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ORIGINAL RESEARCH
Pediatric Cardiology

The impact of maternal age on congenital heart defects and their severity in Down syndrome

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ABSTRACT

Objective: Advanced maternal age is known to be a risk factor for Down syndrome. This study aimed to investigate whether maternal age affects the development and severity of congenital heart defects in patients with Down syndrome.

Material and Methods: A total of 394 patients with Down syndrome who presented to our center between 2018 and 2024 and underwent at least one echocardiographic examination in the pediatric cardiology outpatient clinic were included in the study. Maternal age, gravidity, parity, gestational age, and birth weight were retrospectively evaluated, and their relationships with the severity of congenital heart defects were analyzed.

Results: The study included 221 boys (53.6%) and 183 girls (46.4%). The mean gestational age was 36.85±2.46 weeks, and the mean birth weight was 2783.25±574.21 g. The mean maternal age among patients for whom this information was available was 37±5.96 years. The most common congenital heart defects were ventricular septal defect (24.87%), atrioventricular septal defect (16.49%), atrial septal defect (10.91%), and tetralogy of Fallot (4.56%). Of the cases, 41.6% required intervention, whereas 35.25% had no cardiac pathology.

Conclusion: No statistically significant correlation was found between maternal age and the type or severity of congenital heart defects. Investigating the influence of other factors and conducting multicenter studies, where possible, may be beneficial.

Keywords: Congenital heart defect; Down syndrome; echocardiography; maternal age.

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Down sendromlu bebeklerde doğuştan kalp kusurları ve şiddeti üzerine anne yaşının etkisi

ÖZET

Amaç: İleri anne yaşı, Down sendromu için bir risk faktörü olarak bilinmektedir. Bu çalışma, anne yaşının Down sendromlu hastalarda doğuştan kalp kusurlarının gelişimi ve şiddeti üzerindeki etkisini araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: 2018–2024 yılları arasında merkezimize başvuran ve pediatrik kardiyoloji polikliniğinde en az bir kez ekokardiyografi yapılan 394 Down sendromlu hasta çalışmaya dahil edildi. Anne yaşı, gebelik ve doğum sayısı, doğum haftası ve doğum ağırlığı retrospektif olarak değerlendirildi ve bunların doğuştan kalp kusurlarının şiddetiyle ilişkisi analiz edildi.

Bulgular: Çalışmaya 221 erkek (%53,6) ve 183 kız (%46,4) hasta dahil edildi. Olguların ortalama doğum haftası 36,85±2,46 hafta, ortalama doğum ağırlığı ise 2783,25±574,21 g idi. Yaşları bilinen annelerin ortalama yaşı 37±5,96 yıldı. En sık görülen doğuştan kalp kusurları sırasıyla ventriküler septal defekt (%24,87), atriyoventriküler septal defekt (%16,49), atriyal septal defekt (%10,91) ve Fallot tetralojisi (%4,56) idi. Olguların %41,6'sına müdahale gerekti. Olguların %35,25'inde herhangi bir kalp patolojisi yoktu.

Tartışma: Anne yaşı ile doğuştan kalp kusurlarının türü ve şiddeti arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. Diğer faktörlerin etkisinin araştırılmasının ve mümkünse çok merkezli çalışmalar yapılmasının yararlı olacağı sonucuna varıldı.

Anahtar Kelimeler: Anne yaşı; doğuştan kalp kusuru; Down sendromu; ekokardiyografi.

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INTRODUCTION

Down syndrome is the most prevalent chromosomal anomaly compatible with life, occurring in approximately 16 per 10,000 live births (1). Congenital heart defects are observed in 40%–60% of patients with Down syndrome (2–4). and approximately 50% of these defects are severe (5).

Advanced maternal age is generally accepted as a risk factor for Down syndrome (6). Age-related changes in oocyte quality are thought to play a role in this association (6). However, it remains unclear whether maternal age, gravidity, parity, and birth characteristics affect the risk and severity of congenital heart defects (6). This study aimed to investigate the relationships between maternal age, gravidity, parity, gestational age, birth weight, and the prevalence and severity of congenital heart defects in patients with Down syndrome.

