


Prevalence and Association of Congenital Anomalies According to the Maternal Body Mass Index: Cross-Sectional Study

Prevalência e associação de anomalias congênitas de acordo com índice de massa corporal materno: Estudo transversal

Carolina Leão de Moraes¹  Carolina Rodrigues Mendonça¹ Natália Cruz e Melo²
Waldemar Naves do Amaral¹

¹ Faculty of Medicine, Department of Obstetrics and Gynecology, Hospital das Clínicas, Universidade Federal de Goiás, Goiânia, GO, Brazil

² Paulista Medical School, Universidade Federal de São Paulo, São Paulo, SP, Brazil

Address for correspondence: Carolina Leão de Moraes, Msc, Av. Esperança, s/n, 74690-900 Chácaras de Recreio Samambaia, Goiânia, GO, Brazil (e-mail: carolina.leao.moraes2@gmail.com).

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Abstract

Objective To evaluate and compare the prevalence of structural congenital anomalies (CAs) according to maternal body mass index (BMI).

Methods The present cross-sectional study involved pregnant women with fetuses diagnosed with structural CAs through morphological ultrasonography between November 2014 and January 2016. The nutritional status of the pregnant women was classified according to the gross value of the body mass index. The pregnant women were categorized into four groups: low weight, adequate weight, overweight, and obesity. Statistical analysis was performed using Stata/SE version 12.0 (Stata Corporation, College Station, TX), with values of $p \leq 0.05$ considered statistically significant.

Results A total of 223 pregnant women had fetuses diagnosed with CAs. The prevalence of structural CAs in pregnant women with low weight was of 20.18%, of 43.50% in pregnant women with adequate weight, of 22.87% in pregnant women with overweight, and of 13.45% in pregnant women with obesity. The prevalence of central nervous system (CNS) anomalies and of genitourinary system anomalies was high for the four groups of pregnant women. A positive association was observed between multiple anomalies in pregnant women with adequate weight (prevalence ratio [PR] = 1.65; $p \leq 0.004$) and between anomalies of the lymphatic system in obese pregnant women (PR = 4.04, $p \leq 0.000$).

Conclusion The prevalence of CNS and genitourinary system anomalies was high in all of the BMI categories. Obese pregnancies were associated with lymphatic system anomalies. Therefore, screening and identification of the risk factors for CAs are important, regardless of the maternal BMI. Our findings reinforce the importance of discussing with pregnant women maternal nutrition and its effect on fetal development and on neonatal outcome.

Keywords

- ▶ congenital anomalies
- ▶ pregnancy
- ▶ obesity
- ▶ body weight
- ▶ fetal ultrasonography

 Carolina Leão de Moraes's ORCID is <https://orcid.org/0000-0003-0755-0753>.

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Resumo

Objetivo Avaliar e comparar a prevalência de anomalias congênitas (ACs) estruturais de acordo com o índice de massa corporal (IMC) materno.

Métodos Estudo transversal envolvendo gestantes com fetos diagnosticados com ACs estruturais por ultrassonografia morfológica entre novembro de 2014 e janeiro de 2016. O estado nutricional das gestantes foi classificado de acordo com o valor bruto do índice de massa corporal. As gestantes foram categorizadas em quatro grupos: baixo peso, peso adequado, sobrepeso e obesidade. A análise estatística foi realizada no programa Stata/SE versão 12.0 (Stata Corporation, College Station, TX), com valores de $p \leq 0,05$ considerados estatisticamente significantes.

Resultados Um total de 223 gestantes tiveram fetos diagnosticados com ACs. A prevalência de AC estrutural em gestantes com baixo peso foi de 20,18%, em gestantes com peso adequado foi de 43,50%, em gestantes com sobrepeso foi de 22,87%, e em gestantes com obesidade foi de 13,45%. A prevalência de anomalias do sistema nervoso central (SNC) e do sistema geniturinário foi alta para os quatro grupos. Observou-se associação positiva entre múltiplas anomalias em gestantes com peso adequado (razão de prevalência [RP] = 1,65; $p \leq 0,004$) e entre anomalias do sistema linfático em gestantes obesas (RP = 4,04, $p \leq 0,000$).

Conclusão A prevalência das anomalias do SNC e do sistema geniturinário foi alta em todas as categorias de IMC. Gestantes obesas foram associadas a anomalias do sistema linfático. Portanto, o rastreamento e a identificação dos fatores de risco para as AC são importantes, independentemente do IMC materno. Nossos achados reforçam a importância de discutir com gestantes sobre a nutrição materna e seu efeito no desenvolvimento fetal e no desfecho neonatal.

