Utilization of third-trimester fetal transcerebellar diameter measurement for gestational age estimation: a comparative study using Bland-Altman analysis

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BACKGROUND: Several studies show that gestational age estimation during the third trimester of pregnancy using fetal transcerebellar diameter is superior to that measured using fetal biometry (biparietal diameter, head circumference, abdominal circumference, and femur diaphysis length). However, the conclusion of the studies stemmed from findings of correlation and regression statistical tests, which are not the recommended statistical analysis methods for comparing the values of 1 variable as measured by 2 different methods.

OBJECTIVE: This study aimed to compare the accuracy of gestational age estimation using transcerebellar diameter to that using fetal biometry during the third trimester of pregnancy using Bland-Altman statistical analysis.

STUDY DESIGN: This was a cross-sectional study on pregnant women who presented for routine antenatal care follow-up in the third trimester of pregnancy (28–41 weeks of gestation) at St. Paul's Hospital Millennium Medical College (Ethiopia) between November 1, 2020, and February 28, 2021. Data were collected prospectively using a structured questionnaire on the Open Data Kit. The primary outcome of our study was the mean bias of gestational age estimation (error in estimating gestational age) using transcerebellar diameter and composite fetal biometry (composite gestational age). Data were analyzed using Stata (version 15; StataCorp, College Station, TX). Simple descriptive analysis, Bland-Altman analysis, and the Kendall τa discordance measurement were performed as appropriate. The mean bias (error) and limits of agreement were used to present the significance of the finding.

RESULTS: A total of 104 pregnant women in the third trimester were included in the study. The mean error (bias) when transcerebellar diameter was used to estimate the gestational age was 0.65 weeks vs a bias of 1.1 weeks using composite biometry, compared with the gold standard method from crown-lump length (in both cases). The calculated estimated limit of agreement was narrower in the case of transcerebellar diameter than in the case of composite fetal biometry (−3.56 to 2.25 vs −4.73 to 2.53). The Kendall τa discordance measurement revealed that gestational age estimations using composite biometry and crown-lump length were 51% to 70%, respectively, more likely to agree than disagree and that gestational age estimations using transcerebellar diameter and crown-lump length were 62% to 77%, respectively, more likely to agree than to disagree ($P \leq .001$).

CONCLUSION: Gestational age estimation using transcerebellar diameter is more accurate than gestational age estimation using composite gestational age (biparietal diameter, head circumference, femur diaphysis length, and abdominal circumference). Transcerebellar diameter should be used to date third-trimester pregnancies with unknown gestational age (unknown last normal menstrual period with no early ultrasound milestone).

Key words: biometry, low-income setting, obstetrical ultrasound, pregnancy dating, transcerebellar diameter, unknown date

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Formal ethical clearance letter was obtained from the institutional review board of St. Paul Hospital Millennium. Written informed consent was obtained from all study participants.

The authors report no conflict of interest.

This study received funding from St. Paul's Institute for Reproductive Health and Rights.

All data generated or analyzed during this study are included in this published article.

Cite this article as: Bekele D, Gudu W, Wondafrash M, et al. Utilization of third-trimester fetal transcerebellar diameter measurement for gestational age estimation: a comparative study using Bland-Altman analysis. Am J Obstet Gynecol Glob Rep 2024;4:100307.

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2666-5778/$36.00

http://dx.doi.org/10.1016/j.xagr.2024.100307

AJOG Global Reports at a Glance

Why was this study conducted?

Previous studies on the use of fetal transcerebellar diameter (TCD) measurement for gestational age (GA) estimation in the third trimester of pregnancy employed correlation and regression analysis, which are not the recommended statistical analyses to measure 1 variable using ≥2 different methods. A large margin of error (3−4 weeks) remains a major concern when it comes to calculating GA using biometry in the third trimester of pregnancy for undated pregnancies. Hence, using a superior alternative GA estimation method is crucial. Our study investigated the accuracy of TCD vs composite GA (biometry: biparietal diameter [BPD], head circumference [HC], abdominal circumference [AC], and femur diaphysis length [FL]) in determining third-trimester GA.

