

PLACENTAL INSUFFICIENCY AND FETAL GROWTH RESTRICTION

Pranvera IZAIRI, Ana KOCEVSKA, Ana Marija SPISIK-PUSEVSKA, Zoran ILIEVSKI

Department of high risk and pathological pregnancy, Faculty of Medical sciences of Tetova

**Corresponding author e-mail: pranvera.izairi@unite.edu.mk*

Abstract

Compromise of placental function causes an unfavorable pregnancy and, in most cases, results in fetal growth restriction. The aim of this research was to find an ultrasound parameter that can determine a placental insufficiency and prevent FGR. It was a cohort prospective study that includes 573 pregnant women between 20-24 gestational week. 523 had no ultrasound changes and comprise the control group, and 50 of them had changes in doppler values and/or placental volume, so they comprise the research group. All pregnant women were monitored during pregnancy for fetal biometry, pulse doppler of both uterine arteries, placental volume, and in delivery for bodily measurement of the newborn. Pregnant women with FGR had significantly higher mean values of the pulsatility index (PI) in the right uterine artery compared with pregnant women in the control group. The obtained results showed that 90% of pregnant women with FGR and 59.2% of pregnant women in the control group had an elevated resistance index (RI) in the right uterine artery. In the left uterine artery, the resistance index was elevated in 78% of women with FGR and in 67.7% of the control group. In the FGR group, significantly higher mean values of the resistance index were measured in both uterine arteries compared with the control group. Compared with the control group, a placental volume below the reference value was significantly more frequent in pregnant women with FGR. The largest mean placental volume was measured in pregnant women from the control group, whereas pregnant women with FGR had a lower mean placental volume.

Keywords: uterine arteries, placenta, fetal growth restriction

Introduction

The placenta is a temporary, very specific organ during pregnancy that carries out physiological growth and processes essential for fetal development. The growth and function of placenta is well regulated for maximal effective exchange of nutrients and metabolic products between maternal and fetal blood circulations. In normal pregnancy, fetoplacental circulation is increased proportionally with the gestational week of pregnancy, thus enabling the physiological intrauterine growth of the fetus.(1) Placental insufficiency arises from disruptions in the maternal-fetal interface that impair the delivery of oxygen and nutrients. Central to this process is a failure in early gestational placentation, characterized by inadequate trophoblast invasion and incomplete spiral artery remodeling.(2) This condition shows a persistence of high-resistance, low-flow uterine arteries, ultimately resulting in reduction of uteroplacental perfusion.

Feto-placental insufficiency is responsible for oxygen decrease and low transport of nutrients to the fetus, so it suffers and stagnates in intrauterine growth, thus increases the possibility of some other complications during pregnancy and during delivery. Using high frequency ultrasound waves is a possibility of measuring the blood circulation in certain organ.(3) In pregnancies with high blood pressure, preeclampsia, intrauterine growth retardation and other adverse outcomes, the circulatory impedance of a. uterine is increased, that is high resistant index or appearance of early diastole notch. Also, it can appear high an impedance of a. umbilicalis, if the obliteration of placental circulation is up to 60%.(4)

Placental insufficiency occurs in approximately 8% to 15% of all pregnancies, worldwide. It is a leading cause of fetal growth restriction (FGR) and some other complications during fetal development and stillbirth.

The most common reasons for placental insufficiency are: gestational diabetes, high blood pressure, maternal heart diseases, blood clotting conditions, preeclampsia, maternal age, using of certain medications, smoking, drinking alcohol, etc.

Placental insufficiency arises from disruptions in the maternal–fetal interface that impair the delivery of oxygen and nutrients. Central to this process is a failure in early gestational placentation, characterized by inadequate trophoblast invasion and incomplete spiral artery remodeling.(5)

This condition shows a persistence of high-resistance, low-flow uterine arteries, ultimately resulting in reduction of uteroplacental perfusion.

