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Original Article

Use of Nuchal Translucency and Supplementary Ultrasound Markers in Chromosomal Abnormality Detection in Consanguineous Pregnancies

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ABSTRACT

Background: First-trimester ultrasound screening plays an important role in early fetal risk assessment, particularly in populations where consanguineous marriage is common and the burden of congenital and genetic disorders may be increased. Nuchal translucency is an established sonographic marker associated with chromosomal abnormalities, while supplementary markers such as nasal bone status and ductus venosus flow may improve early risk stratification. Objective: To evaluate the association of nuchal translucency and supplementary first-trimester ultrasound markers with chromosomal abnormality status among pregnant women undergoing early fetal assessment. Methods: This cross-sectional observational study included 59 pregnant women assessed during the first trimester. Maternal age, gravida, crown-rump-length-based gestational age, nuchal translucency, fetal heart rate, consanguinity status, nasal bone status, ductus venosus flow, and chromosomal abnormality status were recorded. Descriptive statistics, independent-samples t-tests, chi-square or Fisher's exact tests, correlation analysis, and exploratory logistic regression model-fit assessment were performed using SPSS version 27. Results: Outcome-valid data were available for 58 participants. Mean nuchal translucency was higher in the chromosomal abnormality presence group than in the absence group (3.85 ± 0.45 mm vs. 1.64 ± 0.37 mm; $p < 0.001$). Consanguineous marriage was significantly associated with chromosomal abnormality status ($p = 0.002$). Absent nasal bone and abnormal ductus venosus flow showed complete concordance with chromosomal abnormality status in the analysed sample ($p < 0.001$). Fetal heart rate, maternal age, and gravida were not significantly associated with the outcome. Conclusion: Increased nuchal translucency, absent nasal bone, abnormal ductus venosus flow, and consanguinity were associated with chromosomal abnormality status. Combined first-trimester ultrasound marker assessment may support early fetal risk stratification, although larger studies with confirmed chromosomal outcomes are needed. Keywords: Nuchal Translucency; Consanguinity; Chromosomal Abnormalities; Nasal Bone; Ductus Venosus; First-Trimester Screening.

INTRODUCTION

Nuchal translucency is a transient sonographic finding representing subcutaneous fluid accumulation behind the fetal neck during early pregnancy and is routinely assessed between 11 and 13+6 weeks of

gestation as part of first-trimester fetal risk evaluation. When measured in the mid-sagittal plane with appropriate fetal positioning, increased nuchal translucency provides clinically useful information about the likelihood of chromosomal abnormalities, structural malformations, congenital heart disease, and selected genetic syndromes. Although threshold definitions vary across clinical protocols, values above the 95th percentile for crown-rump length or measurements commonly exceeding approximately 2.5–3.5 mm are generally regarded as abnormal and warrant further risk assessment, counselling, and diagnostic consideration (1,2).

The biological basis of increased nuchal translucency is multifactorial and reflects complex interactions between fetal lymphatic development, cardiovascular haemodynamics, extracellular matrix composition, venous pressure, and genetic regulation of embryological development. During the late first trimester, changes in placental vascular resistance, ductus venosus flow, fetal cardiac function, and lymphatic drainage influence fluid distribution in the fetal neck region. As gestation advances beyond the early first-trimester screening window, maturation of lymphatic drainage and venous return may lead to spontaneous reduction of nuchal translucency in some fetuses, whereas persistent or markedly increased fluid accumulation may indicate a higher probability of aneuploidy, cystic hygroma, congenital heart defects, or syndromic conditions (3,4).

First-trimester screening has evolved from reliance on maternal age alone to integrated risk assessment using sonographic markers, maternal serum biochemistry, and, where available, cell-free fetal DNA testing. Nuchal translucency remains clinically important because it can identify risk patterns not limited to common aneuploidies and may also indicate structural or syndromic abnormalities that would not be fully excluded by aneuploidy-focused non-invasive prenatal testing. Previous studies have shown that increased nuchal translucency is associated with trisomy 21, trisomy 18, trisomy 13, monosomy X, congenital heart disease, miscarriage, and adverse fetal outcome, with risk increasing as the degree of translucency thickening becomes greater (5–7). Therefore, first-trimester ultrasound continues to serve as a central component of early fetal assessment, particularly in settings where access to advanced molecular testing may be variable.