Key findings

A total of 104 pregnant women in the third trimester of pregnancy were included in the study. The mean error (bias) when TCD was used to estimate the GA was 0.65 weeks, which was lower than the mean error (bias) of 1.1 weeks when composite biometry was used. The calculated estimated limits of agreement were narrower in the case of TCD than in the case of composite fetal biometry (−3.56 to 2.25 vs −4.73 to 2.53, respectively). GA estimations using TCD and crown-lump length (the gold standard method) were 62% to 77%, respectively, more likely to agree than to disagree ($P \leq .001$).

What does this add to what is known?

Our results support previous reports on the superiority of TCD vs biometry (HC, AC, BPD, and FL) at estimating GA with far more significant results derived from an ideal statistical method of analysis.

Introduction

Accurate gestational age (GA; a term used to describe how far advanced a pregnancy is) estimation using sonographic fetal parameters is one of the great achievements in the history of modern obstetrics.[1,2] From the fetal ultrasound parameters, first-trimester fetal crown-rump length (CRL) correlates closely with GA and is often mentioned as the gold standard for dating pregnancy in some studies.[3] For pregnant women who had missed the opportunity to have this gold standard measurement in the first trimester of pregnancy and for pregnant women whose last normal menstrual period (LNMP) is unknown, fetal biometric parameters have been used to estimate the GA at later pregnancy. Although the most commonly used fetal biometric parameters to measure GA during the second and third trimesters of pregnancy are biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur diaphysis length (FL),[4] fetal transcerebellar diameter (TCD) measurement has been described as an alternative parameter to these most frequently used biometric parameters to date pregnancy.[5,6] Beyond being an alternative, several studies indicate that fetal TCD is a more accurate and better predictor of GA in normal fetuses and fetuses with intrauterine growth restriction (IUGR) than the other biometry parameters.[7,8] In cases of growth restriction, the cerebellum is usually spared, making TCD a reliable indicator of GA even when other parameters fall off the appropriate growth curve.[9]

However, all the previous studies that documented the accuracy of TCD at estimating GA during the third trimester of pregnancy had a common major limitation. Correlation and regression were the statistical tests used to derive the conclusions in those studies. None of the studies used Bland-Altman (B&A) analysis, which is the recommended statistical analysis used to compare the measurement of 1 variable using 2 different methods. Correlation and regression analysis show the relationship between 1 variable and another, not the differences, and they are not recommended as the methods for assessing the comparability between the methods of measurement.[10−12] This study aimed to address this concern and investigated the accuracy of GA estimation using TCD vs biometric measurement, compared with the gold standard (first-trimester CRL), using the B&A analysis.

Materials and Methods

Study design, study setting, and study period

This was a cross-sectional comparative study of pregnant women in the third trimester of pregnancy who had their GA estimated using fetal biometry and TCD, and this study was conducted at St. Paul's Hospital Millennium Medical College (SPHMMC), Addis Ababa, Ethiopia from November 1, 2020, to February 28, 2021. The SPHMMC is a tertiary public hospital and a leading medical college in Ethiopia. The obstetrics department within this hospital has a maternal-fetal medicine (MFM) unit that deals with managing high-risk pregnant mothers and performs advanced fetal diagnostic ultrasound by MFM specialists and fellows, including estimating GA using fetal biometry and TCD measurement for pregnancies with unknown GA. Annually, close to 3000 mothers attend antenatal care at the obstetrics department of this hospital. Moreover, the hospital has one of the highest delivery rates in Ethiopia, as more than 10,000 deliveries are attended per annum at this hospital.

Participants

Pregnant mothers in their third trimester of pregnancy attending antenatal care at our hospital (SPHMMC) were enrolled in the study. The inclusion criteria were patients with singleton pregnancy, patients with a GA of ≥28 weeks, patients who had early ultrasound milestones (CRL before 13 6/7 weeks of gestation), and patients who volunteered to participate in the study. The exclusion

criteria were fetal congenital anomaly, chromosomal or genetic abnormalities, preeclampsia, IUGR, and women with emergency conditions that required urgent attention.

