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Current median values of double and triple screening test parameters for Antalya region

İkili ve üçlü tarama testi parametrelerinin Antalya bölgesi için güncel medyan değerleri

Sibel Kulaksizoğlu[1], Nazife Öztürk[2], Ferda Işikçelik[3], Meliha Meliş Günaltay[4]

[1]Department of Medical Biochemistry, Antalya Health Application and Research Center, University of Health Sciences,
[2]R&D Unit, Antalya Training and Research Hospital,
[3]Department of Health Management, Faculty of Economics and Administrative Sciences, Burdur Mehmet Akif Ersoy University,
[4]Department of Health Management, Ankara University Institute of Health Sciences
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Correspondence: Ferda Işikçelik
Burdur Mehmet Akif Ersoy University, Faculty of Economics and Administrative Sciences, Department of Health Management, Turkey
e-mail: ferdabuluc@gmail.com

ORCID ID: SK 0000-0001-8374-5769
NÖ 0000-0001-7552-5723
FI 0000-0002-7975-4141
MMG 0000-0002-2883-4416

SUMMARY

Aim: The study aims to ascertain the regional medians of the double and triple screening test parameters in the Antalya region's population, thereby providing significant insights into prenatal care and public health.

Material and Methods: The study, meticulously conducted with pregnant women who applied to the Antalya Training and Research Hospital's labs, involved the calculation of the Median for alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), unconjugated estriol (uE3), plasma protein-A (PAPP-A), and free beta-human chorionic gonadotropin (fβ-hCG).

Results: Compared with other years, the median value computed for fß-hCG in 2022 was lower, whereas the median value calculated for 2020 was greater. The median value computed for PAPP-A in 2022 was found to be lower than previous years, similar to the finding for fß-hCG, and the median value calculated for 2020 was found to be greater than other years. The newly calculated AFP median value peaked in 2018 and decreased in 2022.

Conclusion: It was observed that the median value calculated for ß-hCG for 2020 was more significant than that estimated for other years and that the median value for 2022 was lower than that for other years. The newly calculated median value of uE3 was the highest in 2018 and the lowest in 2022. Regional median values of prenatal screening tests should be updated at regular intervals. In particular, it is essential to develop awareness-raising policies to disseminate prenatal screening tests and to consider biological variability in these tests.

Keywords: Noninvasive prenatal testing, prenatal screening, screening

ÖZET

Amaç: Çalışmanın amacı, Antalya bölgesi nüfusundaki ikili ve üçlü tarama testi parametrelerinin bölgesel ortalamalarını tespit etmek ve böylece doğum öncesi bakım ve halk sağlığı konusunda önemli bilgiler sağlamaktır.

Materyal ve Metodlar: Antalya Eğitim ve Araştırma Hastanesi laboratuvarlarına başvuran hamile kadınlarla titizlikle yürütülen çalışmada alfa-fetoprotein (AFP), beta-insan koryonik gonadotropin (β-hCG), konjuge olmayan estriol (uE3), plazma protein-A (PAPP-A) ve serbest beta-insan koryonik gonadotropin (fβ-hCG) medyan değerleri hesaplandı.

Bulgular: Diğer yıllarla karşılaştırıldığında, 2022 yılında fß-hCG için hesaplanan medyan değeri daha düşük, 2020 yılı için hesaplanan medyan değeri ise daha yüksektir. PAPP-A için 2022 yılında hesaplanan medyan değeri, fß-hCG için bulunan bulguya benzer şekilde önceki yıllara göre daha düşük, 2020 yılı için hesaplanan medyan değeri ise diğer yıllara göre daha yüksek bulunmuştur. Yeni hesaplanan AFP medyan değeri 2018'de zirve yapmış ve 2022'de düşmüştür.

Sonuç: ß-hCG için 2020 yılı için hesaplanan medyan değerin diğer yıllar için tahmin edilen değerden daha anlamlı olduğu ve 2022 yılı için medyan değerin diğer yıllara göre daha düşük olduğu görülmüştür Yeni hesaplanan uE3 medyan değeri 2018'de en yüksek, 2022'de ise en düşüktür. Prenatal tarama testlerinin bölgesel medyan değerleri düzenli aralıklarla güncellenmelidir. Özellikle, prenatal tarama testlerinin yaygınlaştırılması için farkındalık artırıcı politikaların geliştirilmesi ve bu testlerdeki biyolojik değişkenliğin dikkate alınması önemlidir.

