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Original Article

Clinical Significance and Variations of Fetal Frontomaxillary Facial Angle Measurement in North Indian Pregnant Females

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Abstract

Objective: This study aims to establish normative reference ranges for FMF angle measurements in North Indian fetuses during first trimester (11-13+6 weeks of gestation) and assess its clinical significance. ***Design:*** A prospective observational study was conducted at GSVM Medical College, Kanpur, involving 161 North Indian pregnant females. ***Methods:*** Transabdominal ultrasound measurements of FMF angle were obtained using standardized mid-sagittal imaging techniques. The relationship between FMF angle and crown-rump length (CRL), gestational age, and maternal factors was analyzed using statistical models. ***Results:*** The mean FMF angle was 83.90° (SD = 1.76°), with a range of 80.0° to 87.3°. A strong inverse correlation was observed between FMF angle and CRL ($r = -0.789$, $p < .001$), confirming a gestational age-dependent decline. No significant influence of maternal age ($p = .574$) or gravida status ($p = .233$) was found on FMF angle measurements. The 5th to 95th percentile reference range for FMF angle was established as 81.3° to 86.5°, providing a clinically relevant baseline for North Indian populations. ***Conclusion:*** FMF angle is a stable and reproducible prenatal screening parameter in North Indian pregnancies. The study establishes normative data essential for refining regional first- trimester screening protocols and improving early detection of fetal anomalies.

Keywords: ***Gestational age, Nasal bone, Nuchal translucency, Crown rump length, Frontomaxillary facial angle.***

Introduction

Soft markers [1,2] are minor ultrasound findings identified during early, mid trimester anomaly scan that are often transient and can be found in normal fetuses. However, their presence may warrant further evaluation depending on the clinical context. The presence of a single soft marker during early anomaly scan does not hold much of significance but two or more soft markers holds importance by increasing the likelihood ratio of aneuploidies.

Recently Frontomaxillary facial angle (FMF angle) [1] is an emerging sonographic marker used for the early detection of chromosomal abnormalities especially trisomy 21 [3].

Various studies have shown significant differences in FMF angle measurements among European, Asian, and African populations [4,5] demonstrating distinct mean values for FMF angle which is attributable to genetic and environmental factors reinforcing the necessity of population-based reference values. As a result, applying universal cut-off values without considering ethnic background may lead to inaccurate risk assessments. This variation makes it imperative to establish normative data for our Indian pregnant female population to improve the sensitivity and specificity of prenatal screening in this geographical area. The clinical significance of the FMF angle extends beyond its role in aneuploidy screening [6]. Apart from trisomy 21, an abnormal FMF angle has been observed in other chromosomal disorders such as trisomy 18, trisomy 13 and spina bifida [7-9] though with lesser specificity. It has also been linked to non- chromosomal syndromes involving craniofacial dysmorphism, such as- Treacher's Collins syndrome and Stickler syndrome.

Studies focusing on Indian populations are limited and most available data are derived from Western cohorts [10]. Considering the diverse genetic composition of India, there is a need for region-specific studies to determine a reliable FMF angle reference range that reflects the normal craniofacial growth pattern in North Indian fetuses.

Gestational age is a key determinant, as the FMF angle naturally decreases as pregnancy progresses [11]. Therefore, establishing trimester-specific reference values is essential to avoid misinterpretation. Maternal characteristics such as body mass index (BMI), diabetes, and nutritional status can also impact craniofacial development, potentially affecting FMF angle measurements. Technical factors such as ultrasound machine resolution, operator

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expertise and fetal position further contribute to variability and underscoring the need for standardized measurement protocols [11].

Despite its potential, the FMF angle is not a standalone diagnostic tool but rather a complementary marker in prenatal screening. When combined with other parameters such as nasal bone assessment, nuchal translucency, and biochemical markers, it enhances the predictive value for chromosomal abnormalities [1,12]. Current guidelines recommend integrating FMF angle measurements into first-trimester screening strategies, particularly in cases where traditional markers yield borderline results. However, further studies are needed to refine its role in screening algorithms and to determine optimal cut-off values for different populations.

Limited data is available in FMF angle in India so we had undertaken this study with an aim to establish a pool of such reference range as well as to evaluate the clinical significance measuring frontomaxillary facial angle.