The diagnostic value of first-trimester ultrasound improves when nuchal translucency is interpreted alongside supplementary sonographic markers. Absence or hypoplasia of the fetal nasal bone, abnormal ductus venosus Doppler waveform, and tricuspid regurgitation have been repeatedly associated with increased risk of chromosomal abnormalities, particularly Down syndrome. These markers are not independent replacements for genetic diagnosis, but they refine risk stratification and help clinicians identify pregnancies requiring additional biochemical screening, non-invasive prenatal testing, chorionic villus sampling, amniocentesis, fetal echocardiography, or targeted anomaly assessment. Evidence indicates that combining nuchal translucency with nasal bone assessment, ductus venosus Doppler, and tricuspid valve evaluation may improve early screening performance compared with nuchal translucency alone, provided that measurements are performed by trained operators using standardized protocols (8–11).

Consanguinity is an important reproductive health consideration in many populations, including Pakistan and other South Asian settings, where cousin marriage and intra-familial unions remain socially and culturally common. Consanguineous unions increase the probability that both parents carry the same autosomal recessive variants inherited from a shared ancestor, thereby increasing the risk of congenital anomalies, inherited metabolic disorders, neurodevelopmental conditions, fetal loss, and adverse perinatal outcomes. Although common chromosomal aneuploidies such as trisomy 21 are usually caused by nondisjunction rather than recessive inheritance, consanguinity may increase the burden of congenital and genetic disorders that can present with abnormal early ultrasound markers, including increased nuchal translucency and abnormal fetal structural development. This makes early sonographic screening particularly relevant in populations with a high prevalence of consanguineous marriage (12,13).

Despite the established role of first-trimester ultrasound markers, there remains a need for local evidence evaluating how nuchal translucency and supplementary sonographic findings relate to chromosomal abnormality status among pregnancies assessed in high-consanguinity clinical settings. Much of the available evidence comes from large tertiary or high-resource screening programmes, while smaller local studies often lack integrated evaluation of nuchal translucency, nasal bone status, ductus venosus flow, fetal heart rate, gestational age, and consanguinity within the same analytical framework. This gap is clinically important because early identification of high-risk pregnancies can support timely counselling, referral, diagnostic testing, and pregnancy management decisions.

The present study was therefore conducted to evaluate the association of nuchal translucency thickness and supplementary first-trimester ultrasound markers with chromosomal abnormality status among pregnant women undergoing early fetal ultrasound assessment. The study specifically examined whether increased nuchal translucency, absent nasal bone, abnormal ductus venosus flow, and consanguineous marriage were associated with chromosomal abnormality status in the study population. The primary objective was to determine the role of nuchal translucency and additional ultrasound markers in first-trimester risk stratification for chromosomal abnormalities, with the hypothesis that fetuses with increased nuchal translucency and abnormal supplementary sonographic markers would show a higher frequency of chromosomal abnormality status than fetuses without these findings.

MATERIAL AND METHODS

This cross-sectional observational study was conducted in a private hospital setting over a period of three months following approval of the study synopsis. The study was designed to evaluate the association of first-trimester nuchal translucency and supplementary ultrasound markers with chromosomal abnormality status among pregnant women undergoing early fetal ultrasound assessment. A total of 59 pregnant women were included. The study population comprised women in the first trimester of pregnancy, with gestational age falling within the 11–14-week screening window, and included both consanguineous and non-consanguineous pregnancies so that the relationship between consanguinity and chromosomal abnormality status could be evaluated.

Pregnant women were considered eligible if they had a singleton pregnancy, a known gestational age, and willingness to provide informed consent for participation and ultrasound-based assessment. Women were excluded if they had multiple pregnancies, unknown gestational age, unwillingness to participate, or clinical circumstances that prevented reliable first-trimester ultrasound assessment. Consanguineous marriage was recorded as an exposure variable rather than an exclusion criterion, because the study aimed to compare chromosomal abnormality status across pregnancies with and without a history of consanguinity. Recruitment was performed among eligible women presenting for first-trimester ultrasound assessment during the study period, and informed consent was obtained before data collection.

Ultrasound examination was performed using a high-resolution ultrasound system equipped with a 3–5 MHz convex transducer. Gestational age was assessed using crown-rump length, and nuchal translucency was measured during the first-trimester screening interval in the mid-sagittal fetal plane with appropriate fetal positioning. Nuchal translucency thickness was recorded in millimetres as a continuous variable. Fetal heart rate was recorded in beats per minute. Supplementary ultrasound markers were assessed systematically, including fetal nasal bone status and ductus venosus flow pattern. Nasal bone status was categorized as present or absent, while ductus venosus flow was categorized as normal or abnormal according to the Doppler waveform observed during the examination. Where abnormal nuchal translucency or supplementary ultrasound markers were identified, the findings were recorded for further clinical assessment and risk classification according to the available diagnostic pathway at the study site.