Although advanced maternal age is a well-established risk factor for Down syndrome, its specific role in determining the phenotypic severity of associated cardiac defects remains poorly understood. This study addresses a critical gap in prenatal counseling by evaluating whether maternal age can serve as a predictor of the clinical management needs of these infants.

MATERIAL AND METHODS

This retrospective cohort study analyzed the effect of maternal age on the severity of congenital heart defects in patients with Down syndrome.

The study included patients with a genetic diagnosis of Down syndrome who presented to our center between 2018 and 2024 and underwent at least one echocardiographic examination in the pediatric cardiology outpatient clinic. Patients who did not undergo echocardiographic examination were excluded from the study. The patients' sex, gestational age, birth weight, maternal age, gravidity, parity, consanguinity, and the type and severity of congenital heart defects detected by echocardiography were evaluated.

The gestational ages of the patients were classified as <28 weeks, 28–32 weeks, 32–37 weeks, and >37 weeks. Birth weights were classified as 1000–1500 g, 1500–2500 g, and >2500 g. Cases with more than one congenital heart defect detected on echocardiography were classified according to the major defect. Congenital heart defects were classified into three groups according to their severity. Group 1 included cases with normal echocardiographic findings, patent foramen ovale, or physiological valvular insufficiency. Group 2 included moderately severe defects that did not require intervention or surgery but required follow-up, hemodynamically insignificant defects (e.g., small ventricular or atrial septal defects), and valvular insufficiencies (e.g., mild insufficiency requiring endocarditis prophylaxis during surgical procedures). Group 3 included cases with severe defects requiring medical, surgical, or catheter-based intervention or those with severe pulmonary hypertension.

A dataset comprising 394 patients with Down syndrome was analyzed to identify associations between congenital heart defect type and other patient characteristics. Maternal age was treated as a continuous variable, whereas sex, gestational age, birth weight, gravidity, parity, twin status, consanguinity, and echocardiographic findings were treated as categorical variables. Analyses were conducted using an available-case approach. Patients with missing data for a specific variable were excluded only from analyses involving that variable. Data entry and storage were performed using Microsoft Excel 2016. Data cleaning, recoding, descriptive summaries, and quality control procedures were performed using R version 4.4.0 with the "dplyr" and "summarytools" packages. All inferential statistical analyses and hypothesis tests were performed using SPSS version 30 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA).

Statistical Analysis

All formal statistical analyses and tests were conducted using SPSS version 30 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) on a personal computer. Data storage, preprocessing, and chart creation were performed using Microsoft Excel 2016. The normality of variable distributions was assessed using the Kolmogorov–Smirnov test, histograms, coefficients of variation, detrended Q–Q plots, and skewness and kurtosis analyses. A p-value of <0.05 was considered statistically significant. Group comparisons were performed using the independent-samples t-test and Mann–Whitney U test, as appropriate, because of the non-Gaussian distribution of the data.

Categorical variables were compared using Pearson's chi-square test when the assumptions of the test were satisfied, namely, when no more than 20% of the expected cell counts were <5 and no expected cell count was <1. For contingency tables larger than 2×2 in which these assumptions were violated because of sparse data or low expected cell frequencies, the Fisher–Freeman–Halton exact test was applied. Before the analyses, expected frequencies were examined for all contingency tables to determine the appropriate statistical test. The association between echocardiographic findings and sex was analyzed using Pearson's chi-square test, whereas comparisons involving variables with sparse categories, including gestational age, birth weight, gravidity, parity, twin status, and consanguinity, were evaluated using the Fisher–Freeman–Halton exact test when the assumptions of the chi-square test were not met. For statistically significant associations identified using the chi-square test, Cramér's V coefficient was calculated to assess the strength of the association between categorical variables.

Ethical Approval

This study was conducted in accordance with the ethical principles outlined in the 2013 revision of the Declaration of Helsinki. All participants provided written informed consent or, in the case of minors, written assent with parental consent before participation in the study.

