J Surg Med. 2025;9(7):93-97.
https://doi.org/10.28982/josam.8060

JOSAM

Research article
https://jsurgmed.com/

Journal of Surgery and Medicine

e-ISSN: 2602-2079

The relationship of PAPP-A and ß-HCG values with fetal gender and fetal birth weight: A single-center experience

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Ethics Committee Approval
The study was approved by the Educational Planning Coordination Board of Istanbul Medipol University Hospital (E -10840098-772.02-780 / January 30, 2023).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2025 July 4

Abstract

Background/Aim: Intrauterine growth restriction (IUGR) is a multisystem disorder that results in perinatal morbidity and mortality due to decreased oxygen transfer from mother to fetus, a consequence of placental dysfunction. The placenta secretes certain unique proteins, the levels of which significantly rise in maternal blood during pregnancy. Among these, free beta-human chorionic gonadotropin (ß-HCG) and Pregnancy-Associated Plasma Protein-A (PAPP-A) are the most frequently analyzed. Our primary aim was to assess the correlation between PAPP-A and free ß-HCG levels, derived from the first-trimester dual-screening test, with fetal sex and birth weight. Our secondary aim was to determine the possibility of predicting IUGR using these markers.
Methods: The first-trimester screening data, along with fetal sex and birth weight, of singleton pregnancies in either primiparous or multiparous women who attended Istanbul Koşuyolu Medipol Hospital and gave birth during the first trimester, were retrospectively analyzed from the hospital file system.
Results: PAPP-A demonstrated a positive correlation with birth weight. It was significantly lower in cases of IUGR compared to normal fetal birth weight. A statistically significant correlation was also found between fetal gender and both ß-HCG and PAPP-A values; they were both higher in girls compared to boys ($P<0.05$).
Conclusions: Pregnancies with low PAPP-A values in first-trimester screenings should be closely monitored for IUGR. As PAPP-A and ß-HCG averages were found to be lower in boys, they appear more risky. At this point, a larger number of multicentric prospective studies are needed to support this conclusion.

Keywords: adverse pregnancy outcomes, pregnancy-associated plasma protein-A, ß-HCG, dual test

How to cite: Altuntaş ŞL, Elçi Atılgan A, Kılıç F. The relationship of PAPP-A and ß-HCG values with fetal gender and fetal birth weight: A single-center experience. J Surg Med. 2025;9(7):93-97.

Introduction

Today, early detection of Intrauterine Growth Restriction (IUGR) is critical during prenatal check-ups to avoid multi-organ failure. It is understood that the fundamental pathophysiological cause of IUGR is placental dysfunction. This dysfunction occurs via excessive vasoconstriction of the uterine and placental spiral arteries, leading to reduced oxygen delivery to the fetus and, thus, limited intrauterine fetal growth [1].

During pregnancy, the placenta secretes unique proteins, and their levels in the maternal blood increase measurably. Among these, free beta-human chorionic gonadotropin (ß-HCG) and Pregnancy-Associated Plasma Protein-A (PAPP-A) are the most commonly used markers in studies [1]. ß-HCG and PAPP-A are measured in pregnant plasma and, combined with maternal age and Nuchal translucency (NT), are used as screening tests to identify the likelihood of various aneuploidies, particularly Down syndrome [2,3]. The first-trimester screening test, also known as the double test, is performed during the 11th to 14th gestational weeks. It provides insights into potential fetal anomalies and enables the termination of pregnancy in earlier weeks. A variety of studies have examined the relationship between fetal weight and PAPP-A [3-5]. However, there has been no study exploring the relationship between the values from the double-screening test and both fetal gender and weight.

In this study, we aimed to explore whether there is any association between maternal PAPP-A and ß-HCG levels, obtained from the dual-screening test in the first trimester of pregnancy, and fetal sex as well as fetal birth weight. We also investigated the possibility of predicting IUGR using these markers.

Materials and methods

This retrospective study was conducted at Koşuyolu Medipol University Hospital from January 1, 2009, to December 31, 2016. The subjects included primiparous and multiparous singleton pregnancies who underwent dual-screening tests and follow-up visits at our hospital and also delivered their babies here. A total of 1022 primiparous or multiparous pregnant women who had such screening tests in our biochemistry laboratory were selected for examination. Informed consent was obtained from all participants. Ethical approval was granted by the Educational Planning Coordination Board of Istanbul Medipol University Hospital (E-10840098-772.02-780).