The primary outcome variable was chromosomal abnormality status, categorized as presence or absence according to the documented clinical or diagnostic assessment available in the study record. The principal exposure variables were nuchal translucency thickness, nasal bone status, ductus venosus flow, and consanguineous marriage. Additional maternal and fetal variables included maternal age, gravida, gestational age based on crown-rump length, and fetal heart rate. Consanguineous marriage was operationally defined as a marital union between biologically related partners as reported by the participant. Increased nuchal translucency was evaluated as a continuous measurement and interpreted in relation to fetal gestational age and abnormality status rather than as an isolated diagnostic test.

To reduce measurement bias, ultrasound variables were recorded using a standardized first-trimester assessment approach, with fetal biometric and marker measurements obtained during the same examination period. Data were checked for completeness, coding accuracy, and consistency before analysis. Categorical variables were coded using explicit binary categories, including consanguineous versus non-consanguineous marriage, nasal bone present versus absent, ductus venosus flow normal versus abnormal, and chromosomal abnormality status present versus absent. Continuous variables were reviewed for range errors and distributional characteristics before inferential testing. Analyses were performed using valid available cases for each variable, and denominators were reported according to the number of complete observations included in each analysis.

Data were analysed using IBM SPSS Statistics version 27. Descriptive statistics were calculated for maternal and fetal variables. Continuous variables, including maternal age, gravida, gestational age based on crown-rump length, nuchal translucency thickness, and fetal heart rate, were summarized using mean and standard deviation with minimum and maximum values. Categorical variables, including consanguineous marriage, nasal bone status, ductus venosus flow pattern, and chromosomal abnormality status, were summarized using frequencies and percentages. Normality of continuous variables was assessed before group comparison. Independent-samples t-tests were used to compare normally distributed continuous variables between chromosomal abnormality groups, while unequal-variance results were interpreted where homogeneity of variance was not satisfied. Chi-square or Fisher's exact tests were used to evaluate associations between categorical ultrasound or clinical variables and chromosomal abnormality status, particularly when expected cell counts were small.

Correlation analysis was performed to assess the relationship between nuchal translucency thickness and selected continuous variables, including gestational age, maternal age, and fetal heart rate. Pearson correlation was used for linear associations involving normally distributed variables, and Spearman correlation was used where rank-based assessment was appropriate. Binary logistic regression was planned to explore the combined predictive contribution of maternal and ultrasound variables to chromosomal abnormality status; however, model interpretation required caution where complete separation occurred due to perfect or near-perfect classification by categorical ultrasound markers. Statistical significance was set at $p < 0.05$. Results were interpreted as associations rather than causal effects because of the cross-sectional observational design.

The study was conducted after approval of the research synopsis, and participation was based on informed consent. Maternal identity and clinical information were handled confidentially, and data were used only for research analysis. The study involved non-invasive ultrasound-based assessment performed within the routine first-trimester screening window. Data integrity was maintained through structured data entry, review of variable coding, verification of valid denominators, and consistency checking across descriptive, comparative, and association analyses.

RESULTS

A total of 59 pregnant women were included in the descriptive analysis. Chromosomal abnormality status and complete categorical marker data were available for 58 participants and were used for group comparison and association testing.

The study population had a mean maternal age of 30.90 ± 7.50 years and a mean gravida of 3.46 ± 1.66. Mean gestational age based on crown-rump length was 85.71 ± 6.44 days. The mean nuchal translucency measurement was 2.07 ± 0.93 mm, with values ranging from 1.00 to 5.10 mm, while the mean fetal heart rate was 159.34 ± 8.92 bpm.

Table 1. Descriptive Statistics of Maternal and Fetal Continuous Variables

Variable	n	Minimum	Maximum	Mean	SD
Maternal age, years	59	18	42	30.90	7.50
Gravida	59	1	6	3.46	1.66
Gestational age by CRL, days	59	77	97	85.71	6.44
Nuchal translucency, mm	59	1.00	5.10	2.07	0.93
Fetal heart rate, bpm	59	135	177	159.34	8.92

SD, standard deviation; CRL, crown-rump length; bpm, beats per minute.