Anahtar kelimeler: Noninvaziv prenatal test, prenatal tarama, tarama

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INTRODUCTION

Health expenditures continue to increase worldwide. However, the resources allocated to health services are limited. This shows that there is no room for waste in the healthcare services. Particular attention should be paid to this issue in diagnostic healthcare services because the diagnosis process constitutes the beginning of the health service delivery and directly affects the subsequent processes. In this direction, each stage in applying diagnostic tests should proceed correctly. More attention is needed to this situation in diagnostic tests that have widespread application for significant health problems that affect a large part of society. Considering the results of genetic diseases will provide material and moral advantages for diagnostic tests to present correct findings for the first time. Since prenatal diagnostic tests, which are widely used to diagnose genetic disorders, are affected by biological variability, it is essential to make the necessary regional measurements to interpret test results.

Genetic disorders are an essential group of disorders producing mental and physical defects (1). Genetic disorders such as Trisomy 21 (Down), Trisomy 18 (Edward), Trisomy 13 (Patau) syndromes, and Neural Tube Defects bring together social and economic problems (2). Trisomy 21 is the most common, and the best-known malformation syndrome (3). The birth prevalence of trisomy 21 syndrome is generally stated to be 1/650 live births, but it varies in different populations from 1/600 to 1/2000 live births (3). Additionally, with the participation of women in the labor force, the percentage of pregnancies in advanced age has increased. As this rate increased, it also increased the risk of age-related congenital anomalies (4).

Generally, the frequency of chromosomal anomaly is reported to be 1 in 150–160 live births (5). Additionally, chromosomal disorders are found in more than 50% of first-trimester spontaneous abortions and 5% of stillbirths (6). Although different prevalences have been reported in different studies conducted in different parts of the world in the literature, the prevalences of Trisomy 18 and Trisomy 21 (Down's syndrome) are 1/6500 and 1/800, respectively. Trisomy 21 (Down syndrome) is the most common fetal chromosomal anomaly, which is compatible with life. However, it is emphasized chiefly because it causes various structural and mental problems, especially mental sequelae (5, 7). MOM values have a significant effect on the risk calculation. Using medians higher than the current median of the population studied will result in falsely low MoM reporting.

Genetic diseases often cause dreadful problems, but their treatment possibilities are limited (8). Because there is no way to genetic disorder treatment, preventive prenatal diagnostic studies have come out (1). The double screening test applied in the first trimester of pregnancy and the triple screening test used in the second trimester are prenatal screening tests used to detect anomalies such as trisomy 21, trisomy 18, and neural tube defects (8-11). The double screening test is performed at the 11th and 14th weeks of pregnancy, and the triple screening test is performed at the 14th and 20th (12-15). The double screening test that determines the risk of aneuploidy and triploidy by combining Pregnancy Associated Plasma Protein-A (PAPP-A) secreted from trophoblasts and free β-human Chorionic Gonadotropin (β-hCG) synthesized by syncytiotrophoblasts, maternal age and NT (nuchal translucency) (6, 16). Measuring maternal serum levels of Alfa-Fetoprotein (AFP), total human chorionic gonadotrophin (hCG), and unconjugated estriol (uE3) is known as triple screening (17).

Double and triple screening test results are formatted as multiples of median (MoM). MoM is used to convert the data obtained from the double and triple screening tests into a more understandable and interpretable unit. First, the median of the data obtained from pregnant women with healthy fetuses is calculated for each gestational week to calculate the MoM value. Then, each test result is divided by the median value of that week, and the MoM value of that test result is determined. The corrected MoM values are calculated by considering the factors (age, weight, and race) that affect the results of the parameters measured during the gestational week for which the MoM value is calculated. The corrected MoM values are compared with the previously determined ones with a computer program, and a risk ratio for trisomy 21, 18, 13, and neural tube defects is reported. Programs use multivariate mathematical rules to calculate risk, and the variables used at each stage of the algorithm affect the result. The quality of the results depends on factors such as the analytical performance of biochemical tests, gestational age, the accuracy with which gestational age is recorded, and whether the program's median and MoM values are population values.

