defects was congenital heart disease, Musculoskeletal system and Urinary system approximately 65.14%, 19.43% and (8.57%) respectively. This is consistent with the data from China's birth defect survey [14].

4.1 Birth Defects Are Related to Age, Perinatal TORCH, and Pregnancy Medication during Pregnancy

In our study, we found that a significant increase in birth defects occurred when the age was over 35 years old and perinatal TORCH were positive. It has been confirmed that advanced maternal age and TORCH were identified as risk factors for birth defects [15,16]. For TORCH, approximately 75% of those infected in utero will be asymptomatic at birth, but as they grow, they will be at significant risk for developing motor dysfunction, cerebellar dysfunction, microcephaly, seizures, chorioretinitis, intellectual disabilities, and sensorineural hearing loss [17].

About pregnancy medication, there are 68 cases with clearly documented medication names and courses, it was observed that 48 participants took prenatal nutrients like iron, calcium, vitamins, and amino acids, whereas 20 participants took progesterone for miscarriage prevention, insulin for blood sugar control, or antihypertensive medications. Karcz *et al.* [18] suggest that maternal nutrient deficiencies might be present during pregnancy and that supplementing adequate nutrients can promote maternal and infant health. Similarly, Hansu *et al.* [19] suggest that supplementing vitamins and minerals during different pregnancy stages can better maintain maternal and infant health. For supplementing iron, calcium, vitamins, and amino acids during pregnancy, we recommend supplementing with nutrients. However, during pregnancy, we recommend avoiding medication during pregnancy. Anderson *et al.* [20] compared women who were exposed to antidepressants during early pregnancy with those who were not and found an association between antidepressant use in early pregnancy and specific birth defects such as congenital heart defects. Huybrechts *et al.* [21] found that the use of hydroxychloroquine in the early stages of pregnancy slightly increased the risk of cleft lip and urinary system defects.

4.2 BMI and GWG Can Affect Birth Defects

In our study, we found that obesity accounted for 5.14% in the birth defect group, compared to 1.14% in the control group. The results suggest that pre-pregnancy obesity is a risk factor for birth defects. However, pre-pregnancy underweight and overweight do not appear to influence the occurrence of birth defects. Research has indicated that pre-pregnancy obesity could impair embryonic development and the health of the offspring [22]. Vena *et al*. [23] conducted a systematic review on the relationship between maternal weight and neural tube defects, revealing a significantly higher risk of neural tube defects in fetuses of obese mothers. However, there is no difference in being overweight or underweight [23]. Additionally, when analyzing congenital heart diseases, Persson *et al*. [24] identified maternal overweight and obesity as high-risk factors. Another cross-sectional study on birth defects also found that overweight and obesity were risk factors [25]. Zhang *et al*. [26] discovered that compared to women with normal weight, the risk of spina bifida significantly increased for both mothers and offspring in obese pregnant women, whereas the risk of anencephaly in offspring significantly increased for underweight pregnant women. However, some researchers did not find a link between maternal pre-pregnancy obesity and the risk of hypospadias or cryptorchidism in male newborns [27].

Considering the results of this study and related literature, BMI, particularly obesity, is identified as a risk factor for birth defects. Nevertheless, BMI is not a universal risk factor for all types of birth defects. Interestingly, in this study, the proportions of insufficient, appropriate, and excessive GWG gain were 9.71%, 34.86%, and 55.43%, respectively. Based on the proportion of GWG in birth defect cases, insufficient or excessive gestational weight gain is considered a potential risk factor for birth defects. Severe insufficient GWG is associated with a higher

Table 4. Subgroup analysis of odds ratio (OR) for birth defects.

