Research Article

The study of the role of maternal and fetal risk factors in the development of placental insufficiency

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ABSTRACT

Objectives: The objectives were to study the role of maternal and fetal risk factors in the development of placental insufficiency (PI) and fetal growth retardation syndrome (FGRS). **Materials and Methods:** The case–control study sample included 497 females in the third trimester of pregnancy recruited during 2009–2013. All the patients were divided into two groups, with the development of fetal growth retardation (n = 250) and without it (n = 247), respectively. **Results:** The prevalence of spontaneous abortions is higher (18.40%) in the group of pregnant women with FGRS compared with the control group (10.12%, χ^2 = 6.29, P = 0.01), due to abortions in the first trimester (14.40% and 8.10%, respectively, χ^2 = 4.33, P = 0.04). The parents of women with FGRS (21.60%) had an anamnesis aggravated by venous thrombosis or stroke/heart attack, which is higher compared to 10.12% of cases among pregnant women without FGRS (10.12%, χ^2 = 11.40, P = 0.002). Spontaneous venous thrombosis occurred in 15.2% of all cases among parents of patients with FGRS compared to 8.10% among parents of patients without FGRS (χ^2 = 5.41, P = 0.02). 8.40% of mothers of patients with FGRS had a burdened obstetric history, which is higher than in control patients (3.24%, χ^2 = 5.12, P = 0.02). **Conclusions:** Thus, as a result of the study, risk factors for the development of PI in FGRS are established. These include a burdened thrombotic history in relatives, a burdened obstetric history in the patient's mother, and a history of spontaneous abortions.

KEY WORDS: Fetal growth retardation, Placental insufficiency, Pregnancy

INTRODUCTION

Placental insufficiency (PI) is a syndrome caused by morphofunctional changes in the placenta, in which progression occurs along with fetal growth retardation syndrome (FGRS), often combined with hypoxia.[1-3] PI is one of the most common complications of pregnancy.[4-6] Perinatal mortality in women having suffered PI is 10.3% among full-term newborns and 49% among pre-term infants.[4-6] FGRS due to PI is the second most common cause of perinatal mortality.[7-8]

According to the literature, risk factors for the development of PI and FGRS are divided into fetal and maternal.[9] The group of maternal factors includes somatic pathology, uterus pathology, family history of FGRS, and the presence of FGRS during a previous pregnancy, aggravated by obstetric-gynecological history.[9] Fetal-related causes include genetic diseases, congenital deformities, multiple pregnancies, and congenital infections.[10,11]

Access this article online

Website: jprsolutions.info | ISSN: 0975-7619

MATERIALS AND METHODS

In total, 497 unrelated pregnant women in the third trimester of pregnancy were recruited for the study during the period 2009–2013. All participants signed an informed consent before entering the study. The clinical and laboratory examination of the participants was conducted in the perinatal center of the Saint Joasaph Belgorod Regional Clinical Hospital. The following inclusion criteria were used to check the eligibility of the participants: singleton pregnancy and Russian ethnicity. Patients having congenital malformations of internal genitals, uterine fibroids, anomalies and placental location, isosensitization of Rh factor or ABO, genetic diseases, and congenital malformations were excluded from the study.

A total of 250 participants were diagnosed with the syndrome of intrauterine growth retardation of varying severity. The diagnosis of the syndrome was based on clinical data, ultrasound fetometry (TOSHIBA Xario

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Received on: 24-08-2018; Revised on: 15-09-2018; Accepted on: 20-01-2019

SSA-660A) and parameters of growth and weight after the birth.

The assessment of the role of maternal and fetal risk factors in the formation of PI and FGRS was carried out using Chi-square test with the Yates correction for continuity. The calculations were performed in 2 × 2 contingency tables.

The statistical data were processed using Statistica 6.0 software package.[12]

RESULTS

Data on concomitant extragenital pathology, obstetric-gynecological pathology, and familial thrombotic and obstetric-gynecological anamnesis are presented in Tables 1-3.

In both the groups, a high prevalence of somatic pathology was observed: Among pregnant women with FGRS, extragenital pathology was found in 60.00% of cases (n = 150) and in the control group - 51.42% (n = 127) (χ^2 = 3.37, P = 0.07). As can be seen from the table, pregnant women with FGRS and the control group do not differ in the prevalence of individual somatic diseases.