All data was analyzed retrospectively from hospital file records. Not included were multiple pregnancies, pregnant women who smoked, those who miscarried or gave birth prematurely, or had their double test at a different center.

Participants were evaluated by a proficient perinatologist with an ultrasound between 11 weeks 4 days to 13 weeks 6 days of pregnancy. First, it was confirmed as a singleton pregnancy by ultrasonography, and the crown-rump length (CRL) and the NT of the fetus were measured. The obtained values were recorded on our hospital's double-screening test printed form, and venous blood samples from the pregnant participants were taken on the same day.

After ultracentrifugation, PAPP-A and free ß-HCG were measured from hemolyzed and non-lipidemic serum samples. Serum biochemical markers were gauged using kits from IMMULITE 2000 and the "solid-phase, enzyme-labeled chemiluminescent immunometric assay" technique, which utilizes the chemiluminescence method. The kit's sensitivity is 0.025 mIU/mL for PAPP-A and 1 ng/mL for free ß-HCG.

The results obtained were tallied with MoM (Multiples of Median) values corrected for case demographic data, maternal age, weight, diabetes, and gestational age. Then, using PRISCA 4.0 (Prenatal risk calculation software from TYPOLOG Software/GmBH, Hamburg, Germany), risks for Biochemical Trisomy 21, age, and a combined risk, which included NT and biochemical parameters, were calculated.

Based on these results, the value of 1/250 was taken as the cut-off value in the first-trimester screening, and patients were counseled whether they were in the high-risk group. At birth, the newborn's Apgar score, gender, fetal length, birth weight, head circumference percentiles, and any congenital deformities and complications at the time of delivery were recorded in the electronic file system.

Statistical analysis

All statistical analyses were conducted using IBM SPSS version 25.0 (SPSS Inc., Chicago, Illinois, USA). The normal distribution of the values was evaluated using the Kolmogorov-Smirnov test with Lilliefors correction. In the tables, continuous variables are presented as mean (standard deviation [SD]), while categorical variables are represented as number (n) and percentage (%). Comparisons between groups were made using the independent t-test for continuous variables. The relationships between continuous variables were analyzed using Pearson correlation. $P<0.05$ was considered statistically significant.

Results

The demographic and clinical characteristics of patients are illustrated in Table 1. The mean age of 1022 singleton pregnant women at birth was 30 (range 17–36) years. The average gestational age at the time of the dual-screening test was 12+4 (11+4–13+6) weeks, or when calculated in days 87.99(3.50) days as shown in Table 2. The median CRL and NT for the fetuses were 60.58 (6.94) mm and 1.67 (0.40) mm respectively. The mean PAPP-A value was 1.01 (0.50) MoM and the mean ß-HCG value was 1.14 (0.73) MoM. The mean gravida was 1.66 (0.80), and the mean body mass index of the patients was 25.20 (11.0) kg/m^2. It was found that 48% (n=490) of the babies born were girls and 51% (n=524) were boys. 19.3% (n=197) of the pregnant women had a normal vaginal delivery, and 80.7% (n=824) had a cesarean section. The mean fetal weight was 3.29 (0.46) kg and the average gestational age at birth was 38.52 (1.54) weeks. A diagnosis of IUGR was given to 10% (n=100) of the pregnant women. As shown in Table 2, there is a significant positive correlation between fetal weight and PAPP-A values (r=0.110, P=0.001). However, no significant relationship was found between fetal weight and ß-HCG values (r=0.016, P=0.303) or NT values and fetal weight (r=0.004, P=0.201). Notably, a negative association was observed between trisomy 21 biochemical risk and fetal weight (r=0.071 P=0.023). Examining the relationship between gender and dual screening test parameters reveals a significant difference between gender and PAPP-A values: a comparative analysis found higher PAPP-A levels in females than in males

(*P*=0.004) (Table 3). Similarly, there is a statistically significant difference between gender and ß-HCG averages: ß-HCG averages were found to be higher in girls than in boys (*P*<0.001) (Table 3).

Table 1: Demographic and clinical features of the subjects included in the study.