Table 1. The frequency and percentages of birth weeks and birth weights

	n	%
Birth week	282	
<28 weeks	2	0.7
28–32 weeks	11	3.9
32–37 weeks	129	45.7
>37 weeks	140	49.6
Birth weight	286	
1–1.5 kg	6	2.1
1.5–2.5 kg	77	26.9
>2.5 kg	203	71.0

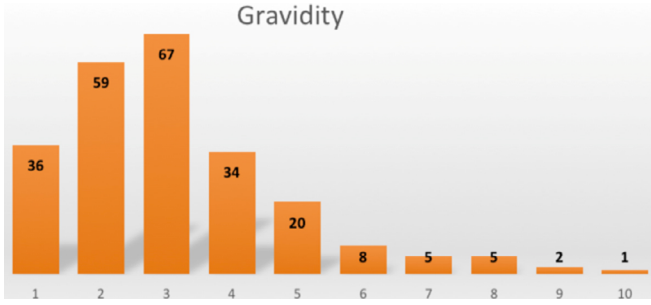

Figure 1. Distribution of gravidity.

Ethical approval was granted by the Clinical Research Ethics Committee of the University of Health Sciences Zeynep Kamil Gynecology and Pediatrics Training and Research Hospital (approval number: 159; date: December 6, 2023).

RESULTS

The study included a total of 394 patients (221 boys [53.6%] and 183 girls [46.4%]) who were genetically and phenotypically diagnosed with Down syndrome. The boy-to-girl ratio was 1.15. The mean gestational age of the cases was 36.85±2.46 weeks, and their mean birth weight was 2783.25±574.21 g.

One hundred and forty cases (49.6%) were born at ≥37 weeks, 129 cases (45.7%) were born between 32 and 37 weeks, 11 cases (3.9%) were born between 28 and 32 weeks, and 2 cases (0.7%) were born before 28 weeks of gestation (Table 1).

The mean age of the mothers whose ages were known was 37±5.96 years (minimum: 21; maximum: 48). Gravidity ranged from 1 to 10, and parity ranged from 1 to 10, as demonstrated in Figures 1 and 2, respectively. Eight cases were twins. Consanguineous marriage was present in the families of 21 cases (11.4%).

As shown in Figure 1, Down syndrome was most frequently observed in the third, second, first, fourth, and fifth pregnancies, respectively. Among 237 cases, 15.2% were G1, 24.9% were G2, 28.3% were G3, 14.3% were G4, 8.4% were G5, 3.4% were G6, 2.1% were G7, 2.1% were G8, 0.8% were G9, and 0.4% were G10. Gravidity data were unavailable for 157 cases.

Table 2. Type of congenital heart defect seen on echocardiography

Type of defect	n	%
Ventricular septal defect	98	24.87
Atrio ventricular septal defect	65	16.49
Atrial septal defect	43	10.91
Tetralogy of fallot	18	4.56
Patent ductus arteriosus	15	3.80
Coarctation of aorta	3	0.76
Hypoplastic left ventricular syndrome	1	0.25
Aortic arch anomaly	3	0.76
Coronary artery fistula	2	0.50
Mitral valve prolapse	1	0.25
Partial anomalous pulmonary venous return	1	0.25
Wolff-Parkinson-white syndrome	5	1.26
Normal/patent foramen ovale	139	35.27

As shown in Figure 2, which demonstrates the distribution of parity, third-, second-, and first-born children were the most common among the 240 cases in our study group. Parity data were unavailable for 154 cases.

Six cases had translocation-type trisomy, six had mosaic trisomy, one had 48,XXY,+21, and one had 48,XXX,+21.

The types of congenital heart defects observed are presented in Table 2. Cases with more than one defect were classified according to the major defect.

Although the most commonly observed congenital heart defect was ventricular septal defect (24.87%), only 53 defects were significant and required treatment, whereas the remaining defects were hemodynamically insignificant and expected to close spontaneously. Five cases of atrioventricular septal defect (AVSD) were accompanied by aortic coarctation, pulmonary stenosis, tetralogy of Fallot, or atrial isomerism. All AVSD cases except one were balanced. Six patients had intermediate or transitional AVSD. Atrioventricular septal defect was more common in girls than in boys (36 girls and 29 boys), whereas

