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Fetal Binocular Distance in Sudanese, Sono-graphic Study

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ABSTRACT

Background: Recent developments in fetal ultrasound technology represent effective tools for gestation age (GA) estimation and screening of abnormalities in fetal development. Fetal orbital measurements as well as binocular distance (BOD) not performed routinely during obstetrical sono-graphy, although not very popular, can aid in GA and fetal weight (FW) estimation. **Objectives:** The aim of this study was to construct reference ranges for fetal BOD in Sudan, and to evaluate the correlations of BOD with GA, FW, sex, and other common biometric measurements. **Subjects and methods:** In this prospective, descriptive, cross sectional study, a total of 385 Sudanese healthy pregnant ladies with regular menstrual cycle and certainty about the time of the last menstrual period and age ranged of 16 – 44 years, within 14 to 41 weeks of gestation; individuals underwent routine sono-graphy were examined at obstetrics and gynecology clinic in Omdurman, Sudan. Normal pregnancies of viable singleton with good sono-graphic visualization of the fetus face were included in this study. Moreover, descriptive statistics, linear regression models were employed by using SPSS version 22 (SPSS Inc, IBM) at 95% confidence intervals. **Results:** Fetal BOD range (15 - 64 mm),mean (40.1 ± 10.7 mm). Linear growth functions were significant between BOD with GA (r=0.930, P < 0.0001), FW (r=0.801, P < 0.0001) and other common fetal biometric parameters such as biparietal diameter (r=0.935, P < 0.0001), head circumference (r=0.879, P < 0.0001), femur length (r=0.939, P < 0.0001) and abdominal circumference (r=0.701, P < 0.0001). Furthermore, BOD showed significant correlation with both fetal sex (P = 0.021) and mother's tribe (P = 0.023). **Conclusion:** BOD significantly increased with increasing GA. Reference ranges developed in the present study will enable accurate evaluation of menstrual age throughout pregnancy. However, nomograms of BOD for Sudanese fetuses of 14–41 weeks gestation have been constructed.

KEYWORDS Binocular distance, Fetal, Biometric measurement, Sudan

INTRODUCTION

Growth of the human eye during fetal life is correlated with growth of the orbit [1]; the parameters that are studied in the fetal face, orbit, and eye follow a roughly linear growth curve [2]; the orbital region plays a predominant role in the evaluation of the craniofacial complex [3]. Since ocular and orbital malformations are often principal signs of generalized syndromes, orbital biometry is helpful for a detailed prenatal investigation of the fetal face [4]. In addition, fetal orbital and ocular anomalies, such as cyclopia, microphthalmia, cataract and anophthalmia may be part of congenital syndromes, such as trisomy 13, trisomy 21, Walker–Warburg syndrome, Frasercryptophthalmos syndrome, or a brain anomaly, such as holoprosencephaly [5]. BOD may be useful in the diagnosis of some abnormalities [6, 7], Trout *et al.*[8] reported that cases with abnormal orbital distances has associated intra- or extracranial abnormalities, including holoprosencephaly, encephalocele, cleft palate, cardiac anomalies, imperforate anus, diaphragmatic hernia, and digit anomalies. Moreover, ocular biometric parameters are useful sonographic markers for trisomy 13, even further evaluation is needed [9]. Both structural anomalies and intraorbital malformations can be identified by using orbital measurements; this method also presents important information about normal eye development and has potentially important place in genetic counseling [10].Knowledge of the examination technique and normal ultrasound anatomy of the eye and orbit is required [11].However, assessment of orbital dimensions is important for a good knowledge of the anatomical disposition of orbital structures and surgical management of orbital pathologies [12].
The binocular distance is a measurement between the lateral inner wall of one orbit to lateral inner wall of the other orbit [13]. BOD has occasionally proven useful in clinical practice; to obtain the right plane; one should start from the conventional section of the BPD and move the transducer caudally until the orbits visualized [14, 7]. Kivilevitch *et al.*[15] used an oblique anterior coronal section to measure the BOD. In the correct plane, both eyes should have the same diameter, and the image should be symmetrical; the plane of the largest diameter of eye should be used [7].In addition, there are no significant differences between automatic and manual orbital measurements [16].Moreover, no statistically significant difference between the right and left orbit is found [17].