In previous studies, it has been found that MoM values vary according to race, origin, and region (18-27). For this reason, it is stated that to interpret the prenatal screening test results accurately, in addition to measuring the analytes accurately, the region should also determine the median values used in the MoM calculation and even the conditions of each laboratory performing the analysis (18). MoM values ensure standardization and comprehensibility of the results (19). Creating a median specific to each race or region is desirable since MOM values differ according to various parameters, such as ethnicity and region (28).

The MoM values obtained from the regional median values are separate for each region's population. This provides a more accurate calculation of risks and prevents unnecessary use of advanced technical methods. Calculating median values for small populations is important because of the existing regional differences in Türkiye. In this context, in our research, we explored the regional medians of the double and triple screening test parameters in the population in the Antalya region between 2018 and 2022.

MATERIAL AND METHODS

It has been observed that the levels of parameters such as fβ-hCG, PAPP-A, AFP, β-hCG, and uE3, which are utilized in double and triple prenatal screening tests, can vary due to population-specific characteristics such as ethnicity, dietary habits, and environmental factors. For this reason, determining region-specific median values is essential for achieving more reliable risk calculations in pregnancy follow-up. For instance, it has been noted that data about the Antalya region may not fully align with national reference ranges in Türkiye. Because changes in laboratory methods over time, shifts in population demographics, and fluctuations in environmental factors can occur, the calculation of annual variation is regarded as important for monitoring trends in these parameters.

Previous studies have demonstrated that region-specific median results are more appropriate for accurate risk assessment in double and triple-screening tests. In this context, an aim was to calculate new region-specific medians for the Antalya region population using data obtained between 2018 and 2022 and to determine the changes in these medians over time. Thus, it was intended to provide updated reference ranges-by detecting any potential upward or downward trends-that could help prevent unnecessary invasive procedures arising from false-positive or false-negative results.

The present study shows that updating the region-specific reference ranges for Antalya double and triple screening tests would significantly contribute to prenatal risk assessments. By utilizing current local median values, both the necessity for invasive interventions and the misguidance of pregnant women can be minimized. The research question has been formulated as follows: "What are the median and percentile distributions of parameters such as fβ-hCG, PAPP-A, AFP, β-hCG, and uE3 among pregnant women in the Antalya region, and what is the annual variation profile of these distributions over time?" Based on this research question, the following hypothesis has been proposed: There are statistically significant differences in the annual median values of fβ-hCG, PAPP-A, AFP, β-hCG, and uE3 biomarkers measured in prenatal screening tests conducted in the Antalya region between 2018 and 2022.

This study is retrospective and descriptive. A total of 20,088 pregnant women residing in Antalya and its surroundings who attended the Antalya Education and Research Hospital laboratories between 2018 and 2022 with a gestational age of 11 weeks + 0 days to 13 weeks + 6 days, were included in the study, in addition to 15,514 pregnant women with a gestational age of 15 weeks + 0 days to 20 weeks + 6 days who presented for triple screening tests. The minimum, maximum, and median values of alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (β-hCG), and unconjugated estriol (uE3) were calculated in the serum samples obtained for the triple screening test. In contrast, the minimum, maximum, and median values of plasma protein A (PAPP-A) and free beta-human chorionic gonadotropin (fβ-hCG) were determined in those collected for the double screening test.

Multiple pregnancies, pregnant women who smoked, individuals with a prior diagnosis of gestational diabetes, and pregnancies achieved through in vitro fertilization (IVF) were excluded from the study. The chemiluminescence immunoassay method measured All biochemical parameters on an IMMULITE 2000 xpi device.

