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Original Research

Prenatal Detection of Common Trisomies Based on Second- and Third-Trimester Ultrasound Scans

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Abstract

Background: Trisomy 18 and trisomy 13 are severe chromosomal abnormalities frequently associated with stillbirth or early neonatal death, whereas trisomy 21 is the most common trisomy among live births. In settings without routine first-trimester aneuploidy screening, second- and third-trimester ultrasound scans often provide the earliest opportunity for detection. This study aimed to assess the incidence and ultrasound detection rates (DRs) of common fetal trisomies diagnosed during late-trimester scans at our center. **Methods:** This retrospective cohort study included all liveborn neonates with a confirmed diagnosis of trisomy 21, 18, or 13 over a five-year period at a single tertiary care center. Maternal clinical records and prenatal ultrasound reports were retrospectively reviewed. Continuous variables were expressed as mean ± standard deviation (SD) and range (minimum-maximum), and categorical variables were reported as frequency and percentage. **Results:** Among 37,540 pregnancies managed at our institute, 126, 17, and 7 cases were diagnosed with trisomy 21, 18, and 13, respectively. Mean maternal age was 38.1 ± 5.9, 40.6 ± 3.7, and 41.5 ± 4.3 years, respectively. Late second- or third-trimester anatomy scans were performed in 63.5% of trisomy 21, 52.9% of trisomy 18, and 71.4% of trisomy 13 cases. Abnormal ultrasound findings were identified in 50/80 (62.5%) among trisomy 21, compared with all 9/9 (100%) trisomy 18 cases and all 5/5 (100%) trisomy 13 cases. Common findings included polyhydramnios, fetal growth restriction (FGR), abnormal Doppler findings, structural anomalies, and soft markers. Notably, 37.5% of trisomy 21 cases had normal ultrasound examinations. Neonatal mortality occurred in all trisomy 18 and trisomy 13 cases. **Conclusions:** Late-trimester ultrasound may support risk assessment but is insufficient for reliable detection of trisomy 21. First-trimester aneuploidy screening and earlier prenatal evaluation are recommended to improve detection, counseling, and multidisciplinary care.

Keywords: trisomy; Down syndrome; Edwards syndrome; Patau syndrome; prenatal diagnosis; ultrasound

1. Introduction

Fetal chromosomal abnormalities have been detected using invasive diagnostic testing since the 1950s. Initially, aneuploidy screening relied solely on maternal age-based risk assessment; however, screening subsequently evolved to incorporate serum biochemical and ultrasound markers [1,2,3,4]. Most prenatal tests were developed as screening tools to identify pregnancies at an increased risk of fetal congenital abnormalities [1,5]. Over the past few decades, early detection of pregnancies at high risk for aneuploidy has become the primary objective of prenatal screening [6,7,8].

First trimester screening typically includes assessment of nuchal translucency (NT) along with biochemical markers such as beta-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein A (PAPP-A). This combined approach achieves a detection rate (DR) of approximately 82% with a 3% false-positive rate [9,10,11]. In contrast, second-trimester screening relies on maternal serum biochemical testing of β-hCG, α-fetoprotein (AFP), unconjugated estriol, and inhibin-A, collectively referred to as the "quadruple test". The quadruple test has a lower DR of approximately 64%, with a 3% false-positive rate [12,13,14].

Prenatal diagnosis (PND) plays a crucial role in providing essential information to expectant parents. It enables informed decision-making regarding pregnancy continuation and facilitates psychological, social, financial, and medical preparation for raising a child with congenital or genetic conditions [1,2]. Moreover, it allows for anticipation and management of potential complications such as stillbirth or intrauterine fetal demise.

Ultrasound examination was initially introduced as a screening tool before the emergence of current biochemical and genetic screening tests. Currently, the role of second-trimester ultrasound screening is more limited and is primarily reserved for centers where first-trimester screening is unavailable, women who missed early screening, those

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identified as high risk after first-trimester testing, and twin pregnancies [15,16]. In multiple gestations, biochemical marker screening is less accurate than in singleton pregnancies because fetoplacental products from an unaffected twin may mask abnormal levels produced by an affected twin. Therefore, some centers rely solely on nuchal fold thickness measurement for aneuploidy screening in twin gestations [16,17].