Fetal Gender	**n (%) or Mean (SD)**
Female	490 (48.3)
Male	524 (51.7)
Type of delivery	
Vaginal delivery	197 (19.3)
Cesarean Section	824 (80.7)
IUGR	
None	899 (90.0)
Present	100 (10.0)
Macrosomia	
None	903 (90.2)
Present	98 (9.8)
Maternal Age (n=1021)	30.55 (4.35)
Gravidity (n=1014)	1.66 (0.80)
Maternal BMI. kg/m²	25.20 (11.03)
Gestational age *(day) (n=1021)	87.99 (3.50)
CRL mm (n=1020)	60.58 (6.94)
NT mm (n=1021)	1.67 (0.40)
PAPP-A, MoM	1.01 (0.50)
ß-HCG, MoM	1.14 (0.73)
Fetal weight, kg (n=1011)	3.29 (0.46)
Gestational age(week) (n=1007)**	38.52 (1.54)

* Gestational Age at Dual screening time, **Gestational Age at birth

Table 2: Correlation analyses between fetal weight, PAPP-A, ß-HCG, NT, maternal weight, and Trisomy 21 values.

		Fetal weight	**PAPP-A**	**ß-HCG**	**NT**	**Maternal BMI**	**Trisomy 21 risky**
Fetal weight	r	1					
PAPP-A	r	0.110**	1				
	P	**<0.001**					
ß-HCG	r	0.016	0.267**	1			
	P	0.603	**<0.001**				
NT	r	-0.004	-0.048	-0.023	1		
	P	0.901	0.128	0.457			
Maternal BMI	r	0.161**	-0.084**	0.031	0.048	1	
	P	**<0.001**	**0.007**	0.327	0.126		
Trisomy 21 risky	r	-0.071*	-0.518**	0.408**	0.080*	0.127**	1
	P	**0.023**	**<0.001**	**<0.001**	**0.011**	**<0.001**	

** Correlation is significant at the 0.05 level (Pearson correlation test), *** Correlation is significant at the 0.01 level (Pearson correlation test)

Table 3: Comparison of PAPP-A and ß-HCG values with fetal gender.

	Female n=490	**Male n=524**	***P*-value**
PAPP-A, MoM	1.06 (0.53)	0.97 (0.48)	0.004
ß-HCG, MoM	1.25 (0.82)	1.04 (0.62)	<0.001

P-value: independent t-test, values: mean (SD)

Discussion

The primary goal of antenatal biochemical screening tests is to minimize maternal and fetal morbidity and mortality [4-6]. Consequently, the number of studies on these placenta-secreted proteins is increasing significantly. PAPP-A, one of these proteins, was first isolated in a laboratory in 1974 [7]. It is secreted from cytotrophoblasts and can be detected in maternal blood starting the 8th week of gestation [4]. In 1999, PAPP-A, an insulin-like growth factor (IGF), was isolated from a human fibroblast culture medium. PAPP-A has been linked to numerous pathophysiological events associated with IGF-1 and 2 [8]. The IGFs are known to play a significant role in trophoblast invasion into the decidua during pregnancy [9]. Any defects in this pathway could potentially affect fetal growth adversely, due to inadequate placental perfusion, and could be the initial mechanism for various pregnancy complications [9,10]. As pregnancy progresses, levels of PAPP-A in maternal blood increase, rapidly decreasing after birth [7]. A decrease in PAPP-A as compared to a typical pregnancy suggests a riskier pregnancy in terms of chromosomal anomalies and negative pregnancy outcomes [11].

In addition to its role in placental and fetal development in pregnant women, PAPP-A plays a significant part in many physiological and pathological processes in non-pregnant individuals. These include bone development and restructuring, wound healing, atherosclerotic plaque formation in the vascular wall, and hyperplasia in smooth muscle cells in the airways of asthma patients [9,12]. Accurate determination of gestational age is indispensable to the health of both mother and infant, and it is crucial to provide comprehensive counseling on safe and effective methods for terminating pregnancy. While the last menstrual period and the first-trimester ultrasound are frequently used to ascertain gestational age, they have inherent limitations in terms of accuracy and usability. Studies on PAPP-A for determining gestational age are ongoing [13]. In pregnancies marked by Down syndrome, maternal serum PAPP-A levels significantly decrease in the first trimester [14]. Moreover, low PAPP-A levels are detected not only in trisomy 21 but also in other fetal aneuploidies [15]. Additionally, low first-trimester PAPP-A levels are closely associated with in-utero fetal death and low birth weight [14]. Consequently, low first-trimester PAPP-A levels have started to be used to monitor pregnancies for adverse fetal outcomes [15]. Parry et al. [16] found a significant correlation between maternal serum PAPP-A levels and detrimental pregnancy outcomes in nulliparous women. However, the tests' analytical properties do not substantiate their usage as clinical biomarkers predicting adverse pregnancy outcomes, either individually or in combination with maternal clinical characteristics [16].