Subgroup	No. (%)		*p*-value	OR (95% CI)
	Birth normal	Birth defects		
Age (years)				
<35	332 (94.86)	146 (83.43)		
≥35	18 (5.14)	29 (16.57)	0.000	3.66 (1.97, 6.81)
Pre-pregnancy BMI				
Normal weight	236 (67.43)	116 (66.29)		
Underweight	63 (18.00)	20 (11.43)	0.12	0.65 (0.37, 1.12)
Overweight	47 (13.43)	30 (17.14)	0.31	1.30 (0.78, 2.16)
Obesity	4 (1.14)	9 (5.14)	0.013	4.58 (1.38, 15.18)
Weight gain during pregnancy				
Adequate	144 (41.14)	61 (34.86)		
Inadequate	31 (8.86)	17 (9.71)	0.45	1.30 (0.67, 2.51)
Excessive	175 (50.00)	97 (55.43)	0.18	1.31 (0.89, 1.93)
Number of pregnancies				
1	104 (29.71)	61 (34.86)		
2	142 (40.58)	46 (26.29)	0.11	0.55 (0.35, 0.88)
≥3	104 (29.71)	68 (38.85)	0.63	1.12 (0.72, 1.73)
Number of birth				
1	134 (38.29)	90 (51.42)		
2	202 (57.71)	74 (42.29)	0.002	0.55 (0.37, 0.80)
≥3	14 (4.00)	11 (6.29)	0.71	1.17 (0.51, 2.69)
Pregnancy-related complications	102 (29.14)	65 (30.29)	0.064	0.70 (0.51, 3.119)
Perinatal TORCH				
Normal	333 (95.14)	13 (7.42)		
Abnormal	13 (3.72)	144 (82.29)	0.000	283.74 (128.36, 627.21)
Not done	4 (1.14)	18 (10.29)		
Medication use during pregnancy				
No	341 (97.43)	123 (70.29)		
Yes	9 (2.57)	52 (29.71)	0.000	16.02 (7.67, 33.47)
Alcohol consumption history				
No	336 (96.00)	168 (96.00)		
Yes	14 (4.00)	7 (4.00)	1.00	1.00 (0.40, 2.52)
Smoking history				
No	318 (90.86)	161 (92.00)		
Yes	32 (9.14)	14 (8.00)	0.66	1.16 (0.60, 2.23)

CI, confidence interval; OR, odds ratio; TORCH, Toxoplass, Other (Syphilis, Hepatitis B), Rubivirus, Cytomegalovirus, Herpesvirus.

Table 5. Proportional analysis of GWG in birth defects.

GWG	Pre-pregnancy BMI in birth defect cases				Percentage (%)
	Low	Normal	Overweight	Obese	
Insufficient	6	6	5	0	9.71
Appropriate	7	46	7	1	34.86
Excessive	7	64	18	8	55.43

GWG, Gestational weight gain.

risk of low birth weight, preterm birth, growth retardation, and microcephaly, whereas excessive GWG is linked to a higher risk of macrosomia and large-for-gestational-age babies, highlighting the close relationship between GWG and fetal birth weight [28,29]. Perumal *et al*. [28] discussed the correlation between GWG and birth defects in 7561 Tanzanian women, suggesting the necessity of interventions for inadequate or excessive GWG to prevent adverse neonatal outcomes. Moreover, some studies have found correlations of decreased pre-pregnancy BMI and insufficient

Table 6. Comparison of pre-pregnancy BMI and gestational weight gain for different types of birth defects.

Factor	Type of birth defect						Fisher χ^2	p
	None	Circulatory system defects	Musculoskeletal system defects	Urinary system defects	Digestive system defects	Other system defects		
Pre-pregnancy BMI group							20.905	>0.05
Normal	236	76	24	10	3	3		
Low body weight	63	12	3	2	1	2		
Overweight	47	21	5	2	1	1		
Obesity	4	5	2	1	1	0		
Pregnancy weight gain grouping							9.346	>0.05
Suitable	144	35	16	6	1	3		
Insufficient	31	11	5	1	0	0		
Excessive	175	68	13	8	5	3		

GWG with the severity of clinical features of optic nerve development, especially bilateral diseases and severe brain anomalies [30].

Although BMI and gestational weight gain did not show statistically significant differences between the control group and the birth defect group in this study, might be attributed to the relatively small sample size and potential influence of confounding biases. Further analysis with larger sample sizes is needed to confirm the impact of pre-pregnancy BMI and GWG on fetal birth defects. Nevertheless, trends in the data still suggest that weight management is crucial for women of reproductive age and pregnant women, as it holds significant implications for reducing adverse pregnancy outcomes and improving the overall quality of the population.