Major structural abnormalities, such as atrioventricular canal defects and duodenal atresia, occur significantly more frequently in fetuses with chromosomal abnormalities than in euploid fetuses [18,19]. Minor abnormalities, often referred to as soft markers, may be observed in otherwise normal fetuses but are also associated with an increased risk of aneuploidy [20,21,22,23,24,25]. These include absent or hypoplastic nasal bone [21,22], intracardiac echogenic focus [18,21], fetal ventriculomegaly [2], choroid plexus cysts, thickened nuchal fold, and echogenic bowel [18,19,26].

The FaSTER (First and Second Trimester Evaluation of Risk) trial demonstrated that a detailed anomaly scan achieved a 59% DR with a 3% false-positive rate. Concurrent biochemical testing further improved diagnostic accuracy. When the quadruple test was combined with an anomaly scan, the DR increased to 80%, and reached 77% when a contingent approach was applied, in which the anomaly scan was performed only in cases with borderline quadruple test results. This combined approach may be particularly beneficial in countries where second-trimester biochemical screening is already established, or as an option for women who missed earlier first-trimester screening [21]. In a prospective study, Nyberg et al. [27] identified urinary tract dilation and shortened long bones as notable findings, with fetuses affected by trisomy 21 being 5.4 times more likely to exhibit a short humerus than euploid fetuses. Furthermore, ultrasound findings associated with chromosomal abnormalities are not limited to major structural malformations but may also include alterations in fetal growth and body proportions. Previous studies have demonstrated differences in fetal biometric characteristics, including the head-to-trunk volume ratio, in chromosomally abnormal fetuses, supporting the potential value of detailed fetal morphologic assessment in identifying pregnancies at increased risk of aneuploidy [28].

Trisomy 21, 18, and 13 are the three most common autosomal trisomies encountered during pregnancy. Trisomy 21 (Down syndrome) is the most common among live births and is associated with intellectual disability and congenital anomalies, with improved survival due to advances in care. Trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome) are less common but are associated with high rates of fetal loss, multiple structural anomalies, and early neonatal mortality [29,30,31,32]. While first-trimester screening allows earlier diagnosis, detailed second- and third-trimester ultrasound examinations remain crucial for detecting structural abnormalities and soft markers suggestive of these trisomies, particularly in settings where early screening is unavailable or has been missed. Late-trimester ultrasound therefore plays a key role in identifying affected fetuses, guiding diagnostic testing, counseling parents, and planning perinatal management. As such, the aim of this study was to analyze the incidence of common trisomies suspected on late-trimester ultrasound scans.

2. Materials and Methods

This retrospective cohort study was conducted over a five-year period (January 2017 to December 2021) at the Department of Obstetrics and Gynecology, Prince Sultan Military Medical City (PSMMC), Riyadh, Saudi Arabia. The inclusion criteria comprised all liveborn neonates with confirmed trisomy 21, 18, or 13 based on pre- and/or postnatal cytogenetic testing. The study included only affected cases and excluded unaffected pregnancies. All women with ultrasound findings suggestive of fetal aneuploidy were counseled regarding available options for prenatal genetic testing, including invasive diagnostic procedures and noninvasive prenatal testing (NIPT). Invasive PND by amniocentesis, followed by karyotyping and/or chromosomal microarray analysis, was recommended as the standard method for definitive cytogenetic confirmation. However, some patients declined invasive testing due to concerns regarding procedure-related risks. In these cases, NIPT was offered as an alternative. Although NIPT is generally classified as a screening test, its high reported DR for common trisomies allowed it to be used as a clinically actionable test within our institutional practice. Consequently, pregnancies with high-risk NIPT results were managed as affected pregnancies, with subsequent counseling, antenatal surveillance, delivery planning, and neonatal management based on these results. Furthermore, only cases of complete trisomy were included, whereas mosaic trisomies were excluded from the analysis. In cases without PND, confirmation was obtained postnatally through genetic testing. This was a retrospective cohort study, and the REB waived the requirement for informed consent, as individual patient data remained undisclosed and confidential.