Data collection and procedures

Data were collected using a structured questionnaire prepared in English on the Open Data Kit. The questionnaire had 3 sections: sociodemographic characteristics, obstetrical characteristics, and GA estimation using biometry parameters and TCD. Nurses assigned to antenatal care (ANC) reviewed the medical records of ANC attendees and identified women who were eligible for the study. Systematic random sampling was used to recruit women among those identified women.

All ultrasound examinations were performed by an MFM fellow or specialist. In this ultrasound, fetal biometry and TCD were measured using a 3.5 MHz C1-6VN curvilinear probe of a LOGIQ S8 GE ultrasound machine. Of note, 1 MFM fellow and 1 MFM specialist did all the measurements (including TCD). Participants were scanned once either by a fellow or by the attending physician (MFM specialist). The sonographers were blinded to the GA derived from the early ultrasound examination (CRL) of the participants. The fetal biometry (BPD, HC, AC, and FL) and TCD measurements were performed as follows:

- BPD and HC: Measured in the transverse section of the head at the level of the thalami and cavum septi pellucidi; the cerebellar hemispheres should not be visible in this scanning plane.
- FL: Measured with the full length of the bone perpendicular to the ultrasound beam, excluding the distal femoral epiphysis.
- AC: Measured in the symmetrical, transverse round section at the skin line, with visualization of the vertebrae and in a plane with visualization of the stomach, umbilical vein, and portal sinus.
- TCD: Using the horizontal plane of the fetal head, the landmark of the thalami and cavum septum pellucidum were identified in the midline. The transducer was slightly rotated caudally to bring the characteristic "butterfly" appearance of the cerebellum into view. TCD was measured as the widest diameter across both hemispheres in an outer-to-outer fashion.

Written informed consent was obtained from the study participants. A formal ethical clearance letter was obtained from St. Paul's Institutional Review Board. Data confidentiality and data anonymity were implemented throughout the data collection procedure.

Outcomes

The primary outcome of our study was the mean bias of GA estimation (error in estimating GA) using TCD and fetal biometry (composite GA) compared with GA estimation using the gold standard (CRL). The secondary outcome was the estimated limits agreement of GA estimation using TCD and composite GA compared with that using CRL.

Statistical analysis

The sample size estimate was calculated with an assumption of a correlation of 0.34 with an alpha 2-tailed level of 0.025 and a β of 0.1 (http://sample-size.net/correlation-sample-size/), as there is no previous similar study that employed identical statistical analysis compared with that used in our study. The calculated sample size was 102. Data were analyzed using Stata (version 15; StataCorp, College Station, TX). Descriptive statistics were used to analyze the baseline characteristics. We used the B&A plot analysis and the Kendall τa discordance measurement to test the accuracy of GA measurement using TCD and fetal biometry (composite GA) compared with the gold standard (estimation using first-trimester CRL). The priori determined acceptable limit of agreement was $\pm$3 weeks for the B&A plot for TCD and composite GA with CRL, whereas for comparison of TCD with composite GA, the limit of agreement was $\pm$2 weeks.

Role of the funding source

Apart from allocating a financial grant to support the conduct of this study, the funder (St. Paul's Institute for Reproductive Health and Rights) had no input into the study design, data interpretation, review, and approval of this report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

A total of 104 pregnant women were enrolled in this study at a GA of 28 to 41 weeks. Their mean age was 28 ($\pm$4.66) years (Table 1). Most participants were parous women (63/104 [60.6%]) and had their address within Addis Ababa (71/104 [68.3%]). The mean GA calculated using CRL was 36.09 weeks, whereas the mean GA estimates calculated using composite third-trimester biometry and TCD were 34.99 and 35.38 weeks, respectively.