Palavras-chave

- ▶ anomalias congênitas
- ▶ gravidez
- ▶ obesidade
- ▶ peso corporal
- ▶ ultrassonografia fetal

Introduction

Nutritional status and adequate maternal weight gain are important aspects for the health and the well-being before, during, and after pregnancy.^{1,2} It is known that women with normal gestational weight gain have fewer complications during pregnancy.³

In contrast, low birthweight and malnutrition in pregnant women have been related to adverse effects during pregnancy, such as spontaneous abortion, hypertensive disorders, and fetal growth restriction and prematurity.^{4,5} Maternal weight gain beyond the recommended limit may lead to complications in the pre- and postpartum period, and may represent an obstetric risk factor, with consequences for the mother and for the fetus.^{3,6} Risks to pregnant women include gestational diabetes mellitus (DM) and preeclampsia, whereas risks to fetuses include congenital anomalies (CAs), macrosomia, stillbirth, neonatal death, and prematurity.^{3,7-9}

Congenital anomalies result in mortality in approximately 276,000 newborns per year worldwide. Currently, 50% of the CAs have an unexplained etiology; however, some etiological factors have been reported, including genetic, nutritional, infectious, and/or environmental factors, among which maternal nutritional status is highlighted.^{10,11} Despite this, there are few epidemiological studies on the prevalence of CAs and the association between the body mass index (BMI) of pregnant women and the development of CAs.¹²⁻¹⁴ These studies include only overweight and obese pregnant women.

Thus, the prevalence of CAs in pregnant women with different nutritional profiles remains unknown.¹⁵⁻¹⁷

Research on maternal BMI and the risk of CAs is important to render assistance to healthcare systems in developing strategies for the prevention of CAs.^{4,18} In this context, the objective of the present study was to evaluate and compare the prevalence and association of structural CAs according to the maternal BMI.

Methods**Type of Study**

The present observational cross-sectional study included pregnant women carrying fetuses with structural CAs at the Hospital das Clínicas of the Faculdade de Medicina of the Universidade Federal de Goiás Goiânia, state of Goiás, Brazil. Data were collected between November 2014 and January 2016. The present study was approved by the research ethics committee of the Hospital das Clínicas.

Study Population

We have included pregnant women at a high-risk prenatal outpatient clinic with fetuses diagnosed with structural CAs through morphological ultrasonography. Pregnant women whose fetuses were not diagnosed with structural CAs, pregnant women who had ultrasound at or after 14 weeks of gestation or who did not remember their pregestational weight were excluded. The selected patients were submitted

to a private interview in which they were informed about the stages of the study and signed the informed consent form.

Data Collection

The sociodemographic data of the pregnant women were collected during the interview through questionnaires. In addition, anthropometric (weight, height) and obstetric (gestational age; fetal gender; previous pregnancies; previous abortion history; children with previous CAs; family history of CAs; maternal DM; alcohol, illicit drug, and tobacco consumption, and teratogenic medication use during pregnancy) data were collected. Gestational age was based on the first obstetrical ultrasonography performed to confirm the gestation, performed up to the 14th week of gestation. The pregestational weight was self-reported by the pregnant women. The height of the pregnant women was measured using a mechanical beam medical scale (Medical Antropométrico Mechanical Scale Welmy, São Paulo, Brazil) in meters. The BMI was calculated by dividing the weight of the pregnant women (kg) by the square of their height (m²). The method of Atalah et al¹⁹ was employed to classify the nutritional status of the pregnant women according to the gross BMI value for the gestational age for the first trimester, which is recommended by the Brazilian Ministry of Health.^{19,20} The pregnant women were categorized into four groups: low weight, adequate weight, overweight, and obesity. After the expected date of delivery, data on the evolution of the gestation and on the confirmation of fetal gender were obtained through telephone interviews with the pregnant women.

Statistical Analysis

The sample size was of 153 women, calculated based on a 5% of error and on a 95% confidence level. Statistical analyses were performed using the software Stata/SE version 12.0 (Stata Corporation, College Station, TX). Differences between distributions in particular groups were also evaluated by the Mann-Whitney test and by the Fisher exact test. In prevalence ratio (PR) calculations, the reference category was the group with the lowest prevalence, considering a 95% confidence interval (CI). Values of $p \leq 0.05$ were considered statistically significant.