Fetal growth restriction is a condition of failure of a fetus to reach its predetermined growth potential. FGR antenatal diagnosis requires a detailed assessment of maternal risk factors, including reproductive history, chronic diseases, maternal risk factors, and serial ultrasounds among women identified as at risk. (6) It should be noted that a large proportion of SGA infants are not actually growth restricted but are either constitutionally small or small due to physiologic reasons, such as congenital malformations. FGR affects an estimated 3–5% of pregnancies. Placental insufficiency, as measured by structural abnormalities and histologic findings, is the most frequent cause of FGR, but fetal factors, including chromosomal abnormalities and congenital infections, and maternal risk factors also contribute to FGR.(7)

Objective: Assess ultrasound doppler and placental imaging findings to determine placental insufficiency and to prevent FGR and/or improve pregnancy outcome.

Methods

This research is realized at the Special Hospital for Obstetrics and Gynecology during the period of time from 01.01.2023 – 31.12.2024. It is a cohort prospective study that includes 573 pregnant women who came for a routine check up at our hospital during 20-24 gestational week of pregnancy. Previously, to all participants was explained the aim of the study and their contribution so all of them assigned an volunteer's agreement for participation in it

Inclusion criteria: singlton pregnancy, age of mother up to 18, gestational age 20-24 weeks, exclude anomalies during ultrasound check up.

Exclusion criteria: twins or multiple pregnancy, fetus mortus in utero, anomaly findings, preegsistential hypertension of mother, other chronic diseases of mother, use of Aspirin during pregnancy.

All of them underwent ultrasound for fetal biometry, volume of placenta and color doppler values of both uterine arteries. From overall number of pregnant women, 523 had no ultrasound changes and comprise the control group, and 50 of them had ultrasound changes in doppler values and/or placental volume, so they comprise the research group. All pregnant women were monitored during pregnancy termination for fetal weight and heigh of the newborn.

It was used ultrasound machine Voluson E8 Expert with 4D convex probe RM6C, GE Healthcare.

Fetal biometry included: biparietal diameter, abdominal circumference, femur length, exclusion of fetal anomalies and placental volume (cm³) measuring by Merwins calculator as standard Apple tool. By pulse doppler were finded the values of pulsatile index (PI) and resistant index (RI) of both uterine arteries.