The mean of BOD for each gestational week has been established [18, 6, 19, 2, 7]. BOD significantly increases with increasing GA, which is statistically significant [6, 19, 2]. Correlation coefficient of BOD with GA has been reported[20, 21, 6, 8, 19, 2, 7]. A linear growth functions observed between GA and BOD,($r^2 = 0.953$; $p < 0.0001$) [6], ($r^2 = 0.88$; $P < 0.001$) [2], ($r^2 = 0.86$; $P < 0.05$) [19].

BOD used as an adjunct in estimating menstrual age, Tongsong *et al.*[7] found linear quadratic function that could be considered an optimal model for predicting menstrual age from BOD (r^2 = 0.94052, P = 0.000) and GA (r^2 = 0.94724, P = 0.000).In addition, BOD closely related to BPD [14]; a linear growth function is observed between BPD and BOD (r^2 = 0.965; $p < 0.0001$) [6].

Ethnic significant differences between mothers are not reflected in fetal biometry at second trimester which support that ultrasound in practical health care can be used to assess GA in various populations with little risk of errors due to ethnic variations [22]. A statistically significant difference for the fetal BOD and other orbital measurements have been reported between the Moroccan versus Belgian and Turkish fetuses; this difference has no clinical importance, and no need to construct reference charts for ethnicity when studying these groups [23]. However, several ethnic differences found, pointing to the necessity of ethnic-specific data [19, 3, 24]. Consequently, significant ethnic differences found for BOD [25, 26].

Fetal gender assessed to evaluate possible significant differences. Sex has no detectable effect on fetal orbital biometry [15, 27, 2].Although sex has no detectable effect on orbital biometry, Gupta *et al.*[28]reported that orbital and ocular parameters are better defined in males.

Subjects and Methods

This study was a prospective, cross-sectional study; performed at obstetrics and gynecology clinic, Omdurman city, Sudan. About 385 healthy pregnant women with known GA based on last normal menstrual period(LNMP) confirmed by ultrasound examination recruited into the study with verbal informed consent. The study population of this study met the following criteria:Regular menstrual cycle with certainty about the time of the LNMP, normal pregnancy, and viable singleton.All sonographic examinations performed using SonoScape A5 portable ultrasound machine (Shenzhen, China), equipped with C352 transabdominal convex array ultrasound transducer probe (2-6MHZ).

BOD measurements obtained by a transverse section of the fetal skull at the orbital plane in which the image is symmetrical with both eyes of equal and largest possible diameter. Probe orientation readjusted during continuous viewing until the optimal view of the orbits is possible. Freeze-frame ultrasound capabilities and electronic on-screen calipers set employed for measurements. BOD measured between the lateral inner wall of one orbit to lateral inner wall of the other orbit. Data collection sheet designed for recording the common fetal biometry parameters and BOD;it also included the maternal age, anthropometric measurements, state of origin, state of residence, tribe and clinical history of the mothers.

All data processed and analyzed with the SPSS version 22 (SPSS Inc, IBM). Reference centiles at each week of gestation calculated in a parametric method. The mean estimated by polynomial linear regression and the goodness-of-fit of the centiles to the data was verified [29]. Nomograms with confidence intervals (5^{th} and 95^{th} percentile) established for BOD with GA.The quality of the prediction evaluated by cross-validation and the goodness-of-fit by the R^2 coefficient. The present study approved by the Ethics Committee of The National Ribat University, Khartoum, Sudan.

Results

About770 measurements of BOD obtained from 385 fetuses of normal Sudanese pregnant women, measurements obtained as shown in figure(1).Fetal binocular distance ranged between 15 to 64 mm, with mean of (40.1±10.7 mm). Additionally different centiles shown table 1.