Results

Characteristics of the Study Sample

A total of 223 pregnant women with fetuses diagnosed with CAs through ultrasonography participated in the present study. The mean gestational age at the time of diagnosis was 12.83 weeks (standard deviation [SD] = 1.16). After the calculation of the BMI, the pregnant women were categorized into groups: low weight (20.18%; $n = 45$), adequate weight (43.50%; $n = 97$), overweight (22.87%; $n = 51$), and obese (13.45%; $n = 30$) (► **Table 1**).

Most of the pregnant women were aged between 19 and 29 years old (58.74%; 121/223) and were of white, brown, or indigenous ethnicity (79.82%; 178/223). A significant difference in age was observed in pregnant women with low weight; a greater proportion of women were aged between 19 and 29 years old (25.19%; 33/45; $p = 0.021$; PR = 3.02;

95% CI:1.24–7.37), and had a family history of CAs (30.00%; 15/45; $p = 0.049$; PR = 1.73; 95% CI = 1.01–2.95). Normal weight was not associated with DM (PR = 3.09; 95% CI = 1.07–8.88; $p = 0.008$); however, obesity was positively associated with DM (PR = 3.09; 95% CI = 1.33–7.20; $p = 0.003$) (► **Table 1**). No significant differences in previous abortion history, children with previous CAs, previous pregnancies, alcohol, illicit drug, or tobacco consumption, teratogenic medication use during pregnancy, and evolution of gestation were found among groups.

Prevalence of Structural Congenital Anomalies

Of the analyzed fetuses with CAs, 51.12% (114/223) were males, and 48.88% were females (109/223). ► **Table 2** presents the prevalence of fetal structural CAs in pregnant women with low and normal weight and in those who were overweight and obese. Ten types of structural CAs were detected, with central nervous system (CNS) (30.94%; 69/223) and genitourinary system (23.77%; 53/223) anomalies being the most prevalent.

Multiple CAs accounted for 17.49% (39/223) of the anomalies, with a statistical difference among the four groups analyzed. The bivariate analysis showed an association between low weight for the gestational age and absence of multiple anomalies in pregnant women. Normal weight was associated with the presence of multiple anomalies and absence of lymphatic system anomalies. Obese pregnant women had the highest prevalence of lymphatic system anomalies (46.15%), and obesity was determined to be associated with lymphatic system anomalies.

Description of Subtypes of Congenital Defects

► **Table 3** presents the prevalence of subtypes of congenital defects in pregnant women with low and adequate weight and in those who were overweight and obese. Hydronephrosis/pyelectasis was the most prevalent anomaly in the study sample (11.66%; 26/223). Renal dysplasia was the most prevalent defect in pregnant women with low gestational weight (20%; 9/45), followed by acrania/anencephaly (11.11%; 5/45), hydrocephalus (11.11%; 5/45), hydronephrosis/pyelectasis (11.11%; 5/45), and gastroschisis (11.11%; 5/45). In pregnant women with adequate weight, hydronephrosis/pyelectasis had the highest prevalence rate (13.40%; 13/97). In overweight pregnant women, CNS anomalies were prevalent; however, hydronephrosis/pyelectasis had the highest prevalence rate (11.76%; 6/51). In obese pregnant women, cystic hygroma had the highest prevalence rate (20%; 6/30).

Discussion

Congenital anomalies represent epidemiological relevance because they result in mortality in ~ 276,000 newborns per year worldwide.^{10,11} Despite this, there are few studies that report the reality of the center-west region of Brazil.

In the present study, we have analyzed patients from a tertiary referral public hospital in the care of high-risk pregnant women in the center-west region of Brazil, and report a higher frequency of CNS anomalies (30.94%; 69/

Table 1 Characteristics of pregnant women and gestational evolution of the fetuses with CAs attending a high-risk prenatal outpatient clinic from 2014 to 2016 according to body mass index