Table 2. Continuous Maternal and Fetal Variables by Chromosomal Abnormality Status

Variable	Absence n	Absence Mean ± SD	Presence n	Presence Mean ± SD	Mean Difference	95% CI	t	df	p-value	Cohen's d
Nuchal translucency, mm	46	1.64 ± 0.37	12	3.85 ± 0.45	-2.22	-2.47 to -1.96	-17.49	56.00	<0.001	-5.67
Fetal heart rate, bpm	46	155.54 ± 7.22	12	157.58 ± 7.66	-2.04	-6.79 to 2.71	-0.86	56.00	0.393	—
Gestational age by CRL, days	46	86.41 ± 4.37	12	77.50 ± 1.45	8.91	7.37 to 10.45	11.61	52.71	<0.001	—

SD, standard deviation; CI, confidence interval; CRL, crown-rump length; bpm, beats per minute. Independent-samples t-test was used. Unequal-variance results were used for gestational age by CRL. Cohen's d was available for nuchal translucency only.

Nuchal translucency was markedly higher among fetuses with chromosomal abnormality status than among those without chromosomal abnormality status, with mean values of 3.85 ± 0.45 mm and 1.64 ± 0.37 mm, respectively. The mean difference was -2.22 mm with a 95% confidence interval from -2.47 to -1.96, and the effect size was very large. Fetal heart rate showed no meaningful group difference, with overlapping mean values and a non-significant p-value. Gestational age by crown-rump length was lower in the chromosomal abnormality group, with a mean difference of 8.91 days between groups.

Table 3. Categorical Clinical and Ultrasound Markers by Chromosomal Abnormality Status

Variable	Category	Absence n (%)	Presence n (%)	Total n (%)	χ^2	df	p-value
Consanguineous marriage	Yes	24 (52.2)	12 (100.0)	36 (62.1)	9.25	1	0.002
Consanguineous marriage	No	22 (47.8)	0 (0.0)	22 (37.9)			
Ductus venosus flow	Normal	46 (100.0)	0 (0.0)	46 (79.3)	58.00	1	<0.001
Ductus venosus flow	Abnormal	0 (0.0)	12 (100.0)	12 (20.7)			
Nasal bone status	Present	46 (100.0)	0 (0.0)	46 (79.3)	58.00	1	<0.001
Nasal bone status	Absent	0 (0.0)	12 (100.0)	12 (20.7)			

Percentages are column percentages for chromosomal abnormality groups and total percentages for the total column. Fisher's exact test was considered where expected cell counts were small.

Consanguineous marriage was significantly associated with chromosomal abnormality status. All 12 fetuses with chromosomal abnormality status were from consanguineous pregnancies, whereas none of the 22 non-consanguineous pregnancies had chromosomal abnormality status. Ductus venosus flow and nasal bone status showed complete concordance with chromosomal abnormality status in this analytic sample. All fetuses with abnormal ductus venosus flow and all fetuses with absent nasal bone had chromosomal abnormality status, while all fetuses with normal ductus venosus flow and present nasal bone were classified in the absence group.

Table 4. Correlation Analysis of Nuchal Translucency with Selected Continuous Variables

Variable Pair	Method	n	r / rho	p-value
Nuchal translucency × Gestational age by CRL	Pearson	58	-0.625	<0.001
Nuchal translucency × Gestational age by CRL	Spearman	58	-0.470	<0.001
Nuchal translucency × Maternal age	Pearson	58	-0.030	0.823
Nuchal translucency × Fetal heart rate	Pearson	58	0.155	0.244

CRL, crown-rump length.

Nuchal translucency showed a statistically significant inverse association with gestational age by crown-rump length. The Pearson correlation was -0.625 and the Spearman correlation was -0.470, indicating that higher nuchal translucency values were observed more frequently at lower crown-rump-length-based gestational ages within this dataset. Maternal age and fetal heart rate were not meaningfully correlated with nuchal translucency.

Table 5. Univariate Association of Maternal and Ultrasound Variables with Chromosomal Abnormality Status

Predictor Variable	Score Statistic	df	p-value
Gestational age by CRL	26.77	1	<0.001
Nuchal translucency	49.02	1	<0.001
Nasal bone status	58.00	1	<0.001
Ductus venosus flow	58.00	1	<0.001
Consanguineous marriage	9.25	1	0.002
Fetal heart rate	0.76	1	0.384
Maternal age	0.03	1	0.862
Gravida	0.78	1	0.378

CRL, crown-rump length.