This study analyzed the fβ-hCG, PAPP-A, AFP, β-hCG, and uE3 values obtained between 2018 and 2022 through descriptive statistical methods. For each year, the minimum, maximum, and median values were determined, and annual variation rates ("Annual variation") were calculated to monitor trends over the years. The study's primary objective was to update the region-specific medians and examine annual changes based on the values obtained. To assess the statistical significance of year-to-year differences in medians, the Kruskal-Wallis H test was applied. Following the Kruskal-Wallis H test, pairwise comparisons were conducted using Dunn's test with Bonferroni correction to identify specific group differences. All statistical analyses were conducted using the SPSS 20 software package. The ethics committee approval has been obtained (Date: 30.06.2022, Decision number: 13/22)

RESULTS

By applying the median values of the regions in a retrospective analysis, the performance of triple screening tests may be improved, prenatal risks can be assessed more precisely, and the necessity for interventional applications can be decreased. In this regard, the population in the Antalya region's double and triple screening test parameters were determined between 2018 and 2022, with the new regional medians and changes in the medians over time. In comparison with other years, it was found that the median value computed for fß-hCG for 2022 was lower, whereas the median value calculated for 2020 was more excellent. Additionally, it was determined that the highest decrease in percentage for fß-hCG occurred between 2021–2022. The median value computed for PAPP-A for 2022 was lower than previous years, similar to the finding for fß-hCG, and the median value calculated for 2020 was more significant than other years. Additionally, it was determined that the highest percentage of decrease for PAPP-A occurred between

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2020–2021. These differences in annual median values were statistically significant for all biomarkers (p< 0.05). (Table 1).

The newly calculated AFP median value peaked in 2018 and decreased in 2022. Additionally, it was determined that the highest percentage of decrease for AFP occurred between 2021–2022. We observed that the median value calculated for ß-hCG for 2020 was more significant than that for other years and that the median value for 2022 was lower than that for other years. It was determined that the highest decrease for ß-hCG occurred between 2020 and 2021. The newly calculated median value of uE3 was the highest in 2018 and the lowest in 2022. Again, like AFP, it was determined that the highest percentage of decrease for uE3 occurred between 2021–2022. These differences in annual median values were statistically significant for all biomarkers (p< 0.05) (Table 2).

Table 1. The Median Values Determined in this Study for fß-hCG and PAPP-A Levels, as well as the Median Changes Between 2018 and 2022

		fß-hCG				PAPP-A			
years	n	min	max	median	Annual variation	min	max	median	Annual variation
2018	5840	2.85	772	36.90		0.16	108	2.71	
2019	4745	3.07	494	37.70	2.17	0.18	111	2.76	1.85
2020	1571	7.09	312	38.90	3.18	0.31	175	2.97	7.61
2021	3794	5.69	492	38.10	-2.06	0.04	31.30	2.59	-12.79
2022	4138	2.05	427	35.00	-8.14	0.13	27.20	2.51	-3.09
Total	20088	2.05	1724	37.32		0.13	108	2.71	

Table 2. The Median Values Determined in this study for AFP, ß-hCG and uE3 levels, as well as the Median Changes Between 2018 and 2022

		AFP				β-hCG				uE3			
years	n	min	max	median	Annual variation	min	max	median	Annual variation	min	max	median	Annual variation
2018	4464	3.50	255	33.50		1578	146822	19789.50		0.07	5.50	0.75	
2019	3548	5.13	99.80	33.20	-0.90	1515	409414	19749.50	-0.20	0.08	3.06	0.72	-4.00
2020	1944	3.62	210	33.30	0.30	2984	119560	20143.00	1.99	0.07	3.06	0.72	0.00
2021	2800	7.34	302	32.85	-1.35	1566	206089	18757.00	-6.88	0.09	3.74	0.73	1.39
2022	2758	6.10	183	31.60	-3.81	2286	154740	18121.00	-3.39	0.07	3.62	0.68	-6.85
Total	15514	3.50	302	32.80		1515	409414	19312		0.07	5.50	0.72	

DISCUSSION

MOM values differ according to various parameters, such as ethnicity and region (28). Median values of MOM specific to each region must be calculated. Additionally, the median values for the same region differ between years. This is especially true for regions that receive immigration from different regions and races. Immigration from national and international areas to Antalya province continues to increase. Immigration to Antalya as foreign nationals has more than doubled from 2017 to 2019 (29). It has mixed socio-demographic and race characteristics due to migration into the city. Therefore, it is essential to follow the median of MOM annually.