Methods

Study Design

It was a prospective observational study, conducted over a duration of one and half years in department of Radio-Diagnosis in collaboration with Department of Obstetrics and Gynaecology. Study utilized Samsung RS80A [fig.1] and GE Versana Balance Touch USG [Fig.2] machines. The examinations were performed by two trained radiologist to ensuring consistency and minimizing interobserver variability in the collected data. Ethical approval was obtained from the Ethics Committee of our institution, before undertaking the study (Ref. No. EC/226/May/2024).All singleton pregnant females from 11+1 to 13+6weeks of gestational age north Indian origin were enrolled. Multiple pregnancies, fetuses with abnormal NT, NB and cases of non north- Indian origin were excluded.

Figure 1: Samsung RS80A USG machine.

Figure 1 shows Samsung RS80A USG machine used in study Manufactured by Samsung Medison Co.,Ltd., year 2017

Figure 2: GE Versana balance USG machine.

Figure 2 Shows GE versana balance USG machine used in study manufactured by GE HealthCare, in year 2023.

Procedure

FMF angle was measured according to IUSOG [6] guidelines in which three-dimensional (3D) volumes of the fetal face were used by two operators to measure the FMF angle in chromosomally normal fetuses. The measurements were taken in the exact mid-sagittal view [**Fig 3,4,5**]and repeated after lateral rotation of the head by 5 degrees, 10 degrees and 15 degrees away from the vertical position of the occipitofrontal diameter axis. Mean difference and 95% limits of agreement between paired measurements of FMF angle by the same and by two different sonographers were determined. All subjects were followed up in the second trimester (16-24 weeks) for a Targeted Imaging for Fetal Anomalies (TIFFA) scan, where the same FMF angle measurements were repeated to track any developmental changes.

Figure 3: FMF angle measured from GE machine.

Figure 3 Shows USG Scan of fetus in first trimester. Nasal bone, Diencephalon, Palate are marked.

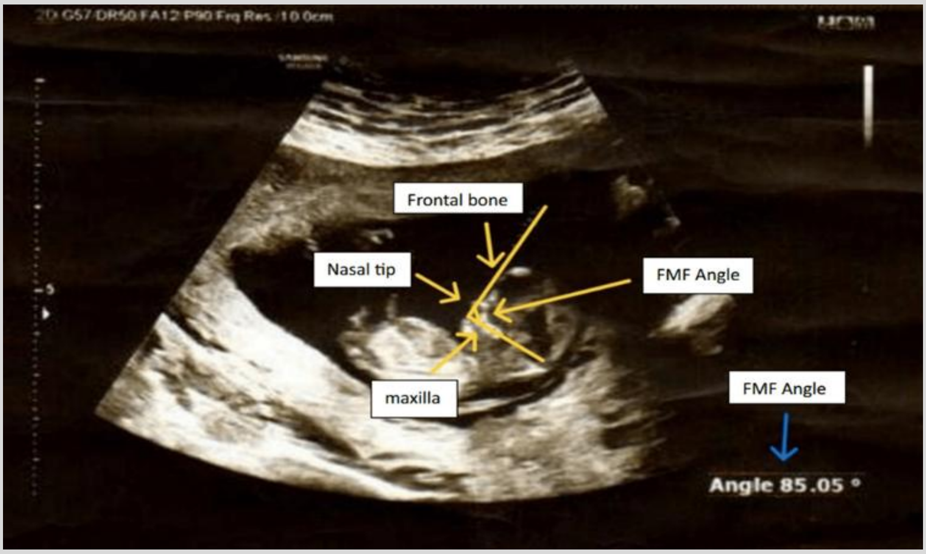

Figure 4: FMF Angle Measurement Using USG Machine.

Figure 4 shows USG Scan of fetus in first trimester. Frontal bone, Nasal tip, FMF angle, Maxilla are marked.