Among the evaluated predictors, nasal bone status, ductus venosus flow, nuchal translucency, gestational age by crown-rump length, and consanguineous marriage were associated with chromosomal abnormality status at the univariate level. Fetal heart rate, maternal age, and gravida did not show statistically significant associations. The strongest score statistics were observed for nasal bone status and ductus venosus flow, reflecting the complete separation seen in the categorical marker analysis.

Table 6. Binary Logistic Regression Model Fit

Model	n	χ^2	df	Cox & Snell R^2	Nagelkerke R^2
Enter method	58	59.14	7	0.639	1.000

The binary logistic regression model was statistically significant overall; however, the model demonstrated complete separation, as reflected by a Nagelkerke R^2 of 1.000 and complete classification of chromosomal abnormality status by selected categorical ultrasound markers. Because nasal bone status and ductus venosus flow perfectly separated outcome groups in this dataset, standard logistic regression estimates should be interpreted cautiously and should not be presented as stable independent adjusted predictors without penalized or exact regression methods.

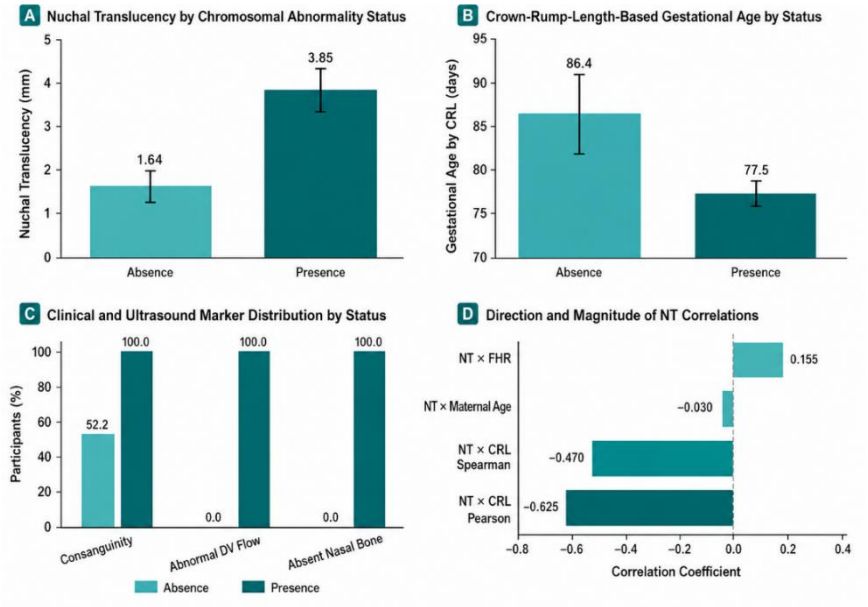

Figure 1. Integrated First-Trimester Ultrasound Marker Profile by Chromosomal Abnormality Status.

The panelled figure demonstrates a distinct ultrasound-risk profile among fetuses with chromosomal abnormality status. Mean nuchal translucency was higher in the presence group than in the absence

group, with values of 3.85 ± 0.45 mm and 1.64 ± 0.37 mm, respectively. Crown-rump-length-based gestational age was lower in the presence group, with mean values of 77.50 ± 1.45 days compared with 86.41 ± 4.37 days in the absence group. Categorical marker distribution showed that all fetuses with chromosomal abnormality status had consanguineous parental history, abnormal ductus venosus flow, and absent nasal bone, whereas abnormal ductus venosus flow and absent nasal bone were not observed in the absence group. Correlation profiling showed an inverse relationship between nuchal translucency and gestational age by crown-rump length using both Pearson and Spearman methods, while maternal age and fetal heart rate showed weak correlations with nuchal translucency. Together, the figure supports the clinical relevance of combined first-trimester marker assessment while requiring cautious interpretation because of the small outcome-positive sample and complete separation of some categorical ultrasound markers.

Overall, the results indicate that increased nuchal translucency, absent nasal bone, abnormal ductus venosus flow, lower crown-rump-length-based gestational age, and consanguineous marriage were associated with chromosomal abnormality status in this sample. The findings support the clinical value of combined first-trimester ultrasound marker assessment for early fetal risk stratification; however, the complete separation observed for nasal bone and ductus venosus flow requires cautious interpretation because of the small analytic sample and the possibility of overestimation of marker performance.