Ultrasound examinations were routinely performed during the second and third trimesters of pregnancy, with gestational age calculated based on the last menstrual period. Examinations were performed using WS80 ultrasound machines (Samsung, HC, Korea) equipped with high-resolution convex (3.5 or 5.0 MHz) and linear transducers. Abnormal ultrasound findings refer to structural anomalies or soft markers. Suspected trisomy refers to cases in which ultrasound or screening raised concern for aneuploidy. Soft markers included increased nuchal fold thickness, echogenic intracardiac focus, ventriculomegaly (>10 mm), absent or hypoplastic nasal bone, choroid plexus cysts, and short femur or humerus.

Scans were performed by qualified sonographers, and all reports were reviewed and confirmed by Maternal-Fetal Medicine (MFM) consultants. Interobserver variability was not assessed, which may affect reproducibility. Maternal and ultrasound-based information was collected from medical records. In this study, the term DR was used as a descriptive measure to indicate the proportion of confirmed trisomy cases with abnormal ultrasound findings among pregnancies that underwent prenatal ultrasound evaluation. DR should not be interpreted as a measure of diagnostic accuracy, including sensitivity, specificity, positive predictive value, or negative predictive value.

Statistical Analysis

Data spanning a five-year period, from January 2017 to December 2021, were collected over six months, between January 2022 and July 2022. The collected data were cleaned, coded, and prepared for analysis over a three-month period (July to September 2022) and subsequently analyzed over the following three months (October to December 2022). Statistical analysis was performed using SPSS Version 22.0 (IBM Corp., Armonk, NY, USA). Ultrasound examinations were performed using WS80 ultrasound machines (Samsung, HC, Korea). Continuous variables were expressed as mean ± standard deviation (SD) and range (minimum–maximum), while categorical variables were presented as frequencies (n) and percentages (%) with corresponding 95% confidence intervals (CI). Exact (Clopper–Pearson) CIs were used for proportions equal to 100%.

3. Results

During the study period, a total of 37,540 pregnancies were managed at our institution, of which 126 (0.3%) were diagnosed with Down syndrome, 17 (0.04%) with Edwards syndrome, and 7 (0.019%) with Patau syndrome, yielding an incidence of 0.4% for common trisomies born alive at our institute. The mean maternal age was 38.1 ± 6, 40.6 ± 4 and 41.5 ± 4 years for Down, Edwards, and Patau syndrome, respectively. The mean gestational age at the time of ultrasound examination was 28 ± 5 weeks (range: 24–39) in Down syndrome, 30 ± 5 weeks (range: 24–39) for Edwards syndrome, and 31 ± 2 weeks (range: 27–34) for Patau syndrome (Table 1). Prenatal ultrasound examinations were performed in 80/126 (63.5%) of Down syndrome cases, 9/17 (52.9%) of Edwards syndrome cases, and 5/7 (71.4%) of Patau syndrome cases. Among cases that underwent prenatal ultrasound evaluation, abnormal findings were observed in 50/80 fetuses (62.5%; 95% CI: 51.9%–73.1%) with trisomy 21, 9/9 (100%; 95% CI: 66.4%–100%) with trisomy 18, and 5/5 (100%; 95% CI: 47.8%–100%) with trisomy 13. The wider CIs for trisomy 18 and 13 reflect the small sample sizes (Table 2).