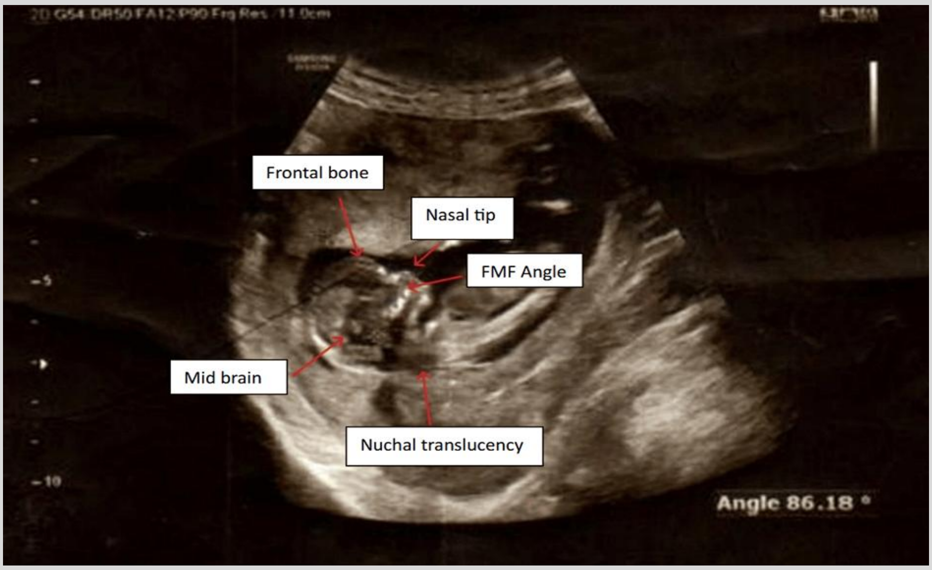

Figure 5: FMF angle measurement using Samsung machine.

Figure 5 shows USG Scan of fetus in First trimester. Frontal bone, Nasal tip, Nuchal translucency, Mid brain FMF angle are marked.

Result

The demographic characteristics and obstetric profiles of the participants are summarized in table no. 1. The mean age of the participants was 27.19 years ± 4.55SD with the youngest participant being 18 years old and the oldest 45 years. Maximum number of participants are under 33 years of age i.e. 88.1%, most of the participants belonged to urban regions i.e. 80.1% and as per B G Prasad socioeconomic classification [13] most of the participants belonged to upper lower class and lower middle class about 38.50% and 36.64% respectively and a lower percentage of participants belongs to lower class and upper class i.e. 2.48% and 5.59% respectively.

Table 1: Demographic data of the participants

Demographic profile of patients			
Variables		**N**	**Percentage**
AGE in years	<33	142	88.1
	≥33	19	11.9
RESIDENCE	Urban	129	80.1
	Rural	32	19.2
Socio Economic Status	Upper class	9	5.59
	Upper middle class	27	16.77
	Lower middle class	59	36.64
	Upper lower class	62	38.50
	Lower class	4	2.48

The mean gestational age at the time of examination was 12.07 ± 0.76 SD weeks, indicating a relatively narrow spread across the sample. CRL values ranged from 42 mm to 85 mm with a mean of 64.37 ± 13.34mm SD. The distribution was slightly positively skewed and leptokurtic, although visual inspection through Q-Q plots suggested near-normal distribution in the midrange.

The FMF angle followed a near-normal distribution (Shapiro-Wilk = 0.968, p =.001), with the mean measurement being 83.90°. The highest recorded angle was 87.3°, and the lowest was 80.0°, supporting a tight and consistent range across the study group.

Table no.2 shows that CRL was categorized into regular intervals to explore the FMF angle variations according to the fetal size and the means of FMF angles were analyzed accordingly. A declining trend was observed in FMF angle with increasing CRL, consistent with prior literature suggesting an inverse relationship.

Table 2: Frontomaxillary facial angle Variations Across CRL Intervals

CRL Interval (mm)	**N**	**Percentage**	**Mean ± SD FMF Angle (°)**
41-50	31	19.2	85.84 ± 1.17
51-60	41	25.4	84.47 ± 1.29
61-70	36	22.3	84.22 ± 0.94
71-80	17	10.5	82.70 ± 1.23
81+	36	22.3	81.84 ± 0.82

An inverse relationship between FMF angle and CRL was observed via Pearson correlation analysis and the findings confirmed a statistically significant negative correlation [**Table 3**]. This suggested that with increasing fetal length during the first trimester, the FMF angle tend to decrease. This trend aligns with previous findings reported in both Asian and Western literature and supported the hypothesis of a gestational progression effect on craniofacial angles.

Table 3: Correalation between Frontomaxillary facial angle and Crown-Rump Length

Variables	**Pearson Correlation (r)**	**Significance (2-tailed)**	**N (%)**
FMF Angle & CRL (mm)	-0.789	<0.001**	161

A similar correlation analysis was conducted between FMF angle and gestational age (in completed weeks), which yielded corroborative findings, albeit of lesser magnitude. While a formal correlation coefficient was not calculated in the output, the observed means suggested a decremental trend in FMF angle with increasing gestational age [**Table 4**]. This pattern is biologically plausible as the fetal midface undergoes structural remodeling during the first trimester.