Independent variable	Total		Low weight		Adequate weight		Overweight		Obesity		p-value*
	n (%)	n (%)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	
Pregnant women	223 (100)	45 (20.18)	97 (43.50)	-	51 (22.87)	-	30 (13.45)	-			
Age (years old)											0.960**
13-18	32 (14.35)	7 (21.88)	18 (56.25)	2.63 (0.90-7.63)	3 (9.38)	1.50 (0.88-2.58)	4 (12.50)	1.00 Ref.		1.00 Ref.	
19-29	131 (58.74)	33 (25.19)	49 (37.40)	3.02 (1.24-7.37)	32 (24.43)	1.00 Ref.	17 (12.98)	2.61 (0.85-7.99)		1.04 (0.37-2.88)	
30-45	60 (26.91)	5 (8.33)	30 (50.00)	1.00 ¹	16 (26.67)	1.34 (0.85-2.11)	9 (15.00)	2.84 (0.89-9.06)		1.2 (0.40-3.60)	
Ethnicity											0.497
White/brown/indigenous	178 (79.82)	38 (21.35)	80 (44.94)	1.37 (0.65-2.87)	39 (21.91)	1.19 (0.79-1.79)	21 (11.80)	1.00 Ref.		1.00 Ref.	
Black	45 (20.18)	7 (15.56)	17 (37.78)	1.00 Ref.	12 (26.67)	1.00 Ref.	9 (20.00)	1.22 (0.70-2.13)		1.70 (0.83-3.45)	
History of abortion											0.201
Yes	180 (80.72)	6 (13.95)	18 (41.86)	1.00 Ref.	13 (30.23)	1.00 Ref.	6 (13.95)	1.43 (0.84-2.45)		1.05 (0.46-2.41)	
No	43 (19.28)	39 (21.67)	79 (43.89)	1.55 (0.70-3.43)	38 (21.11)	1.05 (0.71-1.55)	24 (13.33)	1.00 Ref.		1.00 Ref.	
Children with previous CAs											0.709**
Yes	17 (7.62)	1 (5.88)	8 (47.06)	1.00 Ref.	5 (29.41)	1.09 (0.64-1.85)	3 (17.65)	1.32 (0.60-2.88)		1.35 (0.45-3.99)	
No	206 (92.38)	44 (21.36)	89 (43.20)	3.63 (0.53-24.86)	46 (22.33)	1.00 Ref.	27 (13.11)	1.00 Ref.		1.00 Ref.	
Family history of CA											0.732
Yes	50 (22.42)	15 (30.00)	22 (44.00)	1.73 (1.01-2.95)	7 (14.00)	1.01 (0.71-1.45)	6 (12.00)	1.00 Ref.		1.00 Ref.	
No	173 (77.58)	30 (17.34)	75 (43.35)	1.00 Ref.	44 (25.43)	1.00 Ref.	24 (13.87)	1.82 (0.87-3.79)		1.16 (0.50-2.68)	
Previous pregnancies											0.178
Yes	131 (58.74)	21 (16.03)	55 (41.98)	1.00 Ref.	34 (25.95)	1.00 Ref.	21 (16.03)	1.40 (0.84-2.36)		1.64 (0.79-3.42)	
No	92 (41.26)	24 (26.09)	42 (45.65)	1.63 (0.96-2.74)	17 (18.48)	0.92 (0.62-1.37)	9 (9.78)	1.00 Ref.		1.00 Ref.	
Diabetes mellitus											0.003
Yes	20 (8.97)	2 (10.00)	3 (15.00)	1.00 Ref.	8 (40.00)	1.00 Ref.	7 (35.00)	1.89 (0.89-4.02)		3.09 (1.33-7.20)	
No	203 (91.03)	43 (21.18)	94 (46.31)	2.12 (0.55-8.12)	43 (21.18)	3.09 (1.07-8.88)	23 (11.33)	1.00 Ref.		1.00 Ref.	

(Continued)

Table 1 (Continued)

Independent variable	Total		Low weight		Adequate weight		Overweight		Obesity		
	n (%)	n (%)	n (%)	PR (95% CI)	p-value*	n (%)	PR (95% CI)	p-value*	n (%)	PR (95% CI)	p-value*
Alcohol consumption											
Yes	21 (9.42)	4 (19.05)	10 (47.62)	1.11 (0.69–1.78)	1.000**	6 (28.57)	1.28 (0.62–2.65)	0.513	1 (4.76)	1.00 Ref.	0.323
No	202 (90.58)	21 (20.30)	87 (43.07)	1.07 (0.42–2.69)		45 (22.28)	1.00 Ref.		29 (14.36)	3.01 (0.43–21.12)	
Drug consumption											
Yes	8 (3.59)	3 (37.50)	3 (37.50)	1.92 (0.75–4.90)	0.204**	0 (0.00)	1.00 Ref.		2 (25.00)	1.92 (0.55–6.71)	
No	215 (96.41)	42 (19.53)	94 (43.72)	1.00 Ref.		51 (23.72)	1.17 (0.47–2.89)		28 (13.02)	1.00 Ref.	
Tobacco consumption											
Yes	16 (7.17)	5 (31.25)	8 (50.00)	1.62 (0.74–3.53)	0.328**	2 (12.50)	1.16 (0.69–1.95)		1 (6.25)	1.00 Ref.	
No	207 (92.83)	40 (19.32)	89 (43.00)	1.00 Ref.		49 (23.67)	1.00 Ref.		29 (14.01)	2.24 (0.32–15.47)	
Medication use											
Yes	6 (2.69)	2 (33.33)	3 (50.00)	1.68 (0.52–5.40)	0.349**	1 (16.67)	1.15 (0.51–2.61)		0 (0.00)	–	
No	217 (97.31)	43 (19.82)	94 (43.32)	1.00 Ref.		50 (23.04)	1.00 Ref.		30 (13.82)	–	
Evolution of gestation											
Birth	155 (69.51)	33 (21.29)	73 (47.10)	1.49 (0.70–3.16)	0.431**	32 (20.65)	1.49 (0.75–2.96)		17 (10.97)	1.00 Ref.	
Intrauterine loss	49 (21.97)	7 (14.29)	18 (36.73)	1.00 Ref.		14 (28.57)	1.38 (0.81–2.38)		10 (20.41)	1.86 (0.91–3.80)	
Judicial interruption of pregnancy	19 (8.52)	5 (26.32)	6 (31.58)	1.84 (0.66–5.11)		5 (26.32)	1.27 (0.56–2.88)		3 (15.79)	1.44 (0.46–4.47)	

