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Pregnancy and Delivery in Women with Uterine Malformations

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;

D – writing the article; E – critical revision of the article; F – final approval of article

Abstract

Background. Uterine defects are the most common malformations of the female reproductive system. They can lead to many obstetric complications, e.g. preterm delivery, intrauterine growth restriction, oligohydramnios and operational delivery.

Objectives. Our aim was to analyze the impact of different types of uterine defects on pregnancy outcomes.

Material and Methods. The study involved 94 pregnant women with different types of uterine defects hospitalized at the Department of Fetal – Maternal Medicine and Gynecology, RIPMMH in Łódź, between 1994 and 2012. The patients were divided into 5 groups on the basis of diagnosed defects: arcuate (n = 6), bicornuate (n = 50), duplex (n = 29), septate (n = 5) and unicornuate uterus (n = 4). In order to avoid correlated data in statistical analysis, our research did not consider the total number of pregnancies and births but the number of patients. The first pregnancy of each patient, if completed after 22-week gestation, was studied and analyzed.

Results. Preterm delivery was the most common complication in pregnancy (55 women, 58.5%). The caesarean section was performed in 73 (78%) women. IUGR was diagnosed in 16% of cases. Placental abruption occurred in 13 (14%) and cervical insufficiency in 10 cases (11%), respectively. Prenatal diagnostic showed abnormalities in 12 fetuses (13%). The Apgar score from 0 to 4 points was assigned to 9 newborns (9.6%), 5–7 to 20 children (21.3%) and 8–10 points to 75 cases (69.1%). Normal birth weight (> 2500 g) was determined in 51 newborns (54.3%).

Conclusions. Women with uterine defects are subject to an increased risk of complications in pregnancy and delivery, including premature births, low birth weights, births by cesarean section (Adv Clin Exp Med 2015, 24, 5, 873–879).

Key words: pregnancy, caesarean section, preterm delivery, uterine malformations.

Malformations of the uterus are the most common defects of the female reproductive system. In the general population of women, they occur with an incidence rate of approximately 4% [1]. Based on the results of the presented study, it was found that different types of uterus defects occurred with the following incidence rates: bicornuate uterus – 37%, uterus with partial septum – 13%, arcuate uterus – 15%, uterus duplex – 11%, uterus with complete septum – 11%, uterus unicornuate – 4.4% [2].

During embryonic development of female fetuses, the growth of two mesonephric Mullerian ducts is observed, while the Wolff ducts disappear. Each mesonephric duct consists of three sections: the upper – rostral, center – horizontal and bottom – caudal. Oviducts are formed from the first two parts and the caudal parts combine with each other to form the uterus [3, 4]. Any abnormalities in the development and connection of the Mullerian tubes lead to defects of the uterus. Compromised or no development of the two Mullerian ducts leads to agenesis of the uterus. In cases where a single duct is developed only, the unicornuate uterus is further developed; if there is no connection between the

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two structures, defects may result, such as duplex uterus or bicornuate uterus. After the connection of the Mullerian ducts, a division is formed, which – under normal circumstances – disappears. Disorders at this stage lead to the survival of a formed uterus with a septum [2, 4, 5]. Buttram et al. presented the first classification of defects of the female reproductive system. Now the classification, created by the American Society for Reproductive Medicine (ASRM), is effective and broadly applied [6].

Defects of the uterus are a broad subject but, in the recent medical literature, only a few studies have been reported on this particular issue. Uterus defects are an important medical problem from the point of view of both gynecology, which focuses on the diagnosis and treatment of these defects, as well as obstetrics, which deals with pregnant patients who suffer from this defect. Currently, no uniform standards can be found in the literature, regarding the treatment of pregnant women with congenital uterine malformations.

The Aim of the Study

The aim of this study was to analyze the impact of different types of defects of the uterus on pregnancy outcomes in patients, hospitalized at the Department of Fetal-Maternal Medicine and Gynecology, RIPMMH, between 1994 and 2012.

Material and Methods

The study involved 94 pregnant women with different types of defects of the uterus.