Table 4: Frontomaxillary facial angle Correlation with Gestational Age

Gestational age	**Mean ± SD FMF Angle (°)**	**N**	**percentage**
11-11+6 weeks	85.10 ± 1.11	41	25.4
12-12+6 weeks	84.02 ± 0.99	67	41.6
≥13 weeks	82.91 ± 083	53	32.9

One-way ANOVA was performed across five binned age categories to determine any correlation between FMF angle and maternal age. The ANOVA test revealed no statistically significant difference in FMF angle across maternal age groups (F = 0.728, p =.574), indicating maternal age was not a modifying factor for fetal FMF angle in this cohort [**Table 5**].

Table 5: Maternal Age and Frontomaxillary facial angle of Participants

Maternal Age Group (Years)	N	percentage	Mean ± SD FMF Angle (°)	
≤20	4	2.4	84.21 ± 1.40	ANNOVA (p-value).574
21-26	74	45.9	83.89 ± 1.72	
27-33	64	39.7	84.06 ± 1.83	
34-39	18	11.1	83.63 ± 1.77	
≥40	1	0.62	83.10	

Participants were grouped into primigravida and multigravida to examine whether obstetric history affects fetal FMF angle, and an independent sample comparison was conducted Although multigravida participants had slightly higher mean FMF angles, this difference was not statistically significant (F = 1.433, p =.233) [**Table 6**]. Thus, parity appears to have no clinically meaningful influence on FMF angle measurements.

Table 6: Frontomaxillary facial angle By Gravid Status

Gravida Category	N	percentage	Mean ± SD FMF Angle (°)	95% CI	
Primigravida	22	13.6	83.49 ± 1.42	82.85 - 84.12	ANNOVA (p-value). 233
Multigravida	139	86.3	83.97 ± 1.81	83.67– 84.27	

The establishment of percentile-based reference values was crucial for clinical screening for FMF angle and percentiles of FMF angle were computed to define normative ranges for this population. The data reveal that approximately 90% of the study population falls within the FMF angle range of 81.5° to 86.0° so a narrow range offers a clinically reliable reference for routine ultrasonographic interpretation during early gestation [**Table 7**]

Table 7: Frontomaxillary facial angle Percentile Distribution Between 11+1 to 13+6 weeks

Percentile	FMF Angle
5th	81.30
10th	81.50
25th	82.30
50th (median)	84.00
75th	85.00
90th	86.00
95th	86.50

A linear regression analysis was conducted with FMF angle as the dependent variable and CRL as the predictor to quantify the predictive relationship between fetal size and FMF angle. This regression model demonstrated that CRL significantly predicts FMF angle (p <.001), accounting for approximately 62.2% of the total variance. For every 1 mm increase in CRL, the FMF angle decreases by approximately 0.104°, affirming the inverse linear relationship [**Table 8**].

Table 8: Linear Regression Analysis Between Crown Rump Length and Frontomaxillary facial Angle

Parameters	Coefficient	Std. Error	t Value	p-Value
Constant (Intercept)	90.617	0.424	213.96	<.001
CRL (mm)	-0.104	0.006	-16.18	<.001
$R^2 = 0.622$, Adjusted $R^2 = 0.620$, F=261.96, P<.001				

Discussion

The distribution of FMF angles was nearly symmetrical and approached normality consistent with findings in other large-scale studies, such as those by Panigassi *et al.* [14]. and Molina *et al.* [3]. This tight distribution reflects the measurement's potential as a reliable quantitative screening marker in early gestation.

One of the key observations in the present study was the strong and statistically significant negative correlation between crown-rump length (CRL) and FMF angle (r = -0.789, p <.001), highlighting that as fetal length increased within the first trimester window, the FMF angle decreased. This inverse relationship has been repeatedly validated in international literatures (Bartosz Czuba *et al.* [7]., Hsiao *et al.* [15], and the regression model derived in the current study further supported this trend. The model equation - FMF angle = 90.617 - 0.104 × CRL (mm)-offers a simple and clinically applicable method for estimating FMF angle based on fetal length in North Indian fetuses. This regression was notably similar in structure and strength to those derived by Hsiao *et al.* in the Chinese population and by Plasencia *et al.* in the UK, thus reinforcing the generalizability of the FMF-CRL relationship across ethnic groups [6].