Table Figures and Equations

Overall number of participants N=573

FGR

N=50

CG

N=523

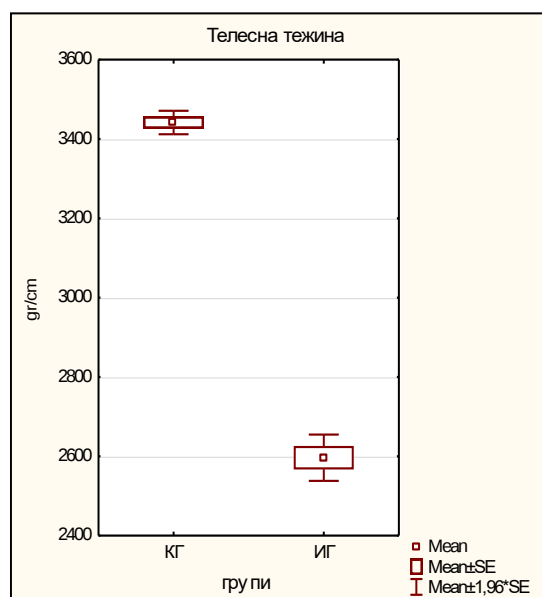


Fig. 1 Graphic depiction of body weight in CG and RG

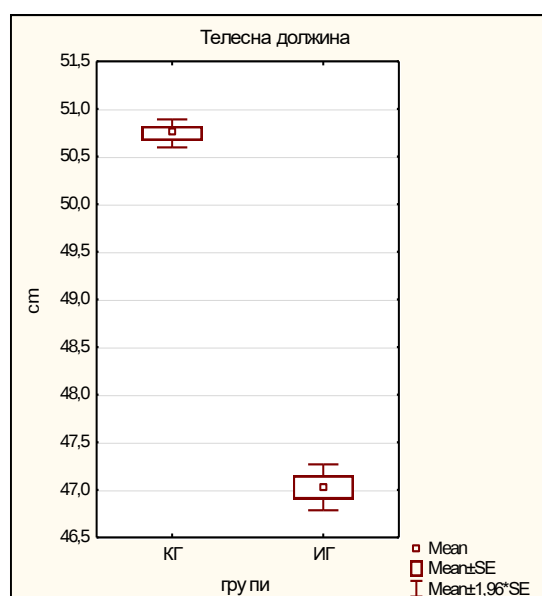


Fig. 2 Graphic depiction of body heigh in CG and RG

Newborn from mothers with FGR newborns had significant smaller fetal bodily measurment (fetal height and weight) comparing to newborns with favorable outcome. (2596.5 ± 364.4 vs 3441.5 ± 344.6 gr/cm, и, 47.0 ± 1.5 vs 50.7 ± 1.7 cm; $p < 0.0001$).

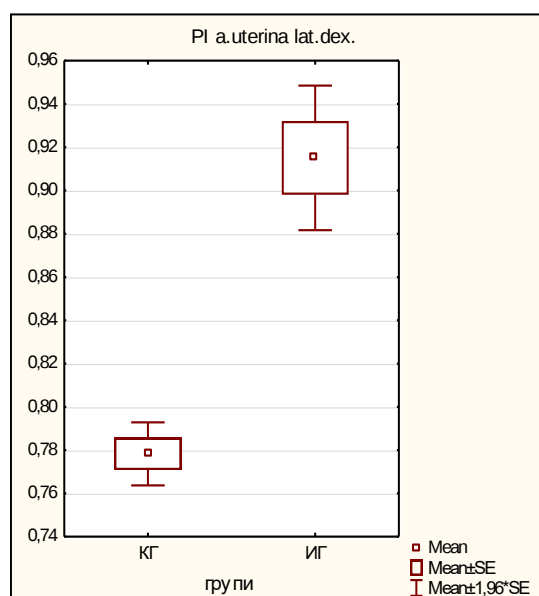


Fig. 3 Graphic depiction of PI PI a. uterine lat. sin. in CG and RG

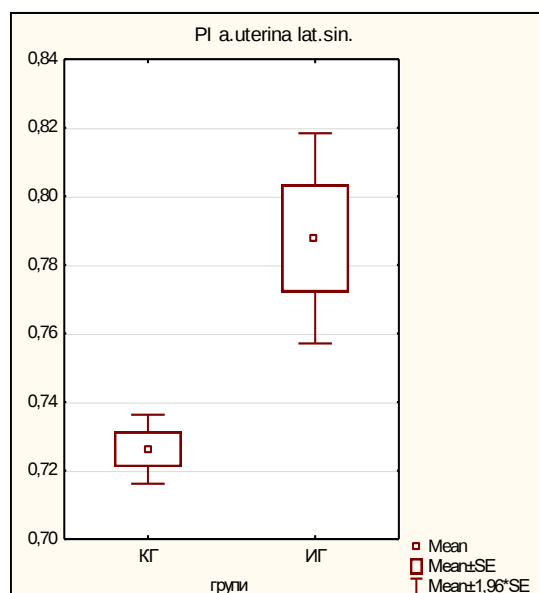


Fig. 4 Graphic depiction of PI a. uterine lat. sin. in CG and RG

The pulsatility index of both uterine arteries differed between the study and control group. The mean PI of the right artery was 0.92 ± 0.2 in pregnant women with an adverse pregnancy outcome, and 0.78 ± 0.2 in pregnant women with a favorable outcome, with the difference of 0.14 confirmed as statistically significant. The mean pulsatility index of the left uterine artery was 0.79 ± 0.2 in pregnant women with an adverse pregnancy outcome, and 0.73 ± 0.1 in pregnant women with a favorable outcome, with the difference of 0.06 confirmed as statistically significant at $p = 0.000002$. (Figures 3 and 4)