Among fetuses with trisomy 21 who underwent prenatal ultrasound evaluation, structural anomalies were identified in 30/80 cases (37.5%; 95% CI: 26.9%–48.1%), while soft markers were observed in 25/80 cases (31.3%; 95% CI: 21.3%–42.6%). Among confirmed cases of trisomy 21, isolated soft markers included short femur and humerus in 5 cases, increased nuchal fold thickness in 5 cases, echogenic intracardiac focus in 4 cases, absent nasal bone in 2 cases, and choroid plexus cyst in 2 cases, with no isolated cases of ventriculomegaly. Furthermore, 7 cases demonstrated more than one soft marker. More than one structural abnormality was present in 23/80 cases (28.8%; 95% CI: 18.8%–38.7%). Less frequent findings included abnormal Doppler studies in 4/80 cases (5.0%; 95% CI: 1.4%–12.3%), polyhydramnios in 2/80 cases (2.5%; 95% CI: 0.3%–8.7%), and fetal growth restriction (FGR)/small for gestational age (SGA) in 1/80 cases (1.3%; 95% CI: 0.03%–6.8%).

Table 1. Perinatal characteristics and outcomes of confirmed common trisomy newborns.

	Down syndrome, n (%), 126 (0.3)	Edwards syndrome, n (%), 17 (0.04)	Patau syndrome, n (%), 7 (0.019)
Maternal age (mean ± SD)	38.1 ± 5.9	40.6 ± 3.7	41.5 ± 4.3
Ultrasound exam			
Yes	80 (63.5)	9 (52.9)	5 (71.4)
No	46 (36.5)	8 (47)	2 (28.5)
Gestational age at exam (weeks) (mean ± SD) (min–max)	28 ± 5 (24–39)	29.75 ± 4.9 (24–39)	31 ± 2 (27–34)
Normal scan	30 (37.5)	0 (0)	0 (0)
Abnormal scan (%)	50 (62.5)	9 (100)	5 (100)
Ultrasound abnormalities			
Polyhydramnios	2 (2.5)	0	0
FGR/SGA	1 (1.3)	0	0
Abnormal Doppler	4 (5)	0	0
Structural anomalies	30 (37.5)	1 (11)	0
Soft markers	25 (31.3)	0	0
Combined >1 abnormality	23 (28.8)	8 (89)	5 (100)
PND			
Normal/not suspected prenatally	30 (37.5)	0	0
Confirmed	12 (15)	5 (55.5)	3 (60)
Suspected/not confirmed prenatally	3 (4)	4 (44.4)	2 (40)
Neonatal death	2 (1.5)	17 (100)	7 (100)

This table summarizes maternal demographic data, including age and gestational age at the time of ultrasound examination, for pregnancies affected by trisomy 21, trisomy 18, and trisomy 13. Values are presented as a number (percentage). Maternal and gestational age at ultrasound examination were expressed as mean ± SD. Abbreviations: FGR, fetal growth restriction; SGA, small for gestational age; PND, prenatal diagnosis; SD, standard deviation.

Table 2. Proportion of confirmed trisomy cases with abnormal ultrasound findings and corresponding 95% confidence intervals.

Condition	Cases with abnormal scan	Cases undergoing ultrasound	Proportion (%)	95% CI
Trisomy 21	50	80	62.5	51.9%–73.1%
Trisomy 18	9	9	100	66.4%–100%
Trisomy 13	5	5	100	47.8%–100%

Abbreviations: CI, confidence interval.

Table 3. Frequency of ultrasound abnormalities in fetuses with trisomy 21, trisomy 18, and trisomy 13.

Ultrasound abnormality	Trisomy 21 (n = 80), n (%)	95% CI	Trisomy 18 (n = 9), n (%)	95% CI	Trisomy 13 (n = 5), n (%)	95% CI
Structural anomalies	30/80 (37.5)	26.9–49.0	1/9 (11.1)	0.3–48.2	0/5 (0)	0–52.2
Soft markers	25/80 (31.3)	21.3–42.6	0/9 (0)	0–33.6	0/5 (0)	0–52.2
Combined abnormalities (>1)	23/80 (28.7)	19.2–40.0	8/9 (88.9)	51.8–99.7	5/5 (100)	47.8–100
Abnormal Doppler	4/80 (5)	1.4–12.3	0/9 (0)	0–33.6	0/5 (0)	0–52.2
Polyhydramnios	2/80 (2.5)	0.3–8.7	0/9 (0)	0–33.6	0/5 (0)	0–52.2
FGR/SGA	1/80 (1.3)	0.03–6.8	0/9 (0)	0–33.6	0/5 (0)	0–52.2