5. Conclusion

In this study, we found advanced age (≥35) and perinatal TORCH positive were risk factors for birth defects. During pregnancy, we recommend supplementing with nutrients. Although BMI and gestational weight gain did not show statistically significant differences between the control group and the birth defect group. We still believe that managing BMI and GWG during pregnancy is crucial.

Availability of Data and Materials

Obtain availability of data and materials through corresponding author email.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MQ, ZY, LM and JL. The first draft of the manuscript was written by ZC and GH, and all authors commented on previous versions of the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Zhuzhou Central Hospital, No: ZZCHEC2020190-02. All patients' consent has been obtained.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Lipinski RJ, Krauss RS. Gene-environment interactions in birth defect etiology: Challenges and opportunities. Current Topics in Developmental Biology. 2023; 152: 1–30.

[2] National Health Commission. National Comprehensive Prevention and Control Program for Birth defects [EB/OL]. 2018. Available at: http://www.nhc.gov.cn/jnr/gfxwjm/201809/9644ce7d2653427790 99d54b6962a4e0.shtml (Accessed: 11 April 2022).

[3] Texas Birth Defects Registry. Texas Birth Defects Registry Annual Report Among 1999–2019 Deliveries. Available at: https://www.dshs.texas.gov/sites/default/files/birthdefects/annualreport/1999-2019-TxBDR-Annual-Report.pdf (Accessed: 2 November 2023).

[4] Centers for Disease Control and Prevention (CDC). Update on overall prevalence of major birth defects–Atlanta, Georgia, 1978-2005. MMWR. Morbidity and Mortality Weekly Report. 2008; 57: 1–5.

[5] Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ, *et al*. National population-based estimates for major birth defects, 2010-2014. Birth Defects Research. 2019; 111: 1420–1435.

[6] D'Ambrosio V, Brunelli R, Vena F, Di Mascio D, Marchetti C, Boccherini C, *et al*. Metformin reduces maternal weight gain in obese pregnant women: A systematic review and meta-analysis

of two randomized controlled trials. Diabetes/metabolism Research and Reviews. 2019; 35: e3164.

[7] Téllez-Rojo MM, Trejo-Valdivia B, Roberts E, Muñoz-Rocha TV, Bautista-Arredondo LF, Peterson KE, *et al*. Influence of post-partum BMI change on childhood obesity and energy intake. PLoS ONE. 2019; 14: e0224830.

[8] Dalrymple KV, Flynn AC, Seed PT, Briley AL, O'Keeffe M, Godfrey KM, *et al*. Associations between dietary patterns, eating behaviours, and body composition and adiposity in 3-year-old children of mothers with obesity. Pediatric Obesity. 2020; 15: e12608.

[9] Wallace JG, Bellissimo CJ, Yeo E, Fei Xia Y, Petrik JJ, Surette MG, *et al*. Obesity during pregnancy results in maternal intestinal inflammation, placental hypoxia, and alters fetal glucose metabolism at mid-gestation. Scientific Reports. 2019; 9: 17621.

[10] Rizzo HE, Escaname EN, Alana NB, Lavender E, Gelfond J, Fernandez R, *et al*. Maternal diabetes and obesity influence the fetal epigenome in a largely Hispanic population. Clinical Epigenetics. 2020; 12: 34.

[11] Lai JQ, Su YX, Yang YX, Wang ZX, Chang SY, Ma LK, *et al*. Standard of Recommendation for Weight Gain during Pregnancy Period. 2022. Available at: https://www.besjournal.com/en/article/doi/10.3967/bes2022.114 (Accessed: 2 November 2023).

[12] Nowak M, Kalwa M, Oleksy P, Marszalek K, Radon-Pokracka M, Huras H. The relationship between pre-pregnancy BMI, gestational weight gain and neonatal birth weight: a retrospective cohort study. Ginekologia Polska. 2019; 90: 50–54.

[13] Fitzpatrick D, Holmes NE, Hui L. A systematic review of maternal TORCH serology as a screen for suspected fetal infection. Prenatal Diagnosis. 2022; 42: 87–96.

[14] Ministry of Health of the People's Republic of China. National Stocktaking Report on Birth Defect Prevention (2012) (China); National Health and Family Planning Commission of the People's Republic of China: Beijing, China. 2012. Available at: http://www.gov.cn/gzdt/att/att/site1/20120912/1c6f6506c7f811bacf9301.pdf (Accessed: 11 April 2022).