DISCUSSION

The present study evaluated the association of nuchal translucency and supplementary first-trimester ultrasound markers with chromosomal abnormality status among pregnant women undergoing early fetal assessment. The principal finding was that fetuses classified with chromosomal abnormality status had substantially higher nuchal translucency measurements than fetuses without chromosomal abnormality status. Mean nuchal translucency was 3.85 ± 0.45 mm in the presence group compared with 1.64 ± 0.37 mm in the absence group, with a mean difference of approximately 2.22 mm and a very large effect size. This finding supports the established role of nuchal translucency as an important first-trimester sonographic marker for fetal chromosomal and structural risk assessment. Previous evidence has shown that increased nuchal translucency is associated with common aneuploidies, including trisomy 21, trisomy 18, trisomy 13, and monosomy X, as well as congenital heart disease and adverse pregnancy outcomes (18,29).

The observed difference in nuchal translucency between outcome groups is clinically meaningful because NT assessment is performed during a narrow gestational window when early referral, counselling, and diagnostic planning remain feasible. Increased NT is not a diagnostic finding by itself, but it provides a measurable early risk signal that can guide decisions regarding further evaluation, including maternal serum screening, non-invasive prenatal testing, chorionic villus sampling, amniocentesis, chromosomal microarray, or targeted fetal echocardiography where clinically indicated. This is especially relevant in clinical settings where advanced genetic testing may not be universally available and where ultrasound remains a first-line screening modality. The present findings therefore reinforce the importance of accurate NT measurement using standardized first-trimester ultrasound technique rather than interpreting NT as an isolated visual impression.

Supplementary ultrasound markers showed strong associations with chromosomal abnormality status in this study. All fetuses with absent nasal bone were classified in the chromosomal abnormality presence group, while all fetuses with present nasal bone were classified in the absence group. This finding is consistent with previous literature showing that absent or hypoplastic nasal bone improves first-trimester risk stratification for trisomy 21 when combined with maternal age, NT, and biochemical markers (9,34). Nasal bone assessment is clinically useful because it is relatively simple to integrate into first-trimester ultrasound protocols when operator training and appropriate imaging planes are available. However, the complete separation observed in the current sample should be interpreted

cautiously because perfect classification is uncommon in larger screening populations and may reflect the small number of outcome-positive cases, selective diagnostic confirmation, or dataset structure.

Ductus venosus flow also showed complete concordance with chromosomal abnormality status, as all fetuses with abnormal ductus venosus flow were classified in the presence group and all fetuses with normal ductus venosus flow were classified in the absence group. This supports the value of Doppler assessment as an additional marker in first-trimester screening. Abnormal ductus venosus waveform has been associated with fetal aneuploidy, cardiac dysfunction, and congenital heart disease, particularly when evaluated alongside NT and other sonographic markers (9,10). In the present study, the finding suggests that ductus venosus Doppler may provide important risk-stratification information beyond NT thickness alone. Nevertheless, because the dataset demonstrated complete separation, the marker should not be described as perfectly diagnostic without validation against a clearly reported genetic reference standard in a larger sample.

Consanguineous marriage was significantly associated with chromosomal abnormality status in this sample. All fetuses classified with chromosomal abnormality status were from consanguineous pregnancies, whereas no chromosomal abnormality status was reported among non-consanguineous pregnancies in the outcome-valid dataset. This finding is clinically relevant in the Pakistani and South Asian context, where consanguineous unions are common and may increase the burden of inherited congenital disorders, autosomal recessive conditions, fetal structural anomalies, and adverse perinatal outcomes (1,11). Although common chromosomal aneuploidies are generally caused by meiotic nondisjunction rather than recessive inheritance, consanguinity can increase the probability of genetic and congenital abnormalities that may manifest through early ultrasound markers such as increased NT, abnormal lymphatic development, structural anomalies, and abnormal cardiovascular physiology. Therefore, consanguinity should be treated as an important contextual risk factor during prenatal counselling and early fetal screening rather than as a stand-alone predictor of chromosomal abnormality.