Abbreviations: CA, congenital anomaly; CI, confidence interval; PR, prevalence ratio.

*Reference, lower prevalence; †chi-squared test

(χ²); **Fisher exact test. Classification of body mass index according to Atalah et al.¹⁹

Table 2 Prevalence and association (χ^2) of structural congenital anomalies in pregnant women attending a high-risk prenatal outpatient clinic from 2014 to 2016 according to body mass index

Congenital anomalies	Total		Low weight		Adequate weight		Overweight		Obesity		P*
	n	(%)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	n (%)	PR (95% CI)	
Central nervous system											0.788
Yes	69	30.94	17 (24.64)	1.36 (0.80-2.31)	26 (37.68)	1.00 Ref.	15 (21.74)	1.00 Ref.	11 (15.94)	1.29 (0.65-2.57)	0.466
No	154	69.06	28 (18.18)	1.00 ¹	71 (46.10)	1.22 (0.86-1.73)	36 (23.38)	1.08 (0.63-1.83)	19 (12.34)	1.00 Ref.	
Genitourinary system											0.602
Yes	53	23.77	15 (28.30)	1.60 (0.94-2.75)	22 (44.12)	0.94 (0.65-1.35)	10 (18.87)	1.00 Ref.	6 (11.32)	1.00 Ref.	
No	170	76.23	30 (17.65)	1.00 Ref.	75 (41.51)	1.00 Ref.	41 (24.12)	1.28 (0.69-2.38)	24 (14.12)	1.25 (0.53-2.89)	
Multiple anomalies											0.310**
Yes	39	17.49	1 (2.56)	1.00 Ref.	26 (66.67)	1.73 (1.30-2.30)	9 (23.08)	1.01 (0.54-1.90)	3 (7.69)	1.00 Ref.	
No	184	82.51	44 (23.91)	9.33 (1.32-65.95)	71 (38.59)	1.00 Ref.	42 (22.83)	1.00 Ref.	27 (14.67)	1.91 (0.61-5.99)	
Abdominal wall											1.000**
Yes	19	8.52	6 (31.58)	1.65 (0.80-3.40)	9 (47.37)	1.10 (0.67-1.81)	4 (21.05)	1.00 Ref.	0 (0.00)	-	
No	204	91.48	39 (19.12)	1.00 Ref.	88 (43.14)	1.00 Ref.	47 (23.04)	1.09 (0.44-2.71)	30 (14.71)	-	
Cardiovascular system											1.000**
Yes	12	5.38	2 (16.67)	1.00 Ref.	4 (33.33)	1.00 Ref.	5 (41.67)	1.91 (0.93-3.92)	1 (8.33)	1.00 Ref.	
No	211	94.62	43 (20.38)	1.22 (0.33-4.47)	93 (44.08)	1.32 (0.58-2.99)	46 (21.80)	1.00 Ref.	29 (13.74)	1.65 (0.24-11.15)	
Lymphatic system											0.000
Yes	13	5.83	1 (7.69)	1.00 Ref.	2 (15.38)	1.00 Ref.	4 (30.77)	1.62 (0.77-3.43)	6 (46.15)	4.04 (2.01-8.12)	
No	210	94.17	44 (20.95)	2.72 (0.41-18.31)	95 (45.24)	2.94 (0.81-10.64)	47 (22.38)	1.00 Ref.	24 (11.43)	1.00 Ref.	
Skeletal system											0.186**
Yes	6	2.69	1 (16.67)	1.00 Ref.	1 (16.67)	1.00 Ref.	2 (33.33)	1.47 (0.46-4.71)	2 (33.33)	2.58 (0.79-8.46)	
No	217	97.31	44 (20.28)	1.22 (0.20-7.45)	96 (44.24)	2.65 (0.44-16.05)	49 (22.58)	1.00 Ref.	28 (12.90)	1.00 Ref.	
Face											1.000**
Yes	9	4.04	1 (11.11)	1.00 Ref.	6 (66.67)	1.57 (0.96-2.56)	1 (11.11)	1.00 Ref.	1 (11.11)	1.00 Ref.	
No	214	95.96	44 (20.56)	1.85 (0.28-12.01)	91 (42.52)	1.00 Ref.	50 (23.36)	2.10 (0.32-13.62)	29 (13.55)	1.22 (0.19-8.02)	