It was established that the prevalence of spontaneous abortions is 1.84 times higher in the group of pregnant women with FGRS (18.40%) compared with the control

Table 1: Characteristics of the extragenital pathology among pregnant women with FGR and without FGR

Extragenital pathology	FGR patients, *n*=250 *n* (%)	Controls, *n*=247 *n* (%)	χ^2, *P*
Hypertonic type and cardiac type of neurocirculatory dystonia	50 (20.00)	29 (11.74)	2.28, 0.13
Hypotonic type of neurocirculatory dystonia	34 (13.60)	28 (11.34)	0.39, 0.53
Chronic pyelonephritis, gestational pyelonephritis, chronic glomerulonephritis	63 (25.20)	55 (22.27)	0.44, 0.51
Obesity	23 (9.20)	22 (8.91)	0.01, 1.00
Congenital heart defects	10 (4.00)	12 (4.86)	0.06, 0.81
Varicose veins	13 (5.20)	10 (4.05)	0.16, 0.69
Venous thromboembolism at pregnancy	4 (1.60)	1 (0.41)	0.78, 0.38
Chronic gastroduodenitis	26 (10.40)	22 (8.89)	0.17, 0.68
Thyroid hyperplasia	13 (5.20)	10 (4.01)	0.16, 0.69
Cerebrovascular disease in history	2 (0.80)	0 (0)	0.45, 0.50

FGR: Fetal growth retardation

Table 2: Characteristics of obstetric-gynecological pathology among pregnant women with FGR and without FGR

Obstetric and gynecological pathology	FGR patients, *n*=250 *n* (%)	Controls, *n*=247 *n* (%)	χ^2, *P*
Medical abortion in history	80 (32.00)	65 (26.32)	1.68, 0.20
Infertility in history	5 (2.00)	8 (3.24)	0.34, 0.56
Miscarriage in history (total)	46 (18.40)	25 (10.12)	6.29, 0.01
Miscarriage in first trimester	36 (14.40	20 (8.10)	4.33, 0.04
Miscarriage in second trimester	10 (4.00)	5 (2.02)	1.05, 0.31
Ectopic pregnancy	10 (4.00)	15 (6.07	0.73, 0.39
Pregnancy loss in first trimester	12 (4.80)	12 (4.86)	0.01, 1.00
IVF pregnancy	2 (0.80)	2 (0.81)	0.01, 1.00
Disorders of the menstrual cycle in history	20 (8.00)	14 (5.67)	0.73, 0.39
Pelvic inflammatory disease in history	58 (23.20)	59 (23.89)	0.01, 0.94
Uterine scar	18 (7.20)	12 (4.86)	0.82, 0.36
Intrauterine infection during pregnancy	83 (33.20)	80 (32.39)	0.17, 0.68
Preeclampsia	55 (22.00)	68 (27.53)	1.75, 0.19
Antenatal intrauterine fetal death	4 (1.60)	0 (0)	2.23, 0.14

FGR: Fetal growth retardation, IVF: In-Vitro Fertilisation

Table 3: Characteristics of a thrombotic family history and a burdened obstetric-gynecologic history of mothers among pregnant women with FGR and without FGR

Family history	FGR patients, *n*=250 *n* (%)	Controls, *n*=247 *n* (%)	χ^2, *P*
I. A depressed thrombotic anamnesis in parents, including:	54 (21.60)	25 (10.12)	11.40, 0.002
1. Spontaneous venous thrombosis in parents, including varicose veins complicated by thrombosis (without phlebitis)	38 (15.20)	20 (8.10)	5.41, 0.02
2. Infants and infarcts in the parents who developed before the age of 50	13 (5.20)	5 (2.02)	2.74, 0.10
3. Combination of spontaneous venous thrombosis and stroke/infarction	3 (1.20)	0 (0)	1.32, 0.25
II. The presence of an obstructed obstetrical anamnesis in the mother (habitual miscarriage, stillbirth, premature birth, severe preeclampsia)	21 (8.40)	8 (3.24)	5.12, 0.02
III. Combination of thrombotic and burdensome obstetric anamnesis	4 (1.60)	0 (0)	2.23, 0.14

FGR: Fetal growth retardation

group (10.12%, $\chi^2 = 6.29$, $P = 0.01$), due to abortions in the first trimester (14.40% and 8.10%, respectively, $\chi^2 = 4.33$, $P = 0.04$) [Table 2]. In terms of the frequency of other obstetric and gynecological pathologies, the studied groups of pregnant women do not differ.

The studies of the thrombotic and aggravated obstetric history of parents of pregnant women with FGRS and without FGRS revealed significant differences [Table 3]. The parents of 54 patients with FGRS (21.60%) had a history of acute venous thrombosis or stroke/heart attack, which was significantly higher compared to 25 (10.12%) cases among pregnant women without FGRS ($\chi^2 = 11.40$, $P = 0.002$). Spontaneous venous thrombosis occurred in 15.2% of all cases among parents of patients with FGRS compared to 8.10% among parents of patients without FGRS ($\chi^2 = 5.41$, $P = 0.02$). 8.40% of mothers of patients with FGRS had a burdened obstetric history, which is higher than in control patients (3.24%, $\chi^2 = 5.12$, $P = 0.02$).