This table shows the frequency of ultrasound abnormalities, including structural anomalies, soft markers, Doppler abnormalities, polyhydramnios and FGR/SGA. Values are presented as n (%). Proportions were calculated using the number of cases that underwent prenatal ultrasound as the denominator (trisomy 21, n = 80; trisomy 18, n = 9; trisomy 13, n = 5). Exact (Clopper–Pearson) 95% CIs were calculated for all proportions. Values are presented as n (%). Abbreviations: CI, confidence interval.

Among fetuses with trisomy 18, structural anomalies were identified in 1/9 cases (11.1%; 95% CI: 0.3%–48.2%), whereas multiple abnormalities were present in 8/9 cases (88.9%; 95% CI: 51.8%–99.7%). No cases demonstrated isolated soft markers, abnormal Doppler findings, polyhydramnios, or FGR/SGA. All fetuses with trisomy 13 demonstrated multiple abnormalities (5/5, 100%; 95% CI: 47.8%–100%), with no isolated structural anomalies, soft markers, abnormal Doppler findings, polyhydramnios, or FGR/SGA observed (Table 3).

Regarding PND, 30/80 (37.5%) of the Down syndrome cases had normal ultrasound findings, and trisomy was therefore not suspected prenatally. 12/80 cases (15%) underwent prenatal genetic testing, including invasive testing (amniocentesis) and NIPT. All women were offered invasive prenatal diagnostic testing. However, some patients declined amniocentesis due to concerns regarding procedure-related risks and subsequently underwent NIPT instead.

Although NIPT is generally considered a screening test, its reported DR for trisomy 21 exceeds 99%. In our institution, pregnancies with high-risk NIPT results in women who declined invasive testing were managed clinically as affected pregnancies, with subsequent counseling, antenatal surveillance, delivery planning, and neonatal management based on these results.

3 cases (4%) were suspected to have trisomy based on ultrasound findings, but diagnostic testing was not performed. 2 neonates (1.5%) with Down syndrome died during the neonatal period. In Edwards syndrome, none of the cases had a normal ultrasound examination. 5 cases (5/9, 55.5%) were confirmed by diagnostic testing, and 4 (4/9, 44.4%) were suspected to have trisomy due to multiple congenital anomalies but were not confirmed invasively. All (100%) Edwards syndrome neonates died during the neonatal period. Similarly, none of the Patau syndrome cases showed normal ultrasound findings. 3 cases (3/5, 60%) were confirmed by diagnostic testing, while 2 (2/5, 40%) were suspected to have trisomy but did not undergo diagnostic testing. All (100%) of the Patau syndrome neonates died during the neonatal period (Figs. 1,2,3).

4. Discussion

It is well established in the literature that the detection of Down syndrome and other trisomies is most effective when performed through combined screening, specifically first trimester NT ultrasound in conjunction with first trimester serum markers, including PAPP-A and free β-hCG [10,11]. Alternatively, second trimester quadruple screening, which measures maternal serum levels of AFP, total hCG, unconjugated estriol (uE3), and inhibin-A, can also be used [11]. The FaSTER trial demonstrated DRs of 82% and 81% for combined and quadruple screening, respectively [10,14,33].

The role of second and third trimester ultrasound screening alone is not well established. This study was conducted in a tertiary specialized center where most pregnancies were initially managed in primary healthcare settings. Consequently, many pregnant women were not referred to our center until later in their second or third trimesters. As a result, first-trimester ultrasound and serum screening were often missed, and prenatal aneuploidy assessment relied