The patients were subjected to a complete diagnostics of infertility, recurrent miscarriages, signs of threatening miscarriage or premature birth. During hospitalization, the following, possible causes of infertility were excluded: hormone disorders, autoimmune diseases or general

disorders of mother. Clinical examinations confirmed uterus defects. Diagnostics was started by ultrasound. In case of any doubt, hysterosalpingography (27 patients) or hysteroscopy (15 women) was performed. In 19 patients, laparoscopy was carried out, which eventually confirmed suspected uterus defects. In 12 patients, the diagnosis of uterus defects was obtained during a cesarean section. None of the patients were subjected to magnetic resonance imaging tests. The data did not indicate that the patients had ever been examined by 3D ultrasound or sonohisterography.

The patients were divided into 5 groups on the basis of diagnosed defects (Table 1). Premature birth was defined as delivery before 37 complete weeks of gestation [7].

Threatening preterm delivery was defined as delivery before the end of the 37th week of pregnancy, with concomitant uterine contractions and changes of the cervix. Amniotic fluid index was determined by according to the protocol by Phelan et al. (the four-quadrant technique) [8].

Intrauterine growth restriction (IUGR) was diagnosed on the basis of the fetal size and weight, which was determined in ultrasound imaging and compared with the gestational age from the date of the last menstrual period and according to the first ultrasound examination. The diagnosis of IUGR was based on the estimated weight of

Table 1. The prevalence of various types of uterus defects

Kind of defect	Number of patients	%
Arcuate uterus	6	6.4
Bicornuate uterus	50	53.2
Uterus duplex	29	30.9
Septate uterus	5	5.3
Unicornuate uterus	4	4.3

Table 2. Results in 94 obstetric patients with different types of uterus defects

Type of the defect							
	Arcuate uterus (n = 6)	Bicornuate uterus (n = 50)	Uterus duplex (n = 29)	Septate uterus (n = 5)	Unicornuate uterus (n = 4)	Total	
Number of all pregnancies	14 (7.2%)	105 (54.1%)	51 (26.3%)	17 (8.8%)	7 (3.6%)	194	
Miscarriages	4 (6.8%)	35 (59.3%)	11 (18.6%)	7 (11.9%)	2 (3.4%)	59	
Premature birth	7 (8.2%)	42 (49.4%)	25 (29.4%)	7 (8.2%)	4 (4.8%)	85	
Deliveries on time	3 (6%)	28 (56%)	15 (30%)	3 (6%)	1 (2%)	50	

measurements in ultrasound imaging: abdominal circumference (AC), head circumference (HC), biparietal diameter (BPD), femur length (FL) and the average transverse dimension of the abdomen. The estimated fetal weight below the 10th percentile for gestational age indicated IUGR [9]. The birth status of newborns was evaluated during the first minute after birth according to the Apgar score.

Excellent birth states were associated with 10–8 score points, 7–5 points – average condition, while 4–0 point score was regarded as a poor condition. Due to the lack of data parameters, such as: APGAR score on the 5th min after birth, assessed acid – base balance, no complications in the neonatal period could be taken into consideration.

For the purposes of this study, the data was obtained from medical records of patients and compared with the data from the literature.

All the analyses were performed using STATIS-TICA 9 program (StatSoft). Pearson's chi-square test and the Fisher exact test were used for statistical analysis of the floor tables. A probability value of < 0.05 was considered to be statistically significant. Descriptive data was presented as frequencies. In examining the relationship between uterine defects and infant birth weight, the data was grouped (two groups – less than 2500 g and greater than 2500 g) for further statistical processing. Only in the case of the incidence of abortion among patients with malformations of the uterus (Table 3) obtained differences were statistically significant (p < 0.05). However, the results of statistical tests

have limited credibility due to the low cardinality of patients with rare uterine defects.

Results

Among the 94 patients, included in the study, 194 pregnancies were reported, which ended with a miscarriage in 59 cases, which accounted for 30.4% of all pregnancy outcomes. Most miscarriages occurred after up to 12 weeks of gestation, while abortions took place in 4 cases only, after 12 weeks of pregnancy. See Table 3 for the incidence of abortions among the patients, examined for various types of uterus defects ($\chi^2 = 18.6$, p < 0.05). Out of the 94 patients, 35 patients (37.24%) experienced one or more miscarriages.

In order to avoid correlated data in statistical analysis, our research did not consider the total number of pregnancies and births but the number of patients. The first pregnancy of each patient, if completed after 22-week gestation, was studied and analyzed.