The comparison of GA measured using composite GA (third-trimester biometry: BPD, HC, FL, and AC) vs GA measured using the first-trimester CRL (gold standard) using B&A analysis showed that the mean calculated GA using composite GA was 1.1 weeks lower than the mean calculated GA using CRL (Figure 1). The estimated limit of agreement (95% confidence interval) was $-$4.73 to 2.53, which indicated that the GA measured using the composite method may measure as much as 4.73 weeks below and 2.53 weeks above the GA measured using CRL. In other words, the mean error in GA estimation using composite GA calculation was 1.1 weeks compared with the gold standard, with the range of error being 4.73 weeks below or 2.53 weeks above that calculated from CRL, with 3.85% of values being outside the limit of agreement. The priori determined acceptable limit of agreement was $\pm$3 weeks. The mean GA estimation using TCD was 0.65 weeks lower than the mean GA estimation using first-trimester CRL. The estimated limit of agreement was $-$3.56 to 2.25, which indicated that the GA measured by the composite method may measure as

TABLE 1
Sociodemographic and obstetrical characteristics of pregnant women whose gestational age was calculated using third-trimester biometry and transcerebellar diameter, 2020−2021, Ethiopia

Variable	Category	n (%)
Age (y)	Mean (±SD)	28 (±4.66)
Parity	Nulliparous	41 (39.4)
	Parous	63 (60.6)
Address	Addis Ababa	71 (68.3)
	Outside Addis Ababa	33 (31.7)
GA (wk)		
GA estimation using LNMP	Mean (±SD)	36.12 (±3.68)
GA estimation using TCD	Mean (±SD)	35.38 (±2.81)
GA estimation using composite GA	Mean (±SD)	34.99 (±2.60)
GA using FL	Mean (±SD)	34.65 (±3.30)
GA using AC	Mean (±SD)	34.80 (±2.95)
GA using HC	Mean (±SD)	34.66 (±2.75)
GA using BPD	Mean (±SD)	34.47 (±2.70)
GA using CRL	Mean (±SD)	36.09 (±3.49)

AC, abdominal circumference; *BPD*, biparietal diameter; *CRL*, crown-lump length; *GA*, gestational age; *HC*, head circumference; *LNMP*, last normal menstrual period; *SD*, standard deviation; *TCD*, transcerebellar diameter.

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much as 3.56 weeks below and 2.25 weeks above the GA measured using CRL, with 4.85% of values being outside the limit of agreement (Figure 2). The priori determined acceptable limit of agreement was ±2 weeks.

When GA estimation using TCD was compared with GA estimation using composite GA, the mean error was −0.38 weeks, with the margin of error being −2.23 to 1.48 weeks (the GA calculation using the composite method was 2.23 weeks below or 1.48 weeks higher than the GA calculation using TCD, with 4.9% of values being outside the limit of agreement (Figure 3). The priori determined acceptable limit of agreement was ±2 weeks.

Using the Kendall τa analysis, we found that GA estimations using the composite method and CRL were 51% to 70%, respectively, more likely to agree than disagree, whereas GA calculated using TCD and CRL were 62% to 77%, respectively, more likely to agree than to disagree ($P \leq .001$) (Table 2).

Discussion

Principal findings

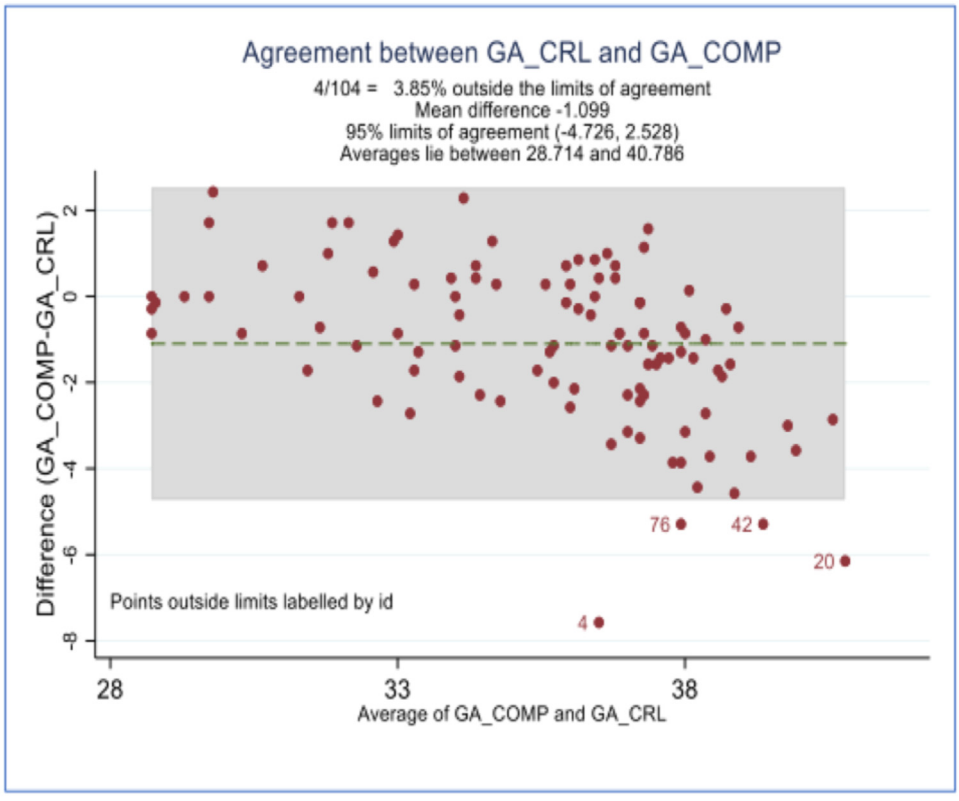
Here, GA estimation using TCD in the third trimester of pregnancy was found to be more accurate at predicting GA than GA estimation using fetal biometry (composite GA estimation using BPD, FL, HC, and AC measurements). GA measurement using TCD was more likely to agree with measurement using CRL than that using composite GA.