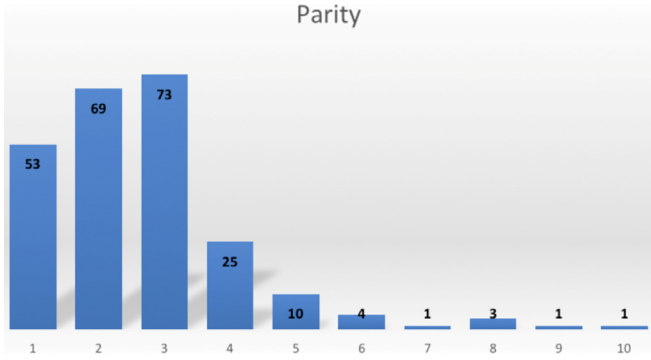

Figure 2. Distribution of parity.

tetralogy of Fallot was more common in boys (11 boys and 7 girls). Tetralogy of Fallot (ToF) was observed in 18 patients. One patient with ToF also had a ventricular septal defect (VSD) and pulmonary atresia.

When the cases were classified according to their echocardiographic findings, 139 cases (35.3%) were in Group 1, 91 cases (23.1%) were in Group 2, and 164 cases (41.6%) were in Group 3, as shown in Figure 3.

The distribution of congenital heart defect groups according to sex is presented in Table 3.

Maternal ages were classified as <35 years, 35–40 years, and >40 years to evaluate the frequency of each congenital heart defect group according to maternal age, as shown in Table 4.

Pearson's chi-square test was used to analyze the association between echocardiographic findings and sex because the assumptions of the chi-square test were satisfied. For variables with sparse categories and low expected cell frequencies, including gestational age, birth weight, gravidity, parity, twin status, and consanguinity, the Fisher–Freeman–Halton exact test was applied. No statistically significant associations were identified between echocardiographic findings and gestational age, birth weight, gravidity, parity, twin status, consanguinity, or maternal age categories ($p>0.05$).

A statistically significant relationship was found between echocardiographic findings and sex ($p<0.05$). The strength of this relationship, evaluated using Cramér's V, was relatively

Table 3. Distribution of congenital heart defect group

	Group 1		Group 2		Group 3		Total	
	n	%	n	%	n	%	n	%
Male	92	23	45	11	74	19	211	53
Female	47	12	46	12	90	23	183	47
Total	139	35	91	23	164	42	394	100

Group 1: Normal echocardiograms, Group 2: Moderately severe or hemodynamically insignificant defects (e.g., small VSD/ASD) and requiring follow-up but no immediate intervention. Group 3: Severe defects requiring medical, surgical, or invasive intervention, or presence of severe pulmonary hypertension. Row% represents the percentage within the gender; Total% represents the percentage within the entire cohort. $\chi^2(2)=14.222$, $p=0.000816$ (Pearson Chi-square); Cramer's V=0.1899926.

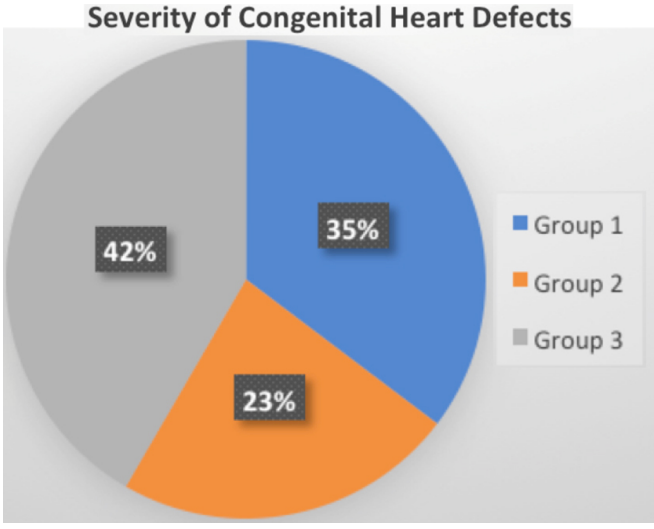

Figure 3. Distribution of congenital heart defects according to severity.

Group 1: Normal echocardiograms, Group 2: Moderately severe or hemodynamically insignificant defects (e.g., small VSD/ASD) and requiring follow-up but no immediate intervention. Group 3: Severe defects requiring medical, surgical, or invasive intervention, or presence of severe pulmonary hypertension.

weak despite being statistically significant (Cramér's V=0.190). Female patients had a higher proportion of severe congenital heart defects than male patients (Group 3: 23% vs. 19%; $p<0.05$).