Kantomaa et al. [17] examined data from a large cohort of pregnant women to assess the relationship between PAPP-A and small for gestational age (SGA). They concluded that a cut-off of 0.4 MoM should be used to gauge the increased risk of SGA [17]. Similarly, Sovio et al. [18] highlighted that lower PAPP-A values were linked with fetal growth restriction. The scenario differs slightly for pregnancies complicated by diabetes: the first-trimester serum screening markers for fetal Down syndrome, PAPP-A, and free ß-HCG, cannot serve as a risk determination tool for obstetric complications like IUGR, macrosomia, and preterm birth [19]. Another crucial point is the assessment of pregnant women who smoke. They were not included in this study due to studies showing that smoker's PAPP-A levels are approximately 15 percent lower than non-smokers [20]. Simulation studies also indicated that the detection of trisomy 21 in smokers using free beta hCG, PAPP-A, and maternal age will decrease by about 5 to 6 percent compared to the general population [20]. A few researchers have also studied the connection between first-trimester maternal PAPP-A levels and adverse obstetric outcomes in cases of isolated preterm oligohydramnios. They concluded that PAPP-A should not be used as a marker in such instances [21].

The present study revealed a statistically significant difference between the mean PAPP-A levels and fetal gender: PAPP-A averages were found to be higher in girls compared to boys. Similarly, we found a statistically significant difference between fetal gender and ß-HCG averages: ß-HCG averages were higher in girls than in boys. In contrast, Çökmez et al. [22] stated that PAPP-A and free β-hCG values were not influenced by the fetal gender. In two studies conducted by Nicolaides in 2000 and 2009, the connection between PAPP-A, ß-HCG, and gender was

discussed. Initially, Cowans et al. [23] examined 2923 normal and 203 Trisomy 21(Tri 21) pregnant women, followed by Spencer et al. [24] who examined 56024 normal and 722 Tri 21 pregnant women in 2009. In both studies, maternal ß-HCG and PAPP-A levels were higher in both normal female fetuses and in female fetuses affected by Tri 21. Since this finding reduced the detection rate of Tri 21 in girls by 1-2%, a gender-based correction was deemed necessary.

Stark et al. [25] demonstrated that maternal physiology varies with fetal sex. Pregnant women carrying a male fetus showed increased vasodilation in response to corticotropin-releasing hormone, as well as greater baseline perfusion than those carrying a female fetus. Preeclamptic women pregnant with a male fetus exhibited significantly reduced vasodilation compared to normotensive women carrying a male fetus. However, microvascular function did not show any significant differences between preeclamptic and normotensive women carrying a female fetus [25].

Broere-Brown et al. [26] discovered that the pulsatility index of the uterine artery in women carrying a male fetus was higher compared to those carrying a female fetus. In addition, women carrying a male fetus were observed notching more often in the Doppler resistance pattern. Reinforcing these findings, Inkster et al. [27] reported that epidemiological studies have identified sex differences linked to various obstetric complications, supporting the broader view of a “male disadvantage” that is more intricate than initially assumed. They also examined potential mechanisms that might explain the development of sex differences in fetoplacental function. In conclusion, they emphasized the need to bridge gaps in the development of appropriate diagnostic tests to predict sex-related obstetric conditions.

The primary strength of this study is that it encompasses a larger number of patients compared to most single-center trials detailed in the literature. Additionally, it represents the pioneering research examining the relationship between dual-screening biochemical parameters and both fetal weight and gender. The limitations of this investigation include its retrospective nature, lack of comparison, and representation of results from single-center data.

Conclusions

Pregnancies with low PAPP-A levels during the first-trimester screening should be thoroughly monitored due to the risk of IUGR. It has been found that PAPP-A levels are lower in boys than in girls. Consequently, male infants may bear a greater risk of poor obstetric outcomes than female infants. However, additional research, especially multicenter, prospective studies, is needed to corroborate these conclusions.