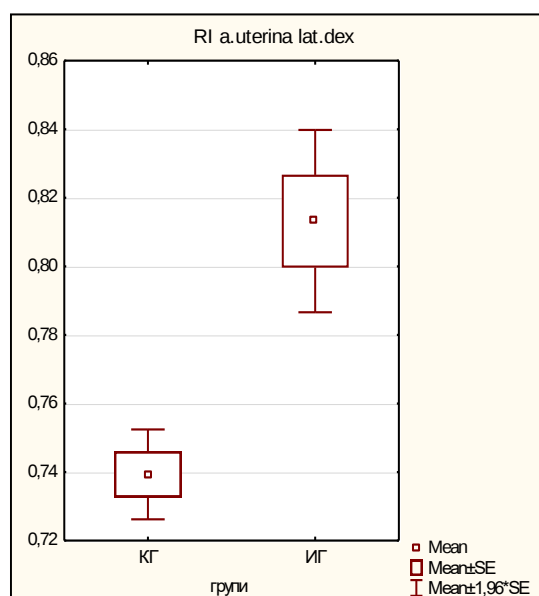


Fig. 5 Graphic depiction of RI a. uterine lat. dex. in CG and RG

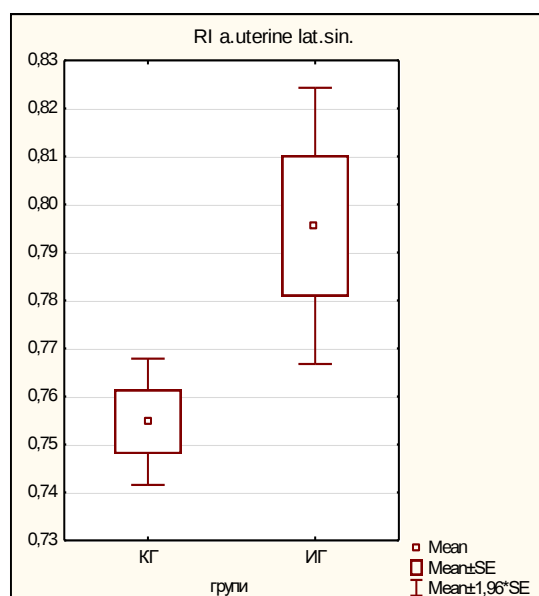


Fig. 6 Graphic depiction of RI a. uterine lat. sin. in CG and RG

Pregnant women with adverse and favorable pregnancy outcomes had different resistance indices in both uterine arteries. The RI of the right uterine artery had a mean value of 0.81 ± 1.2 in the study group (SG) and 0.74 ± 0.15 in the control group (CG), and the difference of 0.07 was confirmed as statistically significant at $p < 0.0001$. The RI of the left uterine artery had a mean value of 0.79 ± 0.2 in the SG and 0.75 ± 0.15 in the CG, and the difference of 0.04 was confirmed as statistically significant at $p = 0.0059$. (Figures 5 and 6)



Fig. 7 Graphic depiction of placental volume in CG and RG

In the study group (SG), the mean placental volume measured was 202.3 ± 49.1 , while in the control group (CG), the mean volume was 211.0 ± 18.2 . The difference in mean placental volumes between the two groups, amounting to 8.7, was confirmed as statistically significant at $p = 0.00085$. A significantly smaller placental volume was measured in pregnant women with FGR. (Figure 7)

Results

Table 1 Resistent index in both uterine arteries

Variable	Calculated parameter	Groups	
		FGR	KG
RI a.uterina lat. dex	mean $\pm$ SD	0.86 ± 0.16	0.74 ± 0.15
	min - max	0.61–1.21	0.37–1.19
	p-level	$t=5.48$ *** $p=0.0000$ sig	
RI a.uterina lat.sin.	mean $\pm$ SD	0.83 ± 0.2	0.75 ± 0.15
	min - max	0.55–1.16	0.47–1.96
	p-level	$t=3.44$ *** $p=0.0006$ sig	

t(Student t-test)

*** $p < 0.0001$

In the FGR group, significantly higher mean values of the resistance index were measured in both uterine arteries compared with the control group (CG): 0.88 ± 0.15 vs. 0.74 ± 0.15 , $p < 0.0001$ for the right uterine artery, and 0.75 ± 0.15 , $p = 0.0009$ and 0.75 ± 0.15 , $p = 0.0006$ for the left uterine artery.