Regional studies have been conducted in Türkiye investigating the medians of prenatal dual tests. İzmir region PAPP-A median was 2.85; â-hCG median was 37.80; AFP median was 32.30; ue3 median was 0.86 (19). Elazıg region's first-trimester fß-hCG median average is 34,4; the PAPP-A median was 3.08 (30). Yozgat region AFP median was 22.8, uE3 median was 1.34 (20). In the Istanbul region, the median value of AFP was 28.4 at week 16, 33.3 at week 17, 36.5 at week 18, and 43.4 at week 19, and the median value of uE3 was 0.58 at week 16, 0.76 at week 17, 0.98 at week 18 and 1.18 at week 19 (21). In the Şırnak region, the mean median Fβ-hCG (IU/l) value was 1.00 at week 11, 0.82 at week 12, and 0.84 at week 13, and the PAPP-A value was 1.05 at week 11, 1.04 at week 12 and 0.88 at week 13 (22). In the Kayseri region, the median PAPP-A values were 1.19 (11th week), 1.15 (12th week), 1.23 (13th week), while the fβ-hCG values were 1.16 (11th week), 1.24 (12th week), 1.26 (13th week) (23). In the

Bingöl region, the mean uE3 value was calculated as 1.61 in week 15, 1.94 in week 16, 2.33 in week 17, 2.81 in week 18, and 3.39 in week 19 (24). In Kırşehir, the AFP median was 32.1 in the 15th week, 34.2 in the 16th week, 39.4 in the 17th week, and 44.7 in the 18th week. β-hCG was 28,543 in the 15th week, 26,826 in the 16th week, 21,189 in the 17th week and 19,460 in the 18th week. The uE3 median was 0.42 in the 15th week, 0.62 in the 16th week, 0.8 in the 17th week, and 1.14 in the 18th week (31). In Çorum, the median β-hCG values were 42.1 in week 10, 35.5 in week 11, 307 in week 12, and 23.8 in week 13. The median PAPP-A values were 1.46 in week 10, 2.05 in week 11, 3.03 in week 12, and 4.74 in week 13. For Samsun, the median fβ-hCG values were 47.0 in the 10th week, 39.0 in the 11th week, 33.1 in the 12th week and 28.2 in the 13th week, while the median PAPP-A values were 1.26 in the 10th week, 1.87 in the 11th week, 2.84 in the 12th week and 3.92 in the 13th week (32). In this study for the Antalya region, the first-trimester fß-hCG median average is 37,32; the PAPP-A median average is 2,71; the second trimester AFP median average is 32,80; â-hCG median average is 19312; uE3 median average was 0,72.

When the median values of prenatal tests obtained in this study for the Antalya region were compared with those from other regions of Türkiye, some similarities and significant differences were observed in various test parameters. In the first trimester, the median values of free β-hCG and PAPP-A in Antalya were consistent with those in the western and central regions, such as Izmir (19) and Elazıg (30). However, lower values were reported in the inland and eastern regions, such as Kayseri (23) and Şırnak (22). In Samsun and Çorum, the median values of PAPP-A and fβ-hCG increased significantly as the weeks progressed (32). In the second trimester, the median AFP value in Antalya was similar to the values observed in weeks 15–17 in Izmir (19), Istanbul (21), and Kırşehir (31). However, it was lower in some regions, such as Yozgat (20), and higher in Istanbul (21) in the 19th week. Regarding uE3, the median value in Antalya is consistent with the early-week values in Istanbul (21). In contrast, in regions such as Bingöl (24), Yozgat, and Kırşehir (31), this parameter is observed to be higher. Additionally, Kırşehir's significant downward trend in β-hCG values by week shows a pattern consistent with the average value observed in Antalya (31). These data reveal that the medians used in prenatal screening tests can vary regionally, suggesting that region-specific medians should be used instead of national or international fixed references. Studies prove that MOM values differ between regions, with each region having different values. Moreover, challenges exist regarding establishing universally accepted cutoffs, as research shows substantial heterogeneity in outcomes when comparing data from diverse populations (33). This variance emphasizes the need for ongoing research to analyze and adjust tested parameters by global standards and local practices (34). This would reduce false positives and enable more accurate indications for invasive procedures.