Results

TCD has been described as a reliable alternative to estimating GA by many studies. In particular, it has been labeled as a useful method of predicting GA in patients who are unsure of dates (unknown date) or suspected to have IUGR.[13,14] A previous large multicenter prospective cohort study (1947 women) conducted in a low-income setting analyzed GA estimation using biometry and TCD. The study found that TCD showed minimal bias in estimating GA and suggested the incorporation of TCD to improve the accuracy of GA estimation in both normal pregnancies and pregnancies complicated by IUGR.[15] This suggestion is further supported by another large study that examined the use of TCD measured using ultrasound for the detection of GA in normal fetuses and fetuses with IUGR. Moreover, the study found that TCD showed a significant correlation with GA in normal pregnancies and pregnancies complicated by IUGR.[16] Similarly, a cross-sectional study of 700 normal pregnancies between 14 and 42 weeks of gestation found a strong correlation between GA and TCD.[17]

In the current study, GA estimation using TCD was found to be more accurate than GA estimation using composite GA (third-trimester biometry). B&A analysis revealed that the bias when TCD was used to estimate GA was less than the bias when composite GA (fetal biometry) was used (mean error of 0.65 vs 1.10 weeks, compared with the gold standard method using CRL). The calculated estimated limit of agreement was narrower in the case of TCD than in the case of composite fetal biometry (−3.56 to 2.25 vs −4.73 to 2.53). Further analysis using the Kendall τa discordance measurement revealed that GA estimations using TCD and CRL were 62% to 77%, respectively, more likely to agree than to disagree ($P \leq .001$), which were higher than that when composite biometry was employed. Similar to our findings, a prospective study from India found that, of all the sonographic parameters (fetal biometry) used to estimate GA, the TCD had the highest correlation ($r=0.979$; $P<0.0001$).[13] In addition, another study of 228 patients showed that TCD gave the correct assessment in more than 90% of the cases (91.7%; $P=.001$) corresponding to the GA using the last menstrual period (LMP).[18] A recent case-control study from Egypt conducted in 2021 analyzed 52 women at 27 and 37 weeks of gestation and found that TCD was a more accurate predictor of GA in the third trimester of pregnancy than other biometric measurements (BPD, AC, and FL).[19] An earlier similar study of 60 women

FIGURE 1
Comparing the measured GA between CRL and composite GA



CRL, crown-lump length; *GA*, gestational age.