The Kruskal–Wallis test was used to analyze the relationship between maternal age as a numerical variable and echocardiographic findings. No statistically significant difference was found among the groups ($p>0.05$).

DISCUSSION

The primary finding of this study is that maternal age does not significantly influence the type or severity of congenital heart defects in children with Down syndrome. Although advanced maternal age increases the risk of nondisjunction, our data suggest that it does not necessarily determine the subsequent cardiac phenotype.

It is widely accepted that the risk of Down syndrome increases with advanced maternal age, particularly after 35 years (7, 8). Approximately 88% of cases result from meiotic nondisjunction and are of maternal origin (9). The remaining cases are attributed to translocation (4.5%), mosaicism (2.3%), and, rarely, duplication (9).

The boy-to-girl ratio of 1.15 in our study was close to the average European ratio of 1.3 (10). Approximately half of the cases were premature births, most of which were late preterm. The birth weights of 70% of the cases were >2500 g. These findings were consistent with those of similar studies (11, 12). Most cases were conceived during the third pregnancy and were third-born children, which may be associated with the increasing risk of Down syndrome with advancing maternal age.

The prevalence of congenital heart defects in patients with Down syndrome is generally reported to be approximately 40%–60% (2–4, 13), ranging from 27% to 79% across different studies and populations (1). With advances in perinatology and the increase in voluntary pregnancy termination, the prevalence and types of congenital heart defects in Down syndrome have changed (14). In societies where pregnancy termination is culturally, religiously, or legally prohibited, however, no such change has been observed (12, 15). In our study, 65% of the cases had cardiac findings, and 42% had severe congenital heart defects.

Atrioventricular septal defect is usually reported as the most common type of congenital heart defect in Down syndrome (3, 6, 16, 17). In 1992, identified a narrow locus on chromosome 21 associated with atrioventricular septal defect (2, 9). However, the etiology of congenital heart defects in Down syndrome has not yet been fully elucidated and is thought to be multifactorial, with contributions from genetic factors and environmental exposures.

A smaller number of studies, however, have reported ventricular septal defect as the most common type of congenital heart defect in Down syndrome (11), with a particularly high prevalence among Asian patients (5, 6, 11). Similarly, ventricular septal defect was the most frequent type of congenital heart defect in our study. However, when hemodynamically insignificant ventricular septal defects were excluded, atrioventricular septal defect was more common.

A statistically significant but weak association was found between sex and congenital heart defect type. Consistent

Table 4. Distribution of congenital heart defect groups according to grouped maternal age

	Group 1		Group 2		Group 3		Total	
	n	%	n	%	n	%	n	%
<35	22	10.3	23	10.7	31	14.5	76	35.5
35-40	22	10.3	16	7.5	35	16.4	73	34.2
>=40	17	7.9	22	10.3	26	12.1	65	30.3
Total	61	28.5	61	28.5	92	43	214	100

Group 1: Normal echocardiograms, Group 2: Moderately severe or hemodynamically insignificant defects (e.g., small VSD/ASD) and requiring follow-up but no immediate intervention. Group 3: Severe defects requiring medical, surgical, or invasive intervention, or presence of severe pulmonary hypertension. p- value >0.05 (Pearson Chi-square). No statistically significant association was found.

with similar studies, atrioventricular septal defect was more common in girls, whereas tetralogy of Fallot was more common in boys (10, 18). Severe congenital heart defects classified as Group 3 were observed in two of the six patients with translocation-type Down syndrome and in two of the six patients with mosaic-type Down syndrome. These rates were not considerably different from those observed in patients with the classical type.

Interestingly, although the prevalence of Wolff–Parkinson–White syndrome has been reported to be 1–3 per 1000 individuals in large-scale general population studies (19), five patients in our study who had normal echocardiographic findings were diagnosed with Wolff–Parkinson–White (WPW) syndrome on electrocardiography. Although this association with WPW syndrome is noteworthy, it may be coincidental given the limited sample size of the present study. Further studies involving larger patient populations are required.