The Antalya region receives much immigration and differs from the regions where other studies are being conducted, both geographically and ethnically (25). Therefore, there is a difference between MOM values. These values also vary over the years. This may be due to the biological variability of the tests, specific population-based differences, or environmental factors. Şerefli et al. state that standardising parameters in screening tests is complex due to differences in social structures and the variety of devices and methods used (31). They therefore suggest that each laboratory determine its median values to increase the tests' effectiveness and improve the accuracy of prenatal risk calculations. Especially since 2020 is a pandemic year, future studies should examine in more detail whether factors such as the health status of pregnant women, social isolation, and stress levels affect biological responses. The study's findings suggest that the regional median values of prenatal screening tests should be updated regularly. Research has emphasized the importance of using local median values, as failure may lead to misinterpretations and inadequate maternal care. Using regional median values in screening tests reduces the false-positive rate, preventing unnecessary interventional procedures, and reduces the false-negative rate, ensuring that high-risk pregnancies are not overlooked. This enhances the clinical accuracy and safety of prenatal risk assessments for both the mother and the fetus (20, 26, 35-37). Furthermore, the integration of local media within clinical processes has been demonstrated to facilitate the process and reduce the psychological burden on prospective parents. This psychological benefit is of significant importance, as it helps parents prepare for a range of pregnancy outcomes through more precise risk assessments (38, 39).

The findings highlight the need to adjust the median values used in prenatal screening tests to account for regional variations in clinical practice. Using region-specific medians in prenatal risk calculations, for example, can reduce false-positive rates and prevent unnecessary invasive procedures, such as amniocentesis. This approach is safer in terms of maternal and foetal health (32, 38), while also increasing the cost-effectiveness of the healthcare system. Calculating regional medians can lead to the more conscious allocation of health resources. Understanding the specific needs of the population through customised median values enables health authorities to prioritise funds and resources effectively. Furthermore, the significance of regional median calculations extends to informing national health policies. From a healthcare policy perspective, it is crucial to establish reliable and up-to-date reference median values for each region across the country and integrate these data into software systems. This would enable prenatal screening programmes to be conducted more accurately, fairly, and scientifically. Adapting healthcare providers' approaches based on local population data can improve counseling and follow-up

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procedures (40). Additionally, revising national screening protocols and creating new guidelines that consider regional biomarker variations will support clinicians' decision-making processes and enhance patient safety.

CONCLUSION

In conclusion, findings regarding regional averages of dual and triple screening test parameters in pregnancy emphasize the importance of local contexts in interpreting biomarker levels, which include demographic considerations, healthcare accessibility, and the necessity to adapt screening protocols to enhance clinical outcomes. A separate median of MOM should be calculated for each region's population, and these calculated medians should be updated regularly every year. Thus, advantages focused on the patient, the physician, the society, and the reimbursement institution can be provided. In particular, this will contribute to correctly using scarce resources to provide health services. In this context, it is recommended that awareness-raising policies be developed to disseminate prenatal screening tests and consider biological variability in these tests.