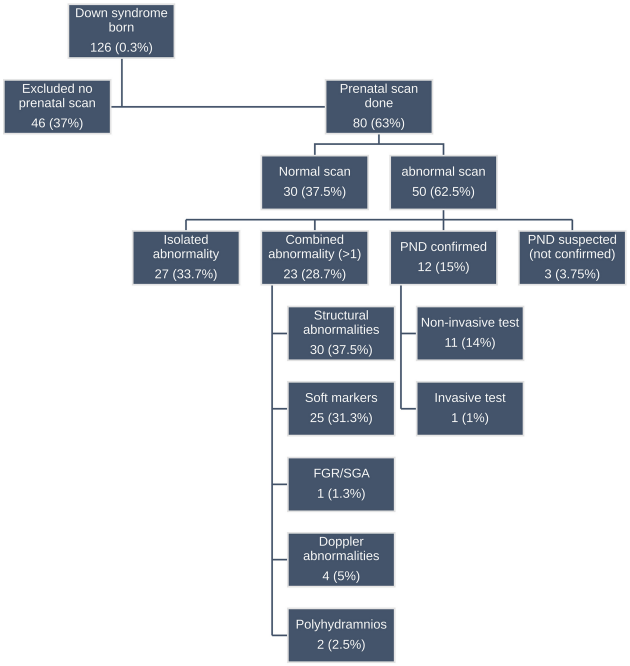


Fig. 1. Flow chart of trisomy 21 (Down syndrome) cases included in the study. Case selection, availability of prenatal ultrasound, and classification of ultrasound findings in fetuses with trisomy 21 are presented. The chart also illustrates the proportion of cases with normal versus abnormal scans, types of abnormalities (structural anomalies, soft markers, Doppler abnormalities, polyhydramnios, and FGR/SGA), and the rate of PND, including confirmed and suspected cases.

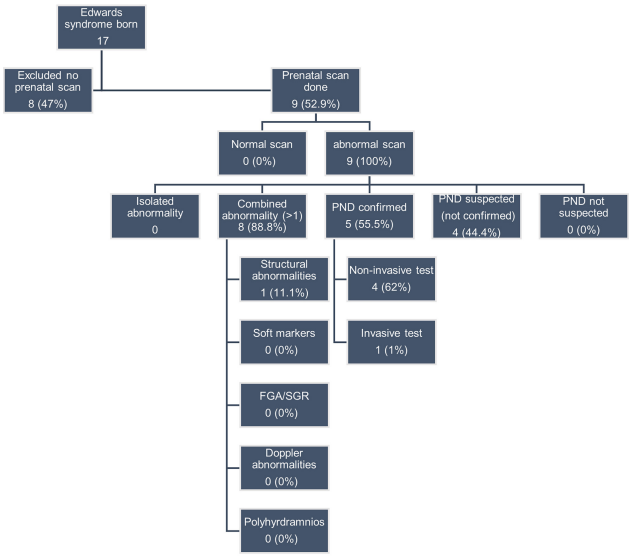


Fig. 2. Flow chart of trisomy 18 (Edwards syndrome) cases and their prenatal ultrasound findings. The majority of cases demonstrated abnormal scans with predominantly multiple structural anomalies. The figure also shows rates of PND confirmation and cases not suspected prenatally.