References

1. Abbara A, Al-Memar M, Phylactou M, Daniels E, Patel B, Eng PC, et al. Changes in Circulating Kisspeptin Levels During Each Trimester in Women With Antenatal Complications. J Clin Endocrinol Metab. 2022 Jan 1;107(1):e71-e83. doi: 10.1210/clinem/dgab617. PMID: 34427658; PMCID: PMC8684464.
2. Abaci Turk E, YunHJ, Feldman HA, Lee JY, Lee HJ, Bibbo C, et al. Association between placental oxygen transport and fetal brain cortical development: a study in monochorionic diamniotic twins. Cereb Cortex. 2024 Jan 14;34(1):bhad383. doi: 10.1093/cercor/bhad383. PMID: 37885155; PMCID: PMC11032198.
3. Movahedi M, Farahbod F, Zarean E, Hajihashemi M, Haghollahi F, Farahmand M. Evaluation of Fetal and Maternal Outcomes in Chorion Villus Sampling (CVS). Adv Biomed Res. 2023 May 19;12:133. doi: 10.4103/abr.abr_229_22. PMID: 37434920; PMCID: PMC10331521.
4. Dias da Silva C, Sarmento Gonçalves I, Ramalho C. Association of low pregnancy associated plasma protein-A with increased umbilical artery pulsatility index in cases of fetal weight between the 3rd and 10th percentiles: a retrospective cohort study. J Perinat Med. 2023 Oct 20;52(1):90-5. doi: 10.1515/jpm-2023-0156. PMID: 37853809.
5. Turrado Sánchez EM, De Miguel Sánchez V, Macía Cortiñas M. Correlation Between PAPP-A Levels Determined During the First Trimester and Birth Weight at Full-Term. Reprod Sci. 2023 Nov;30(11):3235-42. doi: 10.1007/s43032-023-01270-4. Epub 2023 May 26. PMID: 37237249; PMCID: PMC10643350.
6. Tsibizova V, Al-Sannan B, Fedorova A, Govorov I, Meyyazhagan A, Di Renzo GC. Can we improve the outcome of pregnancies with low serum PAPP-A in the first trimester? J Matern Fetal Neonatal Med. 2024 Dec;37(1):2326303. doi: 10.1080/14767058.2024.2326303. Epub 2024 Mar 19. PMID: 38503546.
7. Conover CA, Oxvig C. The Pregnancy-Associated Plasma Protein-A (PAPP-A) Story. Endocr Rev. 2023 Nov 9;44(6):1012-28. doi: 10.1210/endrev/bnad017. PMID: 37267421.
8. Prasad P, Romero R, Chaiworapongsa T, Gomez-Lopez N, Lo A, Galaz J, et al. Further Evidence that an Episode of Premature Labor Is a Pathologic State: Involvement of the Insulin-Like Growth Factor System. Fetal Diagn Ther. 2023;50(4):236-47. doi: 10.1159/000530862. Epub 2023 May 10. PMID: 37231893; PMCID: PMC10591834.
9. Davenport BN, Wilson RL, Jones HN. Interventions for placental insufficiency and fetal growth restriction. Placenta. 2022 Jul;125:4-9. doi: 10.1016/j.placenta.2022.03.127. Epub 2022 Apr 4. PMID: 35414477; PMCID: PMC10947607.
10. Hord TK, Tanner AR, Kennedy VC, Lynch CS, Winger QA, Rozance PJ, et al. Impact of Chorionic Somatomammotropin In Vivo RNA Interference Phenotype on Uteroplacental Expression of the IGF Axis. Life (Basel). 2023 May 26;13(6):1261. doi: 10.3390/life13061261. PMID: 37374044; PMCID: PMC10302269.
11. Dal Y, Akkuş F, Karagün Ş, Nessar AZ, Karaca SG, Coşkun A. The role of second trimester uterine artery Doppler in predicting obstetric and neonatal outcomes in abnormal first-trimester maternal serum pregnancy-associated plasma protein-A and free β-human chorionic gonadotropin values. J Clin Ultrasound. 2024 Feb 14. doi: 10.1002/jcu.23644. Epub ahead of print. PMID: 38353146.
12. Liu J, Zhang X, Yu Z, Zhang T. Exosomes Promote Atherosclerosis Progression by Regulating Circ_100696/miR-503-5p/PAPPA Axis-Mediated Vascular Smooth Muscle Cells Proliferation and Migration. Int Heart J. 2023;64(5):918-27. doi: 10.1536/ihj.23-089. PMID: 37778995.
13. Buhimschi IA, Zhao G, El Helou Y, Frye LJ, Winikoff B, Raymond EG. Analytical Comparison of Pregnancy-Associated Plasma Protein-A (PAPP-A) Immunoassays for Biochemical Determination of Gestational Age. J Appl Lab Med. 2021 Nov 1;6(6):1517-32. doi: 10.1093/jalm/jfab057. PMID: 34329446.