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REFERENCES

1.Gorlin RJ, Cohen M, Hennekam RCM. Syndromes of the Head and Neck. 4th ed. Oxford: Oxford University Press, 2001.
2.Wald NJ, Cuckle H, Brock JH, Peto R, Polani PE, Woodford FP. Maternal serum-alpha-fetoprotein measurement in antenatal screening for anencephaly and spina bifida in early pregnancy. Report of U.K. collaborative study on alphafetoprotein in relation to neural-tube defects. Lancet. 1977;1(8026):1323-32.
3.Hsiao CH, Chen JS, Shiao YM, Chen YJ, Chen CH, Chu WC, et al. Prenatal diagnosis using chromosomal microarray analysis in high-risk pregnancies. J Clin Med. 2022;11(13):3624.
4.Kim YJ, Lee JE, Kim SH, Shim SS, Cha DH. Maternal age-specific rates of fetal chromosomal abnormalities in Korean pregnant women of advanced maternal age. Obstet Gynecol Sci. 2013;56(3):160-6.
5.Akolekar R, Syngelaki A, Gallo DM, Poon LC, Nicolaides KH. Umbilical and fetal middle cerebral artery Doppler at 35–37 weeks' gestation in the prediction of adverse perinatal outcome. Obstet Gynecol Sci. 2015;46(1):82-92.
6.Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. Prenat Diagn. 2011;31(1):7-15.
7.Taylor-Phillips S, Freeman K, Geppert J, Agbebiyi A, Uthman OA, Madan J, et al. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. BMJ Open. 2016;6(1):e010002.
8.Ministry of Health. Genetik Hastalıklar Sağlık Personeli İçin El Kitabı, Ankara, 2002.
9.Aydın T, Aksoy H, Aktürk E, Aksoy Ü, Öz L. Birinci ve ikinci trimester prenatal tarama test sonuçlarının karşılaştırılması. Okmeydanı Tıp Derg. 2016;32(3):130-3.
10.Zaytseva ES, Zhukova TP, Ratnikova SY, Artemicheva IL. Analysis of trisomy 21 risk in early prenatal screening. Med Genet. 2020;19(3):79-80.
11.Karami Matin B, Kazemi Karyani A, Soltani S, Akbari S, Toloui Rakhshan S, Mohammadi Moghadam M. Sağlık sistemi işlevleri ile küresel ölçekte Down sendromu prevalansı arasındaki ilişki. Rehabilitasyon Arş. 2022;23(2):186-203.
12.Driscoll DA, Gross SJ. First trimester diagnosis and screening for fetal aneuploidy. Genet Med. 2008;10(1):73-5.
13.Watt HC, Wald NJ, Smith D, Kennard A, Densem J. Effect of allowing for ethnic group in prenatal screening for Down's syndrome. Prenat Diagn. 1996;16(8):691-8.
14.Cuckle HS, Wald NJ, Thompson SG. Estimating a woman's risk of having a pregnancy associated with Down's syndrome using her age and serum alpha-fetoprotein level. BJOG. 1987;94(5):387-402.
15.Peled Y, Melamed N, Krissi H, Eitan R, Yogev Y, Pardo J. The impact of severe hyperemesis gravidarum on the triple test screening results. J Matern Fetal Neonatal Med. 2012;25(6):637-8.
16.Aytan H, Çalışkan AC, Demirtürk F, Aysal DT, Hısım Y. The relation between first trimester screening markers and maternal folic acid and vitamin B12 levels. Nobel Med. 2011;7(2):55-60.
17.Bogart MH, Pandian MR, Jones OW. Abnormal maternal serum chorionic gonadotropin levels in pregnancies with fetal chromosome abnormalities. Prenat Diagn. 1987;7(6):623-30.
18.Alp HH, Huyut Z, Çokluk E, Şekeroğlu MR. İkili ve üçlü prenatal tarama testi medyan değerleri: Van ölçekli retrospektif bir çalışma. Turk Klin Biyokim Derg. 2018;16(1):17-24.
19.Üğe M, Demir L, Aksun S. Izmir province first and second trimester prenatal screening test current median values. Turk J Womens Health Neonatol. 2022;4(1):1-7.
20.Akarsu GD, Çetin A, Öztürk A, Akarsu RH. Yozgat bölgesinde üçlü tarama testi parametrelerinin medyan değerlerinin belirlenmesi. Turk Biyokim Derg. 2014;39(4):534-7.
21.Sucu V, Yıldırmak S, Vardar M, Mihmanlı V. İkili ve üçlü tarama testi biyokimyasal parametrelerinin hastanemize ait medyanlarının değerlendirilmesi. Abant Med J. 2018;7(2):35-40.
22.Tahiroğlu V, Alayunt NÖ, Coşkun E. Şırnak ili birinci trimester prenatal tarama testi güncel medyan verilerinin