The study also found that gestational age by crown-rump length differed between groups, with the chromosomal abnormality presence group presenting at a lower mean CRL-based gestational age than the absence group. Correlation analysis demonstrated an inverse relationship between nuchal translucency and gestational age by CRL in this dataset. This finding should be interpreted carefully because NT normally varies with crown-rump length during the first-trimester screening window, and raw NT measurements may be affected by gestational-age distribution. The inverse association observed here may reflect the concentration of high-risk cases at earlier measured CRL values or the influence of abnormal fetal development on biometric dating. Future analyses should ideally evaluate NT using gestational-age-adjusted percentiles, multiples of the median, or standardized Z-scores rather than relying exclusively on raw millimetre values. Such adjustment would improve comparability across fetuses scanned at different points within the 11–13+6-week screening interval.

Maternal age, gravida, and fetal heart rate were not significantly associated with chromosomal abnormality status in this sample. This finding suggests that ultrasound-based structural and Doppler markers were more informative than demographic or basic fetal physiological variables in the present dataset. However, the absence of statistical association should not be interpreted as absence of clinical relevance, particularly for maternal age, which remains a recognized component of many prenatal risk algorithms. The lack of association may be due to the small sample size, limited outcome-positive cases, and the strong discriminative pattern of ultrasound markers in this dataset.

The binary logistic regression model was statistically significant overall but demonstrated complete separation, reflected by a Nagelkerke R^2 of 1.000 and perfect classification by selected categorical ultrasound markers. This is a major statistical issue because standard logistic regression estimates become unstable when one or more predictors perfectly separate the outcome groups. Under such conditions, conventional adjusted odds ratios may be inflated, non-estimable, or misleading. Therefore,

the regression results should be presented as exploratory model-fit information only, rather than as proof that nasal bone status or ductus venosus flow independently predicts chromosomal abnormality status. Penalized logistic regression, exact logistic regression, or larger multicentre datasets would be more appropriate for estimating adjusted associations in future research.

The findings of this study support the clinical value of combined first-trimester ultrasound marker assessment for early fetal risk stratification. NT thickness, nasal bone status, ductus venosus flow, and consanguinity together provided a coherent risk profile in the study population. However, the study should be interpreted as an association-based screening study rather than a definitive diagnostic accuracy study unless chromosomal abnormality status is confirmed through a clearly documented reference standard such as karyotyping, chromosomal microarray, chorionic villus sampling, amniocentesis, or validated non-invasive prenatal testing. Without universal reference-standard confirmation, diagnostic terms such as sensitivity, specificity, detection rate, and screening accuracy should be used cautiously or omitted.

This study has several limitations. The sample size was small, and the number of fetuses classified with chromosomal abnormality status was limited. Several analyses used 58 valid cases rather than the full descriptive sample of 59, indicating missing or incomplete outcome data for at least one participant. The original dataset also required denominator correction, particularly for consanguinity and chromosomal abnormality categories, which emphasizes the need for careful data verification before final submission. The single-centre design limits generalizability to other clinical settings, geographic regions, and populations with different background risks. The cross-sectional design allows evaluation of association but does not establish causality. In addition, if genetic confirmation was not performed for all participants, verification bias may have affected outcome classification.

Despite these limitations, the study addresses an important clinical issue in a high-consanguinity context and provides useful preliminary evidence supporting integrated first-trimester ultrasound assessment. The results suggest that increased NT, absent nasal bone, abnormal ductus venosus flow, and consanguinity are strongly associated with chromosomal abnormality status in the analysed sample. Future studies should use larger multicentre cohorts, standardized NT percentile reporting, complete genetic confirmation where feasible, predefined diagnostic pathways, and penalized or exact regression methods when marker-outcome separation is present. Such improvements would strengthen the evidence base for early prenatal screening and counselling in populations where consanguineous marriage is common.

CONCLUSION

Nuchal translucency measurement was strongly associated with chromosomal abnormality status among pregnant women undergoing first-trimester ultrasound assessment, with substantially higher NT values observed in fetuses classified in the chromosomal abnormality presence group. Supplementary ultrasound markers, particularly absent nasal bone and abnormal ductus venosus flow, showed complete concordance with chromosomal abnormality status in the analysed sample, while consanguineous marriage was also significantly associated with the outcome. These findings support the clinical usefulness of combining NT measurement with nasal bone assessment, ductus venosus Doppler, and consanguinity history for early fetal risk stratification. However, because of the small sample size, complete separation of categorical markers, and the need for clearly documented genetic confirmation, the results should be interpreted as screening associations rather than definitive diagnostic accuracy evidence. Larger studies with standardized ultrasound protocols and confirmed chromosomal outcomes are recommended to validate these findings.

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