In 16 cases (17%), deliveries occurred before 33 weeks of gestation, most commonly in the patients with uterine duplex or unicornuate. Birth between 33 and 37 weeks of gestation occurred in 39 pregnant women (41.5%). In 39 women (41.5%), births took place after 37 weeks of pregnancy.

Out of the whole study group, 16 women (17%) presented with uneventful pregnancy. The most common complication during pregnancy

Tuble 5. The prevalence	or imocarriages a	mong women wi	th dicinic delects						
Table 3. The prevalence of miscarriages among women with uterine defects									

n = number of patients	Arcuate uterus (n = 6)	Bicornuate uterus (n = 50)	Uterus duplex (n = 29)	Septate uterus (n = 5)	Unicornuate uterus (n = 4)	Total	
Number of miscarriages							
0	4 (66.67%)	29 (58.00%)	22 (75.86%)	2 (40.00%)	2 (50.00%)	59 (62.76%)	
1	0 (0.00%)	13 (26.00%)	3 (10.34%)	0 (0.00%)	2 (50.00%)	18 (19.15%)	
2 or more	2 (33.33%)	8 (12.00%)	4 (13.79%)	3 (60.00%)	0 (0.00%)	17 (18.09%)	

Table 4. The prevalence of preterm delivery

	Arcuate uterus n = 6	Bicornuate uterus n = 50	Uterus duplex n = 29	Septate uterus n = 5	Unicornuate uterus n = 4	Total	
	Threatening preterm delivery						
No	1 (16.66%)	12 (24%)	10 (34.48%)	2 (40%)	1 (25%)	26 (28.42%)	
Yes	5 (83.33%)	38 (76)	19 (65.52%)	3 (60%)	3 (75%)	68 (71.58%)	

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and childbirth was a threat of a premature labor (Table 4) – χ^2 = 4.2, p = 0.51. Premature abruption of placenta occurred in 13 patients (13.8%) and premature rupture of membranes complicated 10 pregnancies (10.6%). Cervical incompetence was diagnosed in 10 pregnant women (10.6%). In 17 cases (18%), oligohydramnios was diagnosed (Table 5). The value of χ^2 test was 3.8, p = 0.64. Intrauterine fetal growth restriction occurred in 15.96% cases – most often in the patients with unicornuate uterus – 50% and in those with a double uterus – 17.24% cases. This complication was not observed among women with uterus with septum.

Caesarean section was carried out in 77.66% of cases. Table 6 shows the completion of pregnancies in patients with respect to the types of uterus defects. After the rejection of the missing data χ 2 = 5.1, p = 0.41. The most common indication for caesarean section was a breech and transverse presentation of the fetus, observed in 49 cases (52.13%). Fetal malposition was found most commonly in the group of patients with uterus with septum. Transverse and pelvic positions were observed least frequently in women with unicornuate uterus. Threatening intrauterine fetal hypoxia was an indication for immediate birth in 10% of cases. This complication was most commonly diagnosed in patients with bicornuate and duplex uterus. Premature separation of placenta was an indication for urgent caesarean section in 8.8% of cases. Among other indications for pregnancy, termination by caesarean section was undertaken for the lack of labor progress in 3 patients (2%) and

pre-eclampsia in 1 woman (0.67%). Cesarean section for fetus-associated reasons was performed in 9 cases (6%).

Perinatal death occurred in 12 newborns. In most cases, these were due to prematurity and all its consequences. In one case, the cause of death was a severe, complex heart defect, a child born at 37-week gestation with birth weight 2670 g. In two newborns, death was due to severe intrauterine infection and concomitant oligohydramnios (births induced at 24 and 33 weeks of gestation). A baby, born after 32 weeks of gestation with birth weight 2480 g, died after 7 days of life from sepsis. Hydrocephalus and hypotrophy were the causes of death of a newborn, delivered after 33 weeks of gestation with a birth weight of 1250 g. Diaphragmatic hernia and pulmonary hypoplasia caused the death of a child born on the 32nd week of pregnancy. One infant died one day after birth - with a birth weight of 2150 g, birth after 37 weeks of gestation, generalized edema of the fetus and a number of dysmorphic defects. In that case, Edwards's syndrome was diagnosed. In other cases, the causes of death were complex - births before 32 weeks of gestation and congenital defects.