14. Caron L, Fillion A, Giguère Y, Audibert F, Forest JC, Gasse C, Girard M, Laforest G, Guerby P, Bujold E. First-trimester screening for Down syndrome using quadruple maternal biochemical markers. Clin Chem Lab Med. 2023 Mar 29;61(9):1630-5. doi: 10.1515/cclm-2022-1305. PMID: 36989429.
15. Kane D, D’Alton ME, Malone FD. Rare chromosomal abnormalities: Can they be identified using conventional first trimester combined screening methods? Eur J Obstet Gynecol Reprod Biol X. 2021 Feb 27;10:100123. doi: 10.1016/j.eurox.2021.100123. PMID: 33733087; PMCID: PMC7937980.
16. Parry S, Carper BA, Grobman WA, Wapner RJ, Chung JH, Haas DM, et al. Placental protein levels in maternal serum are associated with adverse pregnancy outcomes in nulliparous patients. Am J Obstet Gynecol. 2022 Sep;227(3):497. e1-497.e13. doi: 10.1016/j.ajog.2022.03.064. Epub 2022 Apr 26. PMID: 35487327; PMCID: PMC9420814.
17. Kantomaa T, Vääräsmäki M, Gissler M, Sairanen M, Nevalainen J. First trimester low maternal serum pregnancy associated plasma protein-A (PAPP-A) as a screening method for adverse pregnancy outcomes. J Perinat Med. 2022 Sep 23;51(4):500-9. doi: 10.1515/jpm-2022-0241. PMID: 36131518.
18. Sovio U, Gaccioli F, Cook E, Charnock-Jones DS, Smith GCS. Association between adverse pregnancy outcome and placental biomarkers in the first trimester: A prospective cohort study. BJOG. 2024 May;131(6):823-31. doi: 10.1111/1471-0528.17691. Epub 2023 Oct 12. PMID: 37822261.
19. Kapustin RV, Kascheeva TK, Alekseenkova EN, Shelaeva EV. Are the first-trimester levels of PAPP-A and fß-HCG predictors for obstetrical complications in diabetic pregnancy? J Matern Fetal Neonatal Med. 2022 Mar;35(6):1113-9. doi: 10.1080/14767058.2020.1743658. Epub 2020 Mar 30. PMID: 32228094.
20. Huang T, Bellai-Dussault K, Meng L, Hull D, Howley H, Reszel J, et al. First and second trimester maternal serum markers for prenatal aneuploidy screening: An update on the adjustment factors for race, smoking, and insulin dependent diabetes mellitus. Clin Biochem. 2023 Aug; 118:110596. doi: 10.1016/j.clinbiochem.2023.110596. Epub 2023 Jun 8. PMID: 37295638.
21. Caron L, Ghesquiere L, Bujold E. Pregnancy associated plasma protein-A for the prediction of small for gestational age. J Perinat Med. 2023 Jan 2;51(5):718-9. doi: 10.1515/jpm-2022-0545. PMID: 36584324.
22. Cokmez H, Yozgat ST. The effect of fetal gender on the biochemical markers of the first-trimester screening. Saudi Med J. 2022 Apr;43(4):348-52. doi: 10.15537/smj.2022.43.4.20210906. PMID: 35414612; PMCID: PMC9998053.
23. Spencer K, Ong CY, Liao AW, Papademetriou D, Nicolaides KH. The influence of fetal sex in screening for trisomy 21 by fetal nuchal translucency, maternal serum free β-hCG and PAPP-A at 10–14 weeks of gestation. Prenatal diagnosis. 2000;20(8):673-5.
24. Cowans NJ, Stamatopoulou A, Maiz N, Spencer K, Nicolaides KH. The impact of fetal gender on first trimester nuchal translucency and maternal serum free β-hCG and PAPP-A MoM in normal and trisomy 21 pregnancies. Prenatal Diagnosis. 2009;29(6):578-81.
25. Stark MJ, Dierkx L, Clifton VL, Wright IM. Alterations in the maternal peripheral microvascular response in pregnancies complicated by preeclampsia and the impact of

fetal sex. The Journal of the Society for Gynecologic Investigation: JSGI. 2006;13:573-8.
26. Broere-Brown ZA, Schalekamp-Timmermans S, Hofman A, Jaddoe VWV, Steegers EAP. Fetal sex dependency of maternal vascular adaptation to pregnancy: a prospective population-based cohort study. BJOG. 2016;123(7):1087-95.
27. Inkster AM, Fernández-Boyano I, Robinson WP. Sex Differences Are Here to Stay: Relevance to Prenatal Care. J Clin Med. 2021 Jul 5;10(13):3000. doi: 10.3390/jcm10133000. PMID: 34279482; PMCID: PMC8268816.