Table 2. Depiction of placental volume in FGR group in relation to control group

Варијабла/ Variable	калкулиран параметар/ calculated parameter	Групи / Groups	
		IUGR	KГ / CG
Волумен на постелка Placental volume /(cm ³)	mean $\pm$ SD	194.83 $\pm$ 14.1	211.01 $\pm$ 18.2
	min - max	172 – 212	120 – 290
	p-level	t=6.12 ***p=0.0000sig	

t(Student t-test)

****p<0.0001

Pregnant women with fetal growth restriction (FGR) had a low mean placental volume (194.83 $\pm$ 14.1). According to the results of the statistical analysis, the differences tested between the examined groups and the control group were statistically significant for the comparison between the FGR group and the control group (CG) (p < 0.0001) (Table 2).

Conclusions

Pregnant women with fetal growth restriction (FGR) had significantly higher mean values of the pulsatility index (PI) in the right uterine artery compared with pregnant women in the control group (mean values: 0.90 $\pm$ 0.15 and 0.78 $\pm$ 0.2 in the FGR and CG groups, respectively).

The obtained results showed that 90% of pregnant women with fetal growth restriction and 59.2% of pregnant women in the control group had an elevated resistance index in the right uterine artery. In the left uterine artery, the resistance index was elevated in 78% of women with intrauterine growth restriction and in 67.7% of the control group.

In the FGR group, significantly higher mean values of the resistance index were measured in both uterine arteries compared with the control group (0.86 $\pm$ 0.16 vs. 0.74 $\pm$ 0.15, respectively, in the right uterine artery, and 0.83 $\pm$ 0.2 vs. 0.75 $\pm$ 0.15, respectively, in the left uterine artery). The FGR group had a similar mean resistance index to the control group in both uterine arteries. Compared with the control group, a placental volume below the reference value was significantly more frequent in pregnant women with fetal growth restriction (100% vs. 73.6%). The largest mean placental volume was measured in pregnant women from the control group (211.01 $\pm$ 18.2), whereas pregnant women with fetal growth restriction had a lower mean placental volume (194.83 $\pm$ 14.1).

Nomenclature

FGR fetal growth restriction

CG control group

RG research group

References

- [1]. Čerkez Habek J et al. Intima media thickness in women with preeclampsia. – Med Jad 2018;48
- [2]. Ohgiya Y, Nobusawa H, Seino N, Miyagami O, Yagi N, Hiroto S, Munechika J, Hirose M, Takeyama N, Ohike N, Matsuoka R, Sekizawa A, Gokan T. MR Imaging of Fetuses to Evaluate Placental Insufficiency. Magn Reson Med Sci. 2016;15(2):212-9. [PMC free article] [PubMed] [Reference list]
- [3]. Gómez O, Figueras F, Martínez JM, del Río M, Palacio M, Eixarch E, Puerto B, Coll O, Cararach V, Vanrell JA. Sequential changes in uterine artery blood flow pattern between the first and second trimesters of gestation in relation to pregnancy outcome. Ultrasound Obstet Gynecol. 2006 Nov;28(6):802-8. doi: 10.1002/uog.2814. PMID: 17063456.
- [4]. Eltsje S. Cnossen, et al. March 11, 2008 178 (6) 701-711; DOI: <https://doi.org/10.1503/cmaj.070430>, Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis