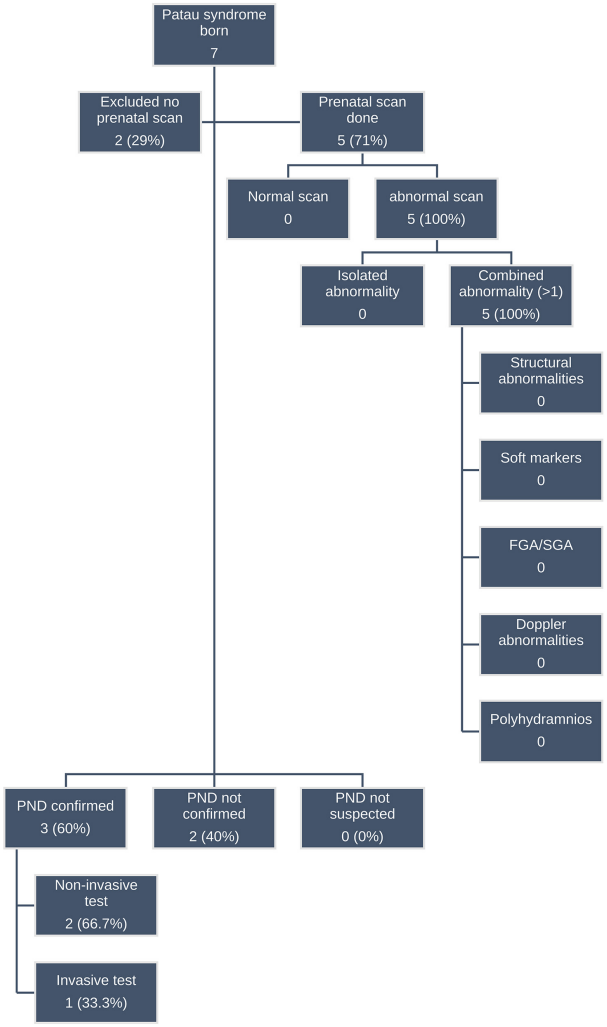


Fig. 3. Flow diagram of trisomy 13 (Patau Syndrome) cases. All fetuses demonstrated abnormal ultrasound findings, typically with multiple anomalies. The chart also presents prenatal diagnostic outcomes, including confirmed and unconfirmed cases.

primarily on mid- and late-trimester ultrasound findings to screen for common trisomies, including trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), and trisomy 13 (Patau syndrome).

A meta-analysis by Smith-Bindman et al. [34] aimed to evaluate the sensitivity of second-trimester ultrasound for the detection of Down syndrome. The analysis focused on six sonographic markers: choroid plexus cysts, thickened nuchal fold, echogenic intracardiac focus, echogenic bowel, renal pyelectasis, and humeral or femoral shortening. The study found that only thickened nuchal fold in the second trimester was useful for detecting Down syndrome, although its overall sensitivity remained too low for practical screening use [34]. In our study, abnormal ultrasound findings were observed in 62.5% of Down syndrome cases, with soft markers such as increased nuchal fold thickness present in 20% of cases. However, 37.5% of Down syndrome cases in our cohort had normal ultrasound find-

ings and were not suspected prenatally. The finding that slightly more than one third of trisomy 21 cases had normal ultrasound examinations highlights the limitations of late-trimester ultrasound. This may be influenced by milder phenotypic expression, earlier gestational age at scanning, or the absence of major structural anomalies. Furthermore, differences in gestational age at the time of ultrasound examination may have influenced DRs, particularly for trisomy 21, where earlier scans may miss subtle findings.

In a more recent cohort study, Smith-Bindman et al. [35] evaluated a high-risk population in whom risk was established by triple-screen testing followed by second-trimester scans. The authors reported that if ultrasound alone had been used to counsel women to avoid amniocentesis, approximately half (115/245) of Down syndrome cases would have been missed. They further concluded that soft markers, other than thickened nuchal fold, showed no association with Down syndrome in the absence of structural anomalies. Similarly, Egan et al. [13] found that when multiple sonographic signs and structural abnormalities were present concurrently, the sensitivity of ultrasound screening for Down syndrome increased to 69%. Consistent with this, our study found more than one abnormal ultrasound finding in 28.8% of Down syndrome cases, reinforcing that the presence of combined markers improves detection performance. Interestingly enough, the relatively low rate of polyhydramnios observed in our study may reflect the late gestational timing of scans, small sample size, or variability in phenotypic expression.

Other investigators have explored the role of second-trimester ultrasound screening in low-risk populations. Schluter and Pritchard [36], in a cohort study from Australia involving 73 Down syndrome cases, reported that after adjusting for gestational and maternal age, all pregnancies with either structural abnormalities or soft markers were significantly associated with Down syndrome. Likewise, a multicenter study by Hobbins et al. [37] involving 176 pregnancies with fetal Down syndrome (134 high risk due to advanced maternal age and 42 with positive triple screens) demonstrated that 71% (125/176) of affected fetuses exhibited either a major structural abnormality or a soft marker. The authors concluded that mid-trimester sonography can complement early screening and serum testing by refining risk estimation for Down syndrome [38].