Although it is widely accepted that advanced maternal age increases the risk of Down syndrome, no association between advanced maternal age and the risk or severity of congenital heart defects in patients with Down syndrome has been reported in the literatüre (6, 9). Similarly, in our study, almost half of the congenital heart defects were severe and required intervention; however, no association was found between the severity of congenital heart defects and maternal age, gestational age, birth weight, gravidity, or parity. No formal sample size calculation was performed because all eligible patients during the study period were included. Consequently, analyses involving rare congenital heart defects may have been underpowered, and nonsignificant findings should be interpreted with caution.

This study has several limitations. First, its retrospective design and the relatively high proportion of missing maternal and perinatal data may have introduced selection bias. Although no significant differences were identified between patients with and without available maternal age data, residual bias cannot be completely excluded. In addition, data regarding certain maternal lifestyle factors were unavailable. Second, as this was a single-center study, the findings may not be fully generalizable to other populations. Third, because of the high proportion of missing data for several covariates, multivariable regression analysis was not performed. Consequently, residual confounding cannot be excluded, and the independent effect of maternal age should be interpreted with caution.

CONCLUSION

In conclusion, our study demonstrates that although maternal age is a critical factor in the occurrence of Down syndrome, it does not significantly influence the clinical severity or specific type of congenital heart defects in these patients. The findings suggest that the cardiac phenotype in trisomy 21 is likely determined by complex genetic and environmental interactions that are independent of maternal age. Within the limitations of this retrospective, single-center cohort, maternal age was not significantly associated with the type or severity of congenital heart defects. However, these findings should not be interpreted as definitive evidence of the absence of an association. Therefore, prenatal and postnatal cardiac management should focus on the specific anatomical defect rather than solely on maternal demographic risk factors. Future prospective, multicenter studies with larger cohorts are needed to further elucidate the multifactorial determinants of congenital heart defect severity in this population.

This study may contribute to the literature by classifying congenital heart defects and birth characteristics, including maternal age, birth weight, gestational age, gravidity, and parity, in patients with Down syndrome. The absence of a statistically significant correlation between these parameters and the severity of congenital heart defects highlights the need for further studies investigating the potential influence of other factors.

Ethics Committee Approval: This study was approved by the Ethics Committee of of University of Health Sciences, Zeynep Kamil Women's and Children's Diseases Training and Research Hospital (Date: Dec 6, 2023, Decision No. 159).

Informed Consent: All participants provided written informed consent or, in the case of minors, written assent with parental consent before participation in the study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

Authorship Contributions: Concept – NE; Design – NE, ZEE; Supervision – NE, ÇE, AA, ZEE; Fundings – NE; Materials – NE; Data Collection and/or Processing – NE; Analysis and/or Interpretation – ÇE; Literature Search – NE; Writing – NE, ZEE; Critical Reviews – NE, AA.

Peer-review: Externally peer-reviewed.

Etik Kurul Onayı: Bu çalışma, Sağlık Bilimleri Üniversitesi Zeynep Kamil Kadın ve Çocuk Hastalıkları Eğitim ve Araştırma Hastanesi Etik Kurulu tarafından onaylanmıştır (Tarih: 6 Aralık 2023, Karar No: 159).

Hasta Onamı: Tüm katılımcılar, çalışmaya katılmadan önce yazılı bilgilendirilmiş onam vermiş; reşit olmayan katılımcılar ise ebeveynlerinin onayıyla yazılı rıza göstermiştir.

Çıkar Çatışması: Yazar, herhangi bir çıkar çatışması bulunmadığını beyan eder.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

Yazma Yardımı için Yapay Zeka Kullanımı: Bu makale için yapay zekadan herhangi bir destek alınmamıştır.

Yazarlık Katkıları: Fikir – NE; Tasarım – NE, ZEE; Denetlemeler – NE, ÇE, AA, ZEE; Kaynaklar – NE; Malzemeler – NE; Veri toplanması ve/veya işleme – NE; Analiz ve/veya yorumlama – ÇE; Literatür araştırması – NE; Yazım – NE, ZEE; Eleştirel incelemeler – NE, AA.

Hakemli inceleme: Harici olarak hakemli.