Table 7 shows neonatal outcomes according to Apgar score and neonatal weights.

More than 3% of newborns were born with very low body weight, below 500 g. Nearly 55% of newborns had normal birth weight above 2500 g ($\chi^2 = 1.7$, p = 0.89). The average Apgar score was 7 points. More than 9% of newborns were delivered in poor condition, ranging at 0 to 4 Apgar score ($\chi^2 = 5.4$, p = 0.86).

Table 5. Oligohydramnios in	patients with	uterus malformations
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	Arcuate uterus n = 6	Bicornuate uterus n = 50	Uterus duplex n = 29	Septate uterus n = 5	Unicornuate uterus n = 4	Total		
	Oligohydramnios							
Yes	1 (16.66%)	9 (18%)	4 (13.79%)	1 (20%)	2 (50%)	17 (18.08%)		
No	5 (83.33%)	41 (82%)	25 (86.21)	4 (80%)	2 (50%)	77 (81.92%)		

Table 6. The prevalence of caesarean sections, depending on the type of uterus malformations

	Arcuate uterus n = 6	Bicornuate uterus n = 50	Uterus duplex n = 29	Septate uterus n = 5	Unicornuate uterus n = 4	Total	
Caesarean section							
Yes	6 (100%)	40 (80%)	20 (68.96%)	3 (60%)	4 (100%)	73 (77.66%)	
No	0	8 (16%)	7 (24.14%)	2 (40%)	0	17 (18.09%)	
No data	0	2 (4%)	2 (6.9%)	0	0	4 (4.25%)	

	Arcuate uterus n = 6	Bicornuate uterus n = 50	Uterus duplex n = 29	Septate uterus n = 5	Unicornuate uterus n = 4	Total
		A	pgar score			
0-4	1 (16.67%)	4 (85)	3 (10.34%)	1 (20%)	0 (0%)	9 (9.57%)
5–7	1 (16.67%)	14 (28%)	4 (13.79%)	0 (0%)	1 (25%)	20 (21.28%)
8–10	4 (66.66%)	32 (64%)	22 (75.87%)	4 (80%)	3 (75%)	65 (69.15%)
		Bi	rth weight			
< 501	0 (0%)	2 (4%)	1 (3.45%)	0 (0%)	0 (0%)	3 (3.19%)
501–1000	1 (16.67%)	2 (4%)	1 (3.45%)	1 (20%)	0 (0%)	5 (5.32%)
1001-2500	1 (16.67%)	20 (40%)	11 (37.94%)	1 (20%)	2 (50%)	35 (37.23%)
> 2500	4 (66.66%)	26 (54%)	16 (55.16%)	3 (60%)	2 (50%)	51 (54.26%)

Table 7. Neonatal outcomes by Apgar score and neonatal weight

Congenital abnormalities were prenatally diagnosed in 12 newborns, with multiple defects in 3 cases. Frequently, as found in five cases, heart defects and abnormalities of the urinary tract were observed, including agenesis and hypoplasia of the kidneys, bladder agenesis, hydronephrosis and obstructive uropathy. Hydrocephalus as umbilical hernia was diagnosed in two cases. In one fetus, a defect in the right lung-cystic degeneration was diagnosed.

The study did not reveal any statistically significant relationship between the type of uterine defect, and obstetric outcome.

Discussion

Malformations of the uterus constitute a risk factor for infertility, miscarriage and complications of pregnancy and childbirth. Among the examined patients, conception occurred in 194 cases, out of which 30% of the pregnancies were finalized in miscarriage. Literature data shows that, in the general population, losses occur with a frequency of approximately 15% [10]. In the group of patients with recurrent miscarriages, malformations of the uterus are diagnosed more often than in the general population (25% vs. 7-8%) [11, 13]. Zlopasa et al. showed in their study a significantly higher miscarriage rate in patients with defects of the uterus than in the control group of healthy women (33.7% vs. 19.5%). The highest percentage of abortions occurred in the group of patients with uterine septum [13].

Women with uterine defects are burdened with an increased risk of complications in pregnancy and childbirth, such as premature birth, breech or transverse position of the fetus, intrauterine fetal growth restriction and operating births [1]. Such complications were also observed in our study.