CONCLUSION

As a result of the study, it was established that pregnant women with FGRS have a higher incidence of spontaneous abortions in history. Furthermore, mothers of pregnant women with FGRS have a higher frequency of venous thrombosis or stroke/heart attack and more common obstetric history.

All these indicate that these maternal factors increase the risk of development of PI and FGRS.

Normal fetal growth depends on a genetically predetermined growth potential and is modulated by fetal, placental, maternal, and external factors. Fetuses with growth retardation syndrome are at high risk of neonatal and infant mortality.[13]

The results of our study are generally consistent with other data, which show that the risk group for FGRS is made up of pregnant women with burdened obstetric history (severe forms of preeclampsia, HELLP syndrome, eclampsia, premature placental abruption, habitual miscarriage, premature birth, antenatal fetal death, and unsuccessful IVF attempts); patients with recurrent thrombosis or an episode of thrombosis in a history or in this pregnancy, as well as a family history burdened by thrombosis.[14-16]

Arterial hypertension and preeclampsia associated with pregnancy cause disorders of the uterine artery perfusion, leading to uterine failure, a decrease in placental blood flow, placental dysfunction, affecting the oxygenation of the fetus, absorption of nutrients. PI can lead to poor circulation in the placenta and nutritional deficiencies, which affects the growth of the fetus and leads to fetal growth retardation.

Thus, as a result of the study, risk factors for the development of PI in FGRS are established. These include a burdened thrombotic history in relatives, a burdened obstetric history in the patient's mother, and a history of spontaneous abortions.

The obtained results broaden the existing ideas about the role of maternal factors in the development of FGRS and make it possible to practice them in obstetrics.

REFERENCES

1. Bamfo J, Odibo A. Diagnosis and management of fetal growth restriction. J Pregnancy 2011:640715.
2. Zollner U, Rehn M, Girschick G, Dietl J. Obstetric management of fetal growth retardation. Z Geburtshilfe Neonatol 2011; 215:49-59.
3. Unanian AL, Arakelov SE, Polonskaia LS, Guriev TD, Illicheva TS, Baburin DV, *et al*. Placental insufficiency: Features of etiopathogenesis, therapy and prevention. Consilium Med 2015;17:37-40.
4. Serov VN. Prevention of maternal mortality. Obstet Gynecol 2011;7:4-10.
5. Simanaov IV. Timing of the main clinical symptoms of pre-eclampsia at the present stage. Research result. Ser Med Pharm 2017;3:51-6.
6. Diner NM, Uzlova TV, Kirsanov MS. Chronic placental insufficiency: Issues of diagnosis and obstetric tactics. Bull Ural Med Acad Sci 2016;3:5-13.
7. Lausman A, Kingdom J. Intrauterine growth restriction: Screening, diagnosis, and management. J Obstet Gynaecol Can 2013;35:741-8.
8. Gureev VV, Martynova OV, Anciferova OE, Martynov MA, Pokrovskaia TG, Malorodova TN, *et al*. Correction of adma-induced preeclampsia with the use of phosphodiesterase 5 and selective inhibitor of arginase II ZB49-0010. Research result. Ser Med Pharm 2015;4:66-8.
9. Albu AR, Anca AF, Horhoianu VV, Horhoianu IA. Predictive factors for intrauterine growth restriction. J Med Life 2014; 7:165-71.
10. Hendrix N, Berghella V. Non-placental causes of intrauterine growth restriction. Semin Perinatol 2008;3:161-5.
11. Baschat AA. Pathophysiology of fetal growth restriction: Implications for diagnosis and surveillance. Obstet Gynecol Surv 2004;8:617-27.
12. Rebrova OI. Statistical Analysis of Medical Data. The Use of Statistical Application Package. Moscow: Mediasfera; 2006. p. 305.
13. Moyambe JN, Bernard P, Khang'Mate F, Nkoy AM, Mukalenge FC, Makanda D, *et al*. Risk factors for intra-uterine growth retardation in Lubumbashi. Pan Afr Med J 2013;14:4.
14. Kujovich JL. Thrombophilia and pregnancy complications. Am J Obstet Gynecol 2004;2:412-24.
15. Liu J, Wang XF, Wang Y, Wang HW, Liu Y. The incidence rate, high-risk factors, and short-and long-term adverse outcomes of fetal growth restriction: A report from Mainland China. Medicine (Baltimore) 2014;93:e210.
16. Horowitz KM, Feldman D. Fetal growth restriction: Risk factors for unplanned primary cesarean delivery. J Matern Fetal Neonatal Med 2015;28:2131-4.

Source of support: Nil; Conflict of interest: None Declared