REFERENCES

1. Dimopoulos K, Constantine A, Clift P, Condliffe R, Moledina S, Jansen K, et al. Cardiovascular complications of Down syndrome: scoping review and expert consensus. Circulation 2023;147:425–41.
2. Bergström S, Carr H, Petersson G, Stephansson O, Bonamy AK, Dahlström A, et al. Trends in congenital heart defects in ınfants with Down syndrome. Pediatrics 2016;138:e20160123.
3. Flanders L, Tulloh R. Cardiac problems in Down syndrome. Paediatr Child Health 2011;21:25–31.
4. Baum RA, Nash PL, Foster JE, Spader M, Ratliff-Schaub K, Coury DL. Primary care of children and adolescents with Down syndrome: an update. Curr Probl Pediatr Adolesc Health Care 2008;38:241–61.
5. Zahari N, Mat Bah MN, A Razak H, Thong MK. Ten-year trend in prevalence and outcome of Down syndrome with congenital heart disease in a middle-income country. Eur J Pediatr 2019;178:1267–74.
6. Freeman SB, Bean LH, Allen EG, Tinker SW, Locke AE, Druschel C, et al. Ethnicity, sex, and the incidence of congenital heart defects: a report from the National Down Syndrome Project. Genet Med 2008;10:173–80.
7. Heinke D, Isenburg JL, Stallings EB, Short TD, Le M, Fisher S, Shan X, et al. Prevalence of structural birth defects among infants with Down syndrome, 2013-2017: A US population-based study. Birth Defects Res 2021;113:189–202.
8. Cuckle H, Morris J. Maternal age in the epidemiology of common autosomal trisomies. Prenat Diagn 2021;41:573–83.
9. Asim A, Agarwal S. Congenital heart defects among Down's syndrome cases: an updated review from basic research to an emerging diagnostics technology and genetic counselling. J Genet 2021;100:45.
10. Santoro M, Coi A, Spadoni I, Bianchi F, Pierini A. Sex differences for major congenital heart defects in Down Syndrome: A population based study. Eur J Med Genet 2018;61:546–50.
11. Ergaz-Shaltiel Z, Engel O, Erlichman I, Naveh Y, Schimmel MS, Tenenbaum A. Neonatal characteristics and perinatal complications in neonates with Down syndrome. Am J Med Genet A 2017;173:1279–86.
12. Nakousi Capurro N, Cares Basualto C, Alegría Olivos A, Gaínza Lein M, López Aristizabal L, Gayan Torrente A, et al. Congenital anomalies and comorbidities in neonates with Down Syndrome. Rev Chil Pediatr 2020;91:732–42. [Article in English, Spanish]
13. 13) Yilmaz Gulec E, Cetin S, Gunes M, Gezdirici A. Down syndrome: From pregnancy through childhood in Türkiye. Mol Syndromol 2026;17:221–37.
14. Bergström S, Carr H, Petersson G, Stephansson O, Bonamy AK, Dahlström A, et al. Trends in congenital heart defects in infants with Down syndrome. Pediatrics 2016;138:e20160123.
15. Huete-García A, Otaola-Barranquero M. Demographic assessment of Down syndrome: A systematic review. Int J Environ Res Public Health 2021;18:352.
16. Baum RA, Nash PL, Foster JE, Spader M, Ratliff-Schaub K, Coury DL. Primary care of children and adolescents with Down syndrome: an update. Curr Probl Pediatr Adolesc Health Care 2008;38:241–61.
17. Stoll C, Dott B, Alembik Y, Roth MP. Associated congenital anomalies among cases with Down syndrome. Eur J Med Genet 2015;58:674–80.
18. Diogenes TCP, Mourato FA, de Lima Filho JL, Mattos SDS. Gender differences in the prevalence of congenital heart disease in Down's syndrome: a brief meta-analysis. BMC Med Genet 2017;18:111.
19. Pediatric and Congenital Electrophysiology Society (PACES); Heart Rhythm Society (HRS); American College of Cardiology Foundation (ACCF); American Heart Association (AHA); American Academy of Pediatrics (AAP); Canadian Heart Rhythm Society (CHRS); et al. PACES/HRS expert consensus statement on the management of the asymptomatic young patient with a Wolff-Parkinson-White (WPW, ventricular preexcitation) electrocardiographic pattern: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Endorsed by the governing bodies of PACES, HRS, the American College of Cardiology Foundation (ACCF), the American Heart Association (AHA), the American Academy of Pediatrics (AAP), and the Canadian Heart Rhythm Society (CHRS). Heart Rhythm 2012;9:1006–24.