Premature births occurred in 30% of cases, whereas, in the general population, this complication rate ranges at about 6–15% [14]. In this study, the most common causes of premature pregnancy termination included, following Goldenberg et al., spontaneous preterm labor, premature rupture of the membranes and the risk of intrauterine fetal hypoxia [15]. We found the highest number of preterm births among women with uterus with a septum. As Raga et al. reported in their study, the majority rate of preterm birth was recorded among women with uterine septum, while in 80% of cases, those deliveries occurred after 28 weeks of gestation [1]. Heinohen presented in his work that preterm births occurred in 25% of cases of women with a unicornuate uterus [16], while in our study, women with a unicornuate uterus were not burdened with an increased risk of preterm delivery.

Among the patients included in our study, births by caesarean section were carried out in more than 75% of cases. During the last 40 years, the caesarean section rate increased significantly from 5% in the 70s, to over 50% in the 90s. The highest rates of caesarean section were observed in Italy (39%), Portugal (25%) and Switzerland (32%) [17, 18]. In 1995, the rate of cesarean deliveries in the United States was 21%, while in 2007 it increased up to 31.8% [19, 20].

In the report of the Center for Disease Control and Prevention, the most common indications for caesarean section included: previous caesarean section (35%), dystocia and maternal disproportion (30%), breech position of the fetus (12%), abnormal cardiotocography (CTG) (9%) [21]. In our study, the main indication was a breech or transverse position of the fetus (47%).

Villar et al. showed in their study that the major indications for cesarean section included

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dystocia, maternal disproportion and lack of progress of labor (20%), similar to the CDC report [21]. In the present study, no such complications were observed, possibly, due to the fact that in patients with congenital uterine malformations, a higher percentage of preterm births and newborns were characterized by lower birth weight. The abovecited authors reported an abnormal fetal position in only 12% of cases, while this complication was much more frequent (47%) among our patients [22]. Reduced space in the uterus and fetal repositioning impeded operations, so there were more transverse and breech positions.

In our analysis, the proportion of death in the perinatal period constituted 5% of newborns. The study by Raga et al. showed that the neonatal mortality rate was much higher, namely around 40% [1]. According to our data, only 54% of infants were born with normal weight > 2500 g. Low birth weight was the result of preterm birth and prematurity of those children. Zlopasa et al. observed significantly worse birth rates in infants of mothers with uterine defects vs. the children from women without such a condition (29% vs. 9%) [13].

Literature provides numerous data on urinary tract defects in women with congenital uterine malformations [1, 23]. Urinary tract defects may affect up to 20–30% of patients with defects of the uterus, which is probably related to the embryonic development of both systems. Urological counseling is advised in all women with congenital uterine defects [2].

Unfortunately, we could not find any reports, dealing with the incidence of urinary tract defects in children from mothers with defects of the uterus.

Malformations of the uterus are rare in the general population. The sample size of women in our study was relatively so small that the obtained results, concerning the comparative analysis of different types of defects in the uterus, were not statistically significant.

In our analysis, 12 newborns were affected by congenital defects, mainly the urinary tract and heart defects. Martinez et al. conducted an analysis of risk factors for birth defects in children born from mothers with uterine defects, mainly two--horned uterus. They demonstrated in their study that birth of a child with birth defect(s) is 4 times higher among mothers with uterine defects than in women without such defect. In the children, examined in our study, the most frequent defects included clubfoot and other defects of the limbs [24]. These defects are due to reduced uterine volumes, where a developing fetus does not have enough space for proper growth, while mechanical pressure impacts the growing fetal structures. In our study, children of mothers with two-horned uterus were diagnosed with birth defects, while no deformation defects were observed in those children.

We believe that due to the importance of the health problem concerning women with uterine malformations, it is worth evaluating their health-related quality of life (HRQL) during the pregnancy and after giving birth [25, 26].

The authors concluded that women with uterine defects are subject to an increased risk of complications in pregnancy and delivery. These complications include premature births, low birth weight babies, births by cesarean section.

Newborns of women with uterine defects show a worse birth status, based on their Apgar score and low birth body mass.

Pregnancy in a woman with uterine defects should be regarded as a high-risk condition. Intensive monitoring of such pregnancy and of delivery, as well as a package of preventive measures to avoid possible complications, is highly indicated.

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