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concluded that TCD is the most accurate biometric measurement in both uncomplicated and complicated pregnancies.[20] This conclusion regarding the accuracy of TCD at estimating GA in the third trimester of pregnancy is further supported by findings from a study conducted in Nepal that found TCD (r^2=0.989; P<.001) to have a higher predictive value than that estimated using BPD (r^2=0.929; P<.01), HC (r^2=0.964; P<.01), AC (r^2=0.931; P<.01), and FL (r^2=0.966; P<.01).[21]

Clinical implication

Consistent with previous reports, we found that TCD is more accurate at estimating GA in the third trimester of pregnancy than other biometric measurements (BPD, HC, AC, and FL). Being performed with far rigorous statistical analysis, the results of our study are also reliable. It implies that TCD measurement at a low-income setting, such as ours, is a feasible and reliable method of estimating GA in the absence of the gold standard of measurement and where the LNMP of the women is unknown. This has relevance to the obstetrical practice across other low-income countries (globally), where undated pregnancies are common.

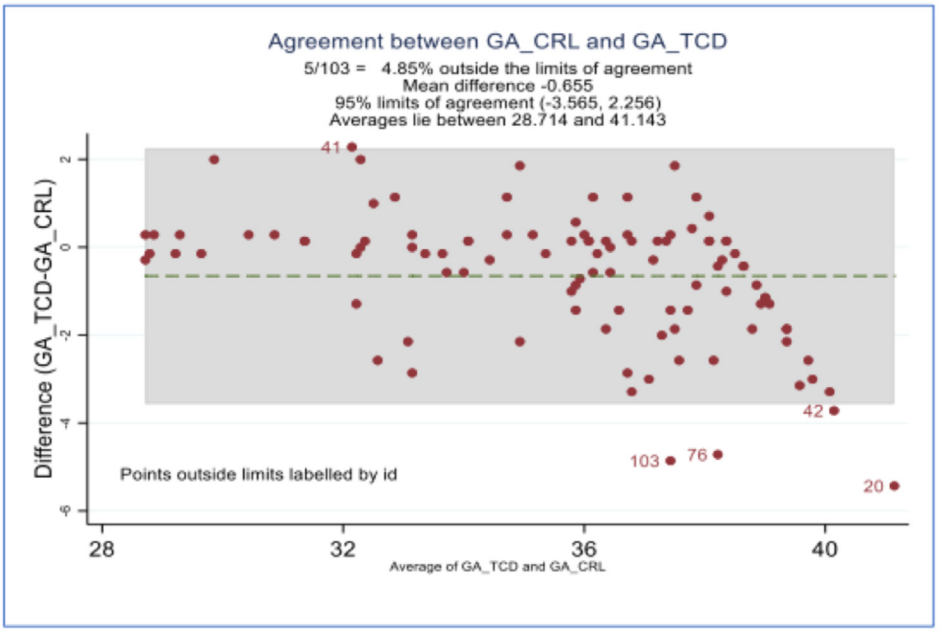
Research implication

Although our study brings in stronger results, there is a research gap that should be addressed in future studies. Although the TCD is a better estimate of GA than fetal biometry in the third trimester of pregnancy, the feasibility and reproducibility of TCD measurements performed by general obstetrics and gynecology providers should be addressed in future studies. In our current analysis using MFM providers specialized in fetal ultrasound, third-trimester TCD measurements were considered technically challenging. In Ethiopia as in other low-income places around the world, people with undated pregnancies are commonly evaluated in hospitals without MFM experts. If future research will identify a difference in the accuracy of third-trimester TCD measurements performed by general obstetrics and gynecology providers vs MFM providers, such findings would support training or general obstetrics and gynecology providers and residents on how to perform TCD (in addition to existing training in fetal biometry).

Strengths and limitations

Our study findings support previous reports regarding the accuracy of TCD at estimating GA in the third trimester of pregnancy but with a more robust statistical analysis method, which was not implemented in any of the studies

FIGURE 2
Comparing the measured GA between CRL and TCD



GA= gestational age; COMP= composite gestational age; CRL= crown lump length ; TCD= trans cerebellar diameter

CRL, crown-lump length; *GA*, gestational age; *TCD*, transcerebellar diameter.