Furthermore, the FMF angle was observed to vary across every week over 11 -13-week gestational age groups, with a gradual decrease in mean angle values from 85.10° at 11 weeks to 82.91° at 13 + 6 weeks. While formal correlation coefficients were not computed for gestational age (converted to weeks), the trend echoes that of CRL, which itself is a surrogate for gestational age in the first trimester. This gestational age- dependent decrease in FMF angle supports the hypothesis that facial bone angulation evolves progressively during fetal craniofacial development, further emphasizing the importance of strict gestational age calibration in clinical use.

Interestingly, neither maternal age nor parity status demonstrated statistically significant association with FMF angle values [16]. Maternal age was stratified into five categories and evaluated via one-way ANOVA, yielding no significant group differences (p =.574). Similarly, comparing FMF angles between primigravida and multigravida women showed no meaningful variation (p =.233). These findings suggested that FMF angle measurements were robust against maternal demographic factors, aligning with the conclusions drawn by Panigassi *et al.* [14], who also reported no significant differences based on maternal ethnicity or demographic background. This reinforces the utility of FMF angle as a fetal-specific marker relatively independent of maternal confounders.

The clinical reproducibility and standardization of the FMF angle were also essential considerations. In the reviewed literature, studies such as that by Plasencia *et al.* [6]. highlighted the impact of off-axis imaging and acquisition technique on FMF angle accuracy. The current study, while not explicitly evaluating reproducibility metrics such as intraclass correlation coefficients (ICCs), maintained strict criteria for mid-sagittal plane acquisition and ensured observer training. The high rate of successful FMF measurements (100%) and the tight clustering of values within a 7.3° range suggested that with appropriate technique, FMF angle can be reliably assessed in routine clinical settings. Even within resource-constrained government institutions with high turnover of patients comparison with previous population-based studies, this study's findings were in alignment with mean FMF angle reported by Molina *et al.* [3], during second trimester screening (83.9°), supporting the idea that in euploid fetuses, the FMF angle remains within a predictable range through mid-gestation. However, the present data pertain strictly to first trimester (11-13+6 weeks), and extrapolation beyond this window should be undertaken with caution. Moreover, the consistently reported decline in FMF angle with increasing CRL, both in this and prior studies, may have implications for determining gestational age-specific cutoffs for screening purposes. In this respect, the percentile data provided in the present study could assist in refining trisomy risk thresholds for local populations.

Despite its strengths, the study had its own limitations. While prior studies have reported ICC (Intraclass correlation coefficient) values between 0.605 and 0.858 (Panigassi *et al.* [14], validation within the current population would further support reproducibility claims. Firstly, the study did not include trisomy or anomaly-confirmed cases, which would have enabled comparison of FMF angle behavior in euploid versus aneuploid fetuses. Consequently, while normative range have been established, the diagnostic utility of the FMF angle in detecting abnormalities within this population remains to be evaluated in future case-control or cohort designs. A follow-up of pregnancy outcomes and correlation of early FMF measurements with postnatal craniofacial development or syndromic features could further elucidate its predictive value.

Furthermore, technological limitations may have impact on measurement of FMF angle. The use of 2D ultrasonography for FMF angle acquisition, while appropriate and validated, lacks the three-dimensional fidelity offered by newer 3D/4D imaging systems. As 3D allows for better mid-sagittal reconstruction, potentially reducing measurement error,however, given that most Indian radiology units in public hospitals use 2D systems, the study's findings remain practical and relevant to real-world screening protocols.

Conclusions

This study concluded that frontomaxillary facial (FMF) angle could be a valuable and reliable ultrasonographic parameter in first trimester of pregnancy, demonstrating consistent measurement characteristics and exhibits significant correlation with other fetal biometric indices in the North Indian population. The findings revealed a statistically strong significant inverse relationship between FMF angle and crown-rump length (CRL), which supported the dynamic nature of fetal craniofacial development during early gestation. Importantly, maternal demographic variables such as age and parity did not significantly influence the FMF angle, indicating its independence from maternal factors and affirming its role as a fetal- specific marker. The study established a normative reference range of 81.3° to 86.5° (5th to 95th percentile) for the FMF angle in euploid fetuses during 11-13+6 weeks of gestation which aligned with international literature, validating the measurement's cross-populational applicability when standardized techniques were followed.

Declarations

Conflict of interest

No conflict of interest

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Acknowledgment

No Acknowledgment

Ethical Clearance

Ethical approval was obtained from the Ethics Committee of our institution, before undertaking the study (Ref. No. EC/226/May/2024).

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