(Continued)

Table 2 (Continued)

Congenital anomalies	Total		Low weight		P [*]	Adequate weight		P [*]	Overweight		P [*]	Obesity		P [*]
	n	(%)	n (%)	PR (95% CI)		n (%)	PR (95% CI)		n (%)	PR (95% CI)		n (%)	PR (95% CI)	
Respiratory system														
Yes	2	0.90	1 (50.00)	2.51 (0.61–10.33)	0.364 ^{**}	1 (50.00)	1.15 (0.28–4.65)	1.000 ^{**}	0 (0.00)	–	–	0 (0.00)	–	–
No	221	99.10	44 (19.91)	1.00 Ref.		96 (43.44)	1.00 Ref.		51 (23.08)	–		30 (13.57)	–	
Digestive system														
Yes	1	0.45	0 (0.00)	–	–	0 (0.00)	–	–	1 (100.00)	1	0.229 ^{**}	0 (0.00)	–	–
No	222	99.55	45 (20.27)	–		97 (43.69)	–		50 (22.52)	0.23 (0.18–0.29)		30 (13.51)	–	

Abbreviations: CI, confidence interval; PR, prevalence ratio.

^{*}Reference, lower prevalence; ^{*}Chi-squared test^{**}Fisher exact test.

223), followed by genitourinary system (23.77%; 53/223), and multiple CAs (17.49%; 39/223). Indian studies showed similar results.^{21–23}

The etiology of CNS malformations is multifactorial, involving complex interactions between genetic and environmental factors, constituting one of the most common congenital defects.^{22,24,25} Sunitha et al²² analyzed 360 pregnant women with fetuses presenting structural abnormalities, and also observed a higher frequency of CNS anomalies (37%), followed by genitourinary system abnormalities (20%) and multiple CAs (11%). In addition, other studies have shown the higher prevalence of genitourinary system malformations and of genitourinary system malformations.^{21,23}

It is known that 50% of the CAs may have an unknown etiology that can be attributed to genetic and environmental factors, including maternal nutritional aspects.^{10,11} This etiological factor has become relevant due the drastic change in the demographics of pregnant women in the last decade, with a higher number of overweight or obese women at conception being observed.²⁶ In the present study, this phenomenon still cannot be observed, since the frequency of obese pregnant women was lower than the frequency of pregnant women of adequate weight. The study population of the present study comes from a tertiary service; therefore, it is likely that, in the analysis of the general population of pregnant women, the frequency of pregnant women who are overweight and obese is higher than the one found here. However, there is a tendency of these data to be altered in future studies. The results of the present study indicated an association between pregnant women with adequate weight and the presence of multiple CAs, and among obese pregnant women with the presence of anomalies of the lymphatic system.

The presence of multiple CAs, in any category of BMI, may be explained by the higher consumption of alcohol, tobacco, and of teratogenic medications during pregnancy in the present study. Although no statistical difference was observed between the groups and the consumption of teratogenic substances, we have noticed that pregnant women with adequate weight consumed more teratogenics than the other groups. The higher consumption of teratogenic substances by this group may have contributed to a higher prevalence of anomalies. However, the comparability of these results with those of national and international studies is limited, mainly because most studies dealing with CAs and gestational BMI have focused more on obese pregnant women.^{17,27–29}

Lifestyle recommendations for couples planning to have children and guidelines for the cessation of smoking, of alcohol consumption, and of the use of illicit drugs, which are teratogenic substances, currently exist.^{18,30} However, it is necessary to reinforce the awareness of the population regarding the harm of teratogenics during pregnancy. Teratogenic substances can cause clinical manifestations such as abortion, CAs, intrauterine growth retardation, and mental deficiency.^{30–32}