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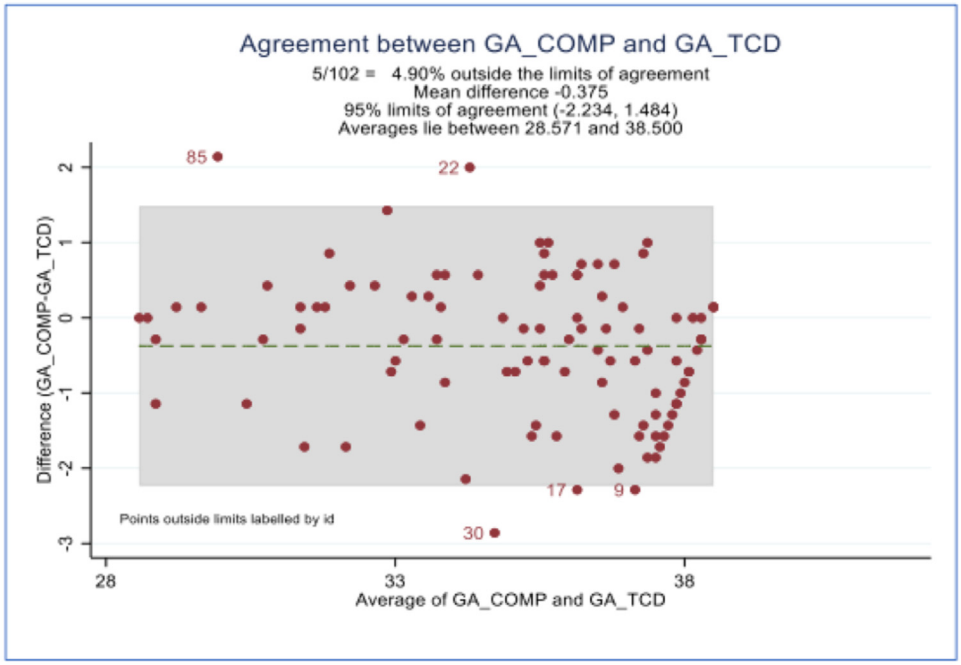
FIGURE 3
Comparing the measured GA between composite GA and TCD



GA= gestational age; COMP= composite gestational age; CRL= crown lump length ; TCD= transcerebellar diameter

GA, gestational age; *TCD*, transcerebellar diameter.

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TABLE 2
Measures of discordance between the test measures (composite GA and TCD) of GA and predicated GA from the first trimester of pregnancy using CRL in weeks

GA estimation method	Coefficient	Jackknife standard error	*z* score	*P* value	95% CI	
GA estimation using CRL	0.98	0.00	325.25	.000	0.98	0.99
GA estimation using composite GA	0.60	0.05	12.55	.000	0.51	0.70
GA estimation using TCD	0.98	0.00	317.73	.000	0.98	0.99

CI, confidence interval; *CRL*, crown-lump length; *GA*, gestational age; *TCD*, transcerebellar diameter.

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reviewed. B&A plot analysis and the Kendall τa discordance measurement were the statistical tests performed in our study (the recommended methods to compare the efficacy of 2 methods of measurement at measuring one variable) but were the correlation statistical tests (used to show correlation between 2 variables) performed in the previous studies. Blinding of sonographers to GA is the other strength of this study. Hence, our study delivers stronger results, and therefore, our conclusions regarding the higher predictive value of TCD at estimating GA are firm and reliable. Lack of comparative analysis in those with normal growth and those with IUGR is a limitation of this study. Using unconventional parameters for sample size calculation is another limitation of this study. We should have used an alpha level of 0.001 instead of an alpha level of 0.025, to be stricter.

Conclusion

For third-trimester pregnancies with unknown GA (unknown LMP and no early dating ultrasound), the use of TCD is more accurate in predicting GA than fetal biometry (BPD, HC, FL, and AC).

CRediT authorship contribution statement

Delayehu Bekele: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Writing — original draft, Writing — review & editing. **Wondimu Gudu:** Conceptualization, Data curation, Methodology, Writing — original draft, Writing — review & editing. **Mekitie Wondafrash:** Formal analysis, Resources, Software, Writing — original draft, Writing — review & editing. **Abdulfetah Abdulkadir Abdosh:** Data curation, Investigation, Writing — original draft, Writing — review & editing. **Abraham Fessehaye Sium:** Formal analysis, Methodology, Validation, Writing — original draft, Writing — review & editing.

ACKNOWLEDGMENTS

We would like to acknowledge the Department of Obstetrics and Gynecology at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.

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