değerlendirilmesi. Ahi Evran Med J. 2023;7(2):128-32.
23.Günay NE. İlk trimester tarama testi parametrelerinin Kayseri bölgesi için güncel medyan değerleri. Turk J Biochem. 2019;17(2):70-8.
24.Duran İ. Bingöl bölgesinde üçlü tarama testi parametrelerinin medyan değerlerinin belirlenmesi. Turk Klin Biyokim Derg. 2017;15(2):37-44.
25.Gün Atak P, Arpacı A, Seydal G. Adıyaman iline ait ikili ve üçlü prenatal tarama testlerinin medyan değerlerinin belirlenmesi. Turk Biyokim Derg. 2014;39(2):231-7.
26.Günay N. Determination of median values of triple screening test hormones for Kayseri region and their cross-regional comparisons. Perinatal J. 2019;27(2):68-76. https://doi.org/10.2399/prn.19.0272004
27.Kwon J, Park I, Park Y, Lee Y, Lee G, Shin J. Korean-specific parameter models for calculating the risk of Down syndrome in the second trimester of pregnancy. J Korean Med Sci. 2011;26(12):1619.
https://doi.org/10.3346/jkms.2011.26.12.1619
28.Spencer K, Heath V, El-Sheikhah A, Ong CY, Nicolaides KH. Ethnicity and the need for correction of biochemical and ultrasound markers of chromosomal anomalies in the first trimester: a study of Oriental, Asian and Afro-Caribbean populations. Prenat Diagn. 2005;25:365-9.
29.TUIK.https://data.tuik.gov.tr/Kategori/GetKategori?p=nufus-ve-demografi 109&dil=1 (Access date: 09.09.2024).
30.Ayyıldız H, Kalaycı M, Yılmaz M, Bozkurt M, Kaya M. İkili tarama testi parametrelerinin bölgesel medyan değerlerinin belirlenmesi. Nobel Med. 2018;14(2):49-53.
31.Şerefli K, Kırbaş A, Babaoğlu ÜT. Kırşehir ili üçlü test tarama parametrelerinin medyan değerlerinin belirlenmesi. Ahi Evran Med J. 2025;9(2):180-5.
32.Erdemli HK, Kocabaş R, Özdemir T, Bedir A. Is median value of double screening test regional?. Turk J Biochem. 2015;40(5):431-7.
33.Patel S, Verma N, Padhi P, Shah S, Nanda R, Mohapatra E. An approach to re-evaluate the reference cutoff of the parameters of newborn screening: an observational study. Cureus. 2023. https://doi.org/10.7759/cureus.45139
34.Liehr T. Non-invasive prenatal testing: what patients do not learn may be due to lack of specialist genetic training by gynecologists and obstetricians. Front Genet. 2021;12. https://doi.org/10.3389/fgene.2021.682980
35.Reynolds T. The triple test as a screening technique for Down syndrome: reliability and relevance. Int J Womens Health. 2010;83. https://doi.org/10.2147/ijwh.s8548
36.Görkem Ü, Güreser A, Toğrul C, Karasartova D, Güngör T, Özkan A, et al. Influence of maternal toxoplasmosis on the second-trimester aneuploidy screening test. Gynecol Obstet Reprod Med. 2018;24(2):71-5.
37.Olukçu G, Hançerlioğulları N, Tanrıverdi MDE, Dadaş Y, Tokmak A. İkinci trimester maternal serum serbest estriol seviyesinin yenidoğan umblikal arter pH değeri ile ilişkisi. Jinekoloji Obstetrik Neonatoloji Tıp Derg. 2024;21(4):267-73.
38.Glynou A, Galatis D, Yalelis V, Sotiriadis A, Pampanos A, Sarella A, et al. Breaking bad news during prenatal screening: the role of professional obstetricians and midwives in Greece. Cureus. 2024.
39.Chitty L, Wright D, Hill M, Verhoef T, Daley R, Lewis C, et al. Uptake, outcomes, and costs of implementing non-invasive prenatal testing for Down's syndrome into NHS maternity care: prospective cohort study in eight diverse maternity units. BMJ. 2016;353:i3426.
40.Hsiao C, Chen C, Cheng P, Shaw S, Chu W, Chen R. The impact of prenatal screening tests on prenatal diagnosis in Taiwan from 2006 to 2019: a regional cohort study. BMC Pregnancy Childbirth. 2022;22(1).

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