- [5]. Figueras F, Gardosi J. Intrauterine growth restriction: new concepts in antenatal surveillance, diagnosis, and management. *Am J Obstet Gynecol.* 2011;204(4):288–300. doi: 10.1016/j.ajog.2010.08.055. [DOI] [PubMed] [Google Scholar]
- [6]. Kinzler WL, Kaminsky L. Fetal growth restriction and subsequent pregnancy risks. *Semin Perinatol.* 2007;31(3):126–134. doi: 10.1053/j.semperi.2007.03.004. [DOI] [PubMed] [Google Scholar]
- [7]. Bartkute Karolina, Dalia Balsyte, Josef Wisser and Juozas Kurmanavicius Pregnancy outcomes regarding maternal serum AFP value in second trimester screening DOI 10.1515/jpm-2016-0101 Received March 17, 2016. Accepted September 29, 2016.
- [8]. Oceania Perinatal Societies, the International Society of Perinatal Obstetricians.
- [9]. 26. 10.3109/14767058.2013.793661.
- [10]. Chen Xiao-He, Shuwen Huang, and David Ken. Integration of biomarkers into epidemiology study design, Biomarkers in clinical medicine, chapter17; 2011
- [11]. D'Anna R, Baviera G, Corrado F, Leonardi I, Buemi M, Jasonni VM. Is mid-trimester maternal serum inhibin-A a marker of preeclampsia or intrauterine growth restriction? *Acta Obstet Gyn Scan,* 2002;81(6):540–3.
- [12]. D'Alton M, Cleary-Goldman J, *Semin Perinatol.* 2005 Aug; 29(4):240-6., and second trimester evaluation of risk for fetal aneuploidy: the secondary outcomes of the FASTER Trial.
- [13]. Daskalakis, J *Neurol Neurophysiol* 2015, 6:1, Serum Markers for the Prediction of Preeclampsia George Daskalakis1 and Angeliki Papapanagiotou2*1 DOI: 10.4172/2155-9562.1000264 Review Article Open Access J Neurol Neurophysiol ISSN:2155-9562 JNN, an open access journal Volume 6 • Issue 1 • 1000264 nr uoJ Journal of Neurology & Neurophysiology
- [14]. Dizdarević-Stojkanović Jadranka, Goran Stojkanović. Savremena terapija hipertenzivnih bolesti u trudnoci. 2014; DOI 10.5644/PI2014-156-04
- [15]. Delmis Josip, Slavko Oreskovic, et al., *Fetalna medicina I opstetricija, Medicinska naklada, Zagreb, 2014*
- [16]. Fang, Shih-Wen, et al. "Second-Trimester Placental Volume and Vascular Indices in the Prediction of Small-for-Gestational-Age Neonates." *Fetal Diagnosis and Therapy*, vol. 37, no. 2, 2015, p. 123+. Gale OneFile: Health and Medicine, link. gale. com/ apps/ doc/ A637147519/ HRCA? U = anon ~ 193 cb134&sid=HRCA&xid=7054c594. Accessed 27 May 2021.
- [17]. Fadl S, Moshiri M, Fligner CL, Katz DS, Dighe M. Placental Imaging: Normal Appearance with Review of Pathologic Findings. *Radiographics.* 2017 May-Jun;37(3):979-998. doi: 10.1148/rg.2017160155. PMID: 28493802.
- [18]. Florio P, Cobellis L, Luisi S, Ciarmela P, Severi FM, Bocchi C, Petraglia F. Changes in inhibins and activin secretion in healthy and pathological pregnancies. *Mol Cell Endocrinol.* 2001 Jun 30;180(1-2):123-30. doi: 10.1016/s0303-7207(01)00503-2. PMID: 11451581.
- [19]. García B, Llorba E, Valle L, Gómez-Roig MD, Juan M, Pérez-Matos C, Fernández M, García-Hernández JA, Alijotas-Reig J, Higuera MT, Calero I, Goya M, Pérez-Hoyos S, Carreras E, Cabero L. Do knowledge of uterine artery resistance in the second trimester and targeted surveillance improve maternal and perinatal outcome? UTOPIA study: a randomized controlled trial. *Ultrasound Obstet Gynecol.* 2016 Jun;47(6):680-9. doi: 10.1002/uog.15873. PMID: 26823208
- [20]. Gómez O, Figueras F, Martínez JM, del Río M, Palacio M, Eixarch E, Puerto B, Coll O, Cararach V, Vanrell JA *Ultrasound Obstet Gynecol.* 2006 Nov; 28(6):802-8. [PubMed] [Ref list]