[15] Baird PA, Sadovnick AD, Yee IM. Maternal age and birth defects: a population study. Lancet (London, England). 1991; 337: 527–530.

[16] Hvide HK, Johnsen J, Salvanes KG. Parental age and birth defects: a sibling study. European Journal of Epidemiology. 2021; 36: 849–860.

[17] Zhang L, Wang X, Liu M, Feng G, Zeng Y, Wang R, *et al*. The epidemiology and disease burden of congenital TORCH infections among hospitalized children in China: A national cross-sectional study. PLoS Neglected Tropical Diseases. 2022; 16: e0010861.

[18] Karcz K, Królak-Olejnik B, Paluszyńska D. Vegetarian diet in pregnancy and lactation - safety and rules of balancing meal plan in the aspect of optimal fetal and infant development. Polski Merkuriusz Lekarski: Organ Polskiego Towarzystwa Lekarskiego. 2019; 46: 45–50.

[19] Hansu K, Cikim IG. Vitamin and mineral levels during pregnancy. Revista Da Associacao Medica Brasileira (1992). 2022; 68: 1705–1708.

[20] Anderson KN, Lind JN, Simeone RM, Bobo WV, Mitchell AA, Riehle-Colarusso T, *et al*. Maternal Use of Specific Antidepressant Medications During Early Pregnancy and the Risk of Selected Birth Defects. JAMA Psychiatry. 2020; 77: 1246–1255.

[21] Huybrechts KF, Bateman BT, Zhu Y, Straub L, Mogun H, Kim SC, *et al*. Hydroxychloroquine early in pregnancy and risk of birth defects. American Journal of Obstetrics and Gynecology. 2021; 224: 290.e1–290.e22.

[22] Han L, Ren C, Li L, Li X, Ge J, Wang H, *et al*. Embryonic defects induced by maternal obesity in mice derive from Stella insufficiency in oocytes. Nature Genetics. 2018; 50: 432–442.

[23] Vena F, D'Ambrosio V, Paladini V, Saluzzi E, Di Mascio D, Boccherini C, *et al*. Risk of neural tube defects according to maternal body mass index: a systematic review and meta-analysis. The Journal of Maternal-fetal & Neonatal Medicine: the Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians. 2022; 35: 7296–7305.

[24] Persson M, Razaz N, Edstedt Bonamy AK, Villamor E, Cnattingius S. Maternal Overweight and Obesity and Risk of Congenital Heart Defects. Journal of the American College of Cardiology. 2019; 73: 44–53.

[25] Lee KW, Ching SM, Ramachandran V, Yee A, Hoo FK, Chia YC, *et al*. Prevalence and risk factors of gestational diabetes mellitus in Asia: a systematic review and meta-analysis. BMC Pregnancy and Childbirth. 2018; 18: 494.

[26] Zhang L, Zhang Y, Li Z, Ren A, Liu J, Ye R. Maternal periconceptional body mass index and risk for neural tube defects: results from a large cohort study in China. The Journal of Maternal-fetal & Neonatal Medicine: the Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians. 2021; 34: 274–280.

[27] Adams SV, Hastert TA, Huang Y, Starr JR. No association between maternal pre-pregnancy obesity and risk of hypospadias or cryptorchidism in male newborns. Birth Defects Research. Part A, Clinical and Molecular Teratology. 2011; 91: 241–248.

[28] Perumal N, Wang D, Darling AM, Wang M, Liu E, Urassa W, *et al*. Associations between Gestational Weight Gain Adequacy and Neonatal Outcomes in Tanzania. Annals of Nutrition & Metabolism. 2022; 78: 156–165.

[29] Hannaford KE, Tuuli MG, Odibo L, Macones GA, Odibo AO. Gestational Weight Gain: Association with Adverse Pregnancy Outcomes. American Journal of Perinatology. 2017; 34: 147–154.

[30] Situ BA, Borchert MS, Brown B, Garcia-Filion P. Association of prepregnancy body mass index and gestational weight gain on severity of optic nerve hypoplasia. Birth Defects Research. 2023; 115: 753–763.