Unlike trisomy 21, second- and third-trimester ultrasound proved highly effective in identifying fetuses with trisomy 18 and trisomy 13 in our cohort [37]. All cases of Edwards syndrome and Patau syndrome that underwent late-trimester scanning showed abnormal sonographic findings, with no normal ultrasound examinations recorded. Moreover, multiple abnormalities were present in most cases (89% in trisomy 18 and 100% in trisomy 13), highlighting that these conditions are typically characterized by major structural anomalies rather than isolated soft markers. This pattern aligns with previous reports indicating that trisomy 18 and 13 are usually detectable on mid-trimester scans due to severe structural malformations and fetal growth abnormalities [29,30,31,32,39].

Although abnormal ultrasound findings were relatively common among affected fetuses in our cohort, ultrasound alone cannot reliably confirm trisomy 21. Several cases with multiple anomalies were suspected but remained unconfirmed prenatally. This highlights a persistent gap between detection and definitive diagnosis in real-world settings and further underscores the need for timely referral to diagnostic testing whenever major structural abnormalities are detected on ultrasound [27,30]. Neonatal mortality, by contrast, was universal in both the trisomy 18 and trisomy 13 groups, consistent with the well-established poor prognosis associated with these conditions [27,29].

Two major findings emerge from this study. First, despite the relatively high proportion of abnormal ultrasound findings observed among affected fetuses, ultrasound alone cannot reliably identify trisomy 21, as a substantial proportion of cases demonstrated normal second- and third-trimester ultrasound examinations [13,34]. Second, although the incidence of trisomy 21 and other chromosomal abnormalities clearly increases with maternal age, many such cases remain undetectable through ultrasound screening alone in the second trimester [12,36,37,38]. A key limitation of this study is the restriction to liveborn neonates. Pregnancies resulting in intrauterine fetal demise (IUFD) or termination were excluded, which may introduce selection bias. This limitation is particularly relevant for trisomy 13 and trisomy 18, in which severe phenotypes are more likely to result in fetal loss or pregnancy termination. Consequently, the spectrum and severity of ultrasound findings reported here may be underestimated.

Limitations

This study provides real-world evidence from a tertiary care setting where first-trimester aneuploidy screening is frequently missed, underscoring the practical reliance on second- and third-trimester ultrasound for prenatal evaluation of common trisomies. Our findings demonstrate that fetuses with trisomy 18 and trisomy 13 commonly present with multiple structural abnormalities readily identifiable during late-trimester ultrasound examination. By contrast, a substantial proportion of fetuses with trisomy 21 had normal ultrasound findings, highlighting the limitations of ultrasound in identifying all affected cases. These findings reinforce that ultrasound alone is insufficient as a standalone screening tool for Down syndrome and highlight the importance of implementing early combined screening strategies. Additionally, this study further emphasizes the clinical value of late-trimester ultrasound in guiding risk stratification, referral for diagnostic testing, and perinatal counseling in settings with delayed access to prenatal care.

5. Conclusions

Late second- and third-trimester scans play an important role in refining risk assessment; however, they should support rather than replace early combined screening and biochemical testing, thereby enabling timely counseling, multidisciplinary planning, and informed decision-making for affected pregnancies.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported. IB designed the research study, drafted the manuscript, and finalized the manuscript for submission. BA and AK acquired the data and drafted the manuscript. TM, FA and AA were involved in study design, acquiring data, drafting, and editing the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Review Committee for Human-related Scientific Research at Prince Sultan Military Medical City (IRB Approval No: 2347). The research was conducted in accordance with the Declaration of Helsinki and adhered to relevant national and international ethical guidelines for research involving human participants' data. The REB waived informed consent because the study was a minimal-risk retrospective review of existing records, obtaining consent was impracticable, and the waiver did not affect participants' rights or welfare. Data were de-identified before analysis.

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Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG54044.

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