Multiple CAs represent a serious category of structural defects and are associated with high rates of stillbirth, preterm birth, and low birthweight.³³ They are usually related to genetic syndromes and are a part of a complex group of anomalies with lethal cumulative effects in the

Table 3 Prevalence of subtypes of congenital anomalies in pregnant women attending a high-risk prenatal outpatient clinic from 2014 to 2016 according to body mass index

Congenital anomalies	Low weight	Adequate weight	Overweight	Obesity	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
Central nervous system					
Acrania/Anencephaly	5 (11.11)	6 (6.19)	5 (9.80)	3 (10.00)	19 (8.52)
Spina bifida/meningocele	3 (6.67)	5 (5.15)	2 (3.92)	0 (0.0)	10 (4.48)
Hydranencephaly	0 (0.0)	0 (0.0)	3 (5.88)	0 (0.0)	3 (1.35)
Hydrocephalus	5 (11.11)	9 (9.28)	4 (7.84)	5 (16.67)	23 (10.31)
Holoprosencephaly	2 (4.44)	3 (3.09)	0 (0.0)	1 (3.33)	6 (2.69)
Others	2 (4.44)	3 (3.09)	1 (1.96)	2 (6.67)	8 (3.59)
Genitourinary system					
Renal dysplasia	9 (20.00)	5 (5.15)	3 (5.88)	3 (10.00)	20 (8.97)
Hydronephrosis/pyelectasis	5 (11.11)	13 (13.40)	6 (11.76)	2 (6.67)	26 (11.66)
Megacystis	1 (2.22)	3 (3.09)	1 (1.96)	0 (0.0)	5 (2.24)
Obstructive uropathy	0 (0.0)	1 (1.03)	0 (0.0)	1 (3.33)	2 (0.90)
Multiple congenital anomalies					
Craniofacial + cardiac	1(2.22)	7(7.22)	3 (5.88)	1(3.33)	12 (5.38)
Craniofacial + digestive	0 (0.0)	2 (2.06)	2 (3.92)	1 (3.33)	5 (2.24)
Craniofacial + renal	0 (0.0)	3 (3.09)	2 (3.92)	0 (0.0)	5 (2.24)
Digestive + renal	0 (0.0)	3 (3.09)	0 (0.0)	1 (3.33)	4 (1.79)
Craniofacial + members	0 (0.0)	11 (11.34)	2 (15.4)	0 (0.0)	13 (5.83)
Abdominal wall					
Gastroschisis	5 (11.11)	6 (6.19)	4 (7.84)	0 (0.0)	15 (6.73)
Diaphragmatic hernia	0 (0.0)	2 (2.06)	0 (0.0)	0 (0.0)	2 (0.90)
Omphalocele	1 (2.22)	1 (1.03)	0 (0.0)	0 (0.0)	2 (0.90)
Cardiovascular system					
Bradyarrhythmia	0 (0.0)	2 (2.06)	2 (3.92)	0 (0.0)	4 (1.79)
Cardiomegaly	1 (2.22)	2 (2.06)	2 (3.92)	0 (0.0)	5 (2.24)
Others	1 (2.22)	0 (0.0)	1 (1.96)	1 (3.33)	3 (1.35)
Lymphatic system					
Cystic hygroma	1 (7.7)	2 (2.06)	4 (7.84)	6 (20.00)	13 (5.83)
Skeletal system					
Thanatophoric dwarfism	0 (0.0)	1 (1.03)	1 (1.96)	0 (0.0)	2 (0.90)
Osteogenesis imperfecta	0 (0.0)	0 (0.0)	1 (1.96)	0 (0.0)	1 (0.45)
Achondroplasia	1 (2.22)	0 (0.0)	0 (0.0)	2 (6.67)	1 (0.45)
Face					
Cleft palate	1 (2.22)	2 (2.06)	0 (0.0)	1 (3.33)	4 (1.79)
Cleft lip	0 (0.0)	4 (4.12)	1 (1.96)	0 (0.0)	5 (2.24)
Respiratory system					
Pulmonary cystic adenomatoid malformation	1 (2.22)	1 (1.03)	0 (0.0)	0 (0.0)	2 (0.90)
Digestive system					
Atresia of the second portion of the duodenum	0 (0.0)	0 (0.0)	1 (1.96)	0 (0.0)	1 (0.45)
Total	45 (100.00)	97 (100.00)	51 (100.00)	30 (100.00)	223 (100.00)

intrauterine period.³⁴ Moreover, pregnant women with normal weight had a higher prevalence of intrauterine loss and of a family history of CAs, which may be related to a genetic predisposition.^{35,36} Although no genetic study was performed, this factor may have contributed to a higher prevalence of multiple CAs and of intrauterine losses.

In the present study, the frequency of obese pregnant women was lower than the frequency of pregnant women of adequate weight. Similar studies indicated that the detection rate for anomalies was lower in obese pregnant women.^{13,37,38} Excessive abdominal adipose tissue is associated with significant limitations in the assessment of fetal anatomy using ultrasonography in the 1st and 2nd trimesters of pregnancy.^{13,14,37,39} This, perhaps, is the factor that has contributed to a reduced sample of obese pregnant women in the present study. Therefore, obese pregnant women should be advised about the risks of inadequate visualization during fetal ultrasonography, requiring more follow-up during the pregnancy.³⁹

The literature indicates that maternal obesity is associated with neural tube defects, including hydrocephalus, cardiac defects, renal cysts, orofacial clefts, anorectal atresia, limb reduction anomalies, omphalocele, and diaphragmatic hernia.^{16,17,28,40} However, obese pregnant women had a significantly high prevalence of lymphatic system anomalies, due to cystic hygroma, and it is important to note that no reports on this association exist in the literature. Lymphatic system anomalies may be associated with chromosomal disorders, and the morbidity of these lesions is dependent on their location.⁴¹ If cystic hygroma does not regress until the 18th week of gestation, the fetus could possibly have chromosomal or nonchromosomal anomalies, with a probability of > 90%.⁴²

Studies have shown that folic acid deficiency can cause changes in DNA synthesis and chromosomal alterations, and that excessive maternal adipose tissue interferes with the folate metabolism.^{43,44} The risk of neural tube defects in the offspring has also been reported.⁴³ However, it was not possible to infer that fetuses of obese pregnant women developed lymphatic system anomalies owing to the interference of adipose tissue with folic acid metabolism.

Overweight and obese pregnant women had a higher prevalence of DM, and an association between obesity and DM was observed. It is hypothesized that hyperglycemia impairs the development of the vitelline sac and of the placenta through increased production and release of oxygen free radicals and inositol and arachidonic acid deficiency, which induce a reduction in placental communication between the pregnant woman and her fetus.^{45,46} Uncontrolled hyperglycemia in the first weeks of gestation causes severe complications such as the risk of miscarriage and CAs, including atrial septal defect, anencephaly, sacral and adrenal agenesis. In the 2nd trimester, maternal hyperglycemia causes exacerbated fetal growth and increased risk of fetal death during the last 4 to 6 weeks of gestation.⁴⁷ In this case, inadequate metabolic monitoring during organogenesis is considered the main factor associated with the development of CAs.⁴⁵ The literature and our findings reinforce the importance of clarifying the

severity of DM and its role in the alteration of obstetric parameters and in the development of CAs in fetuses of overweight and of obese pregnant women during prenatal visits.^{48,49}

The present study has some limitations. First, performing fetal genetic tests was impossible, as they were not available for the patients in our study population who visited a public outpatient clinic. The genetic evaluation would have better clarified the anomalies detected. Second, the estimation of the sample size was not performed for abnormalities in the different systems, which may compromise the association of gestational BMI classifications, according to the system or subtypes of CAs. Third, the newborns in the present study were not evaluated for early or late neonatal mortality, and vitamin deficiencies were not evaluated in the pregnant women and in the newborns.

However, as a positive point, the present study presents the reality of a tertiary center in the center-west region of Brazil, the stratification of the prevalence of CAs in pregnant women with different BMIs considering the four groups, since some studies unify the groups of overweight and obese pregnant women, as well as the sample number, and the follow-up of the patients until the birth of the fetus.

Conclusion

In conclusion, the present study demonstrated that there are differences between the profiles of CAs in the groups of pregnant women according to the maternal BMI. Obese pregnant women had more abnormalities of the lymphatic system. In addition, it has also been verified that multiple CAs, generally caused by genetic defects, are independent of lower or higher maternal weight. In this case, it is observed that genetic counseling should be made available to all couples in order to prevent certain malformations. These findings reinforce the need for the identification and screening of risk factors for CAs, regardless of BMI, as well as the importance of discussing with pregnant women maternal nutrition and its effect on fetal development and on neonatal outcome. The implementation of public policies is needed to have more planned pregnancies, and genetic testing in the public health system can contribute to the optimization of the diagnosis of CAs and may elucidate the association between CAs and maternal BMI.

Contributors

All of the authors contributed with the project and data interpretation, the writing of the article, the critical review of the intellectual content, and with the final approval of the version to be published.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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