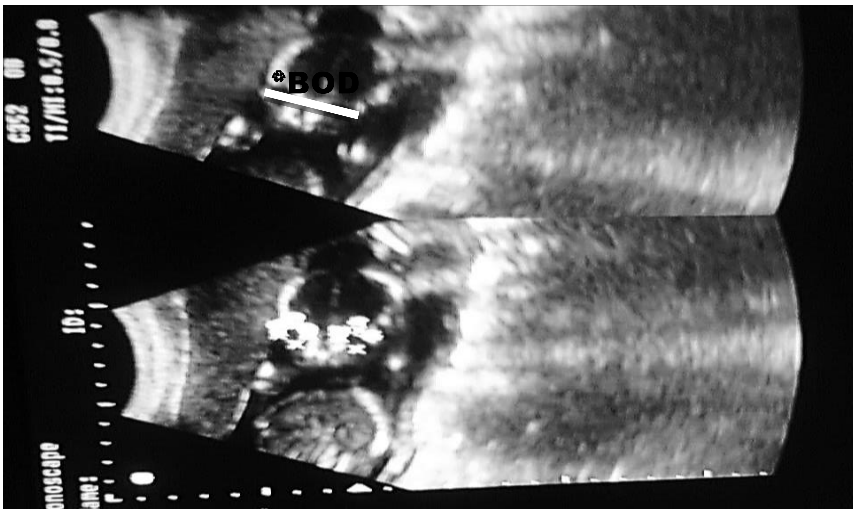

Fig (1): Sonographic measurement of BOD.

Table 1: BOD centiles:

Fetal age using LNMP (weeks)	Percentiles						
	5	10	25	50	75	90	95
14	18.00	18.00	18.00	19.00	20.00.	.	.
15	20.00	20.00	20.25	21.00	22.00	.	.
16	22.00	22.00	22.00	23.00	25.00	26.80	.
17	20.50	23.00	25.00	27.00	28.00	30.00	.
18	20.00	21.00	25.50	28.00	31.25	34.00	.
19	23.50	23.50	30.00	32.00	33.00	34.40	36.00
20	25.00	25.00	31.00	34.00	34.50	39.20	.
21	26.50	26.50	33.25	36.00	37.00	38.70	39.35
22	28.00	28.00	34.00	37.00	38.50	40.00	40.70
23	31.40	33.40	36.00	38.00	40.00	43.80	45.00
24	31.00	31.00	36.00	39.50	42.00	45.10	.
25	36.20	37.40	40.00	41.00	46.00	49.40	51.00
26	34.00	36.80	41.00	43.50	45.00	46.00	46.65
27	31.00	32.35	36.63	43.00	46.75	50.70	.
28	43.00	43.00	44.25	47.00	48.00	52.10	.
29	38.50	38.50	41.75	47.00	49.50	51.40	.
30	42.00	42.00	44.25	49.50	54.25	59.80	.
31	41.50	41.50	45.75	49.50	53.75	57.00	.
32	45.00	45.30	48.00	52.00	54.75	57.00	.
33	49.00	49.30	51.25	53.00	56.50	60.10	.
34	46.00	46.00	51.25	54.50	57.50	.	.
35	47.50	47.70	53.50	56.00	61.00	63.00	.
36	49.00	49.00	50.25	55.00	62.00	.	.
37	50.50	51.90	54.00	57.00	59.00	61.20	.
38	52.00	52.00	53.00	54.00	60.00	.	.
39	59.00	59.00	59.00	59.50	60.00	.	.
41	56.50	56.50	56.50	56.50	58.25	.	.

*Fetal BOD is constant in 13 and 40 weeks, they have been omitted.

Regarding measurements of common fetal biometrics (BPD, HC, AC and FL)in addition to FW as shown in table 2.

Table 2: Descriptive statistics of fetal BPD, HC, FL, AC and FW.

Parameter	Minimum	Maximum	Mean	Std. Deviation
BPD	25	98	62.15	17.673
HC	120	330	194.17	38.666
FL	13	74	42.89	15.4617
AC	200	360	260.79	30.545
FW	91.0	3203.8	1059.67	771.9296

Analysis of Variance (ANOVA) has been made for BOD and GA, BPD, HC, FL and AC, the P value was < 0.0001 for all parameters at 95% confidence interval, considered extremely significant. The best correlations found between BOD and FL (r=0.939), then BOD and BPD (r=0.935), and correlation between BOD and GA (r=0.925). In addition, GA/BOD ratio remained roughly constant. Furthermore, FL/BOD ratio was remained constant throughout gestation.
Linear regression with 95% confidence interval between BOD and GA has been made. correlation coefficient (r = 0.9248. r^2 = 0.8553. Standard deviation of residuals from line = 2.419). P value < 0.0001, considered extremely significant. the following equation formulae were constructed:

1. $Y = 3 + 0.55 \times X$. When Y is GA, X is BOD. R= 0.925, R^2= 0.855, Standard deviation ±2.4 weeks (P= 0.0003).
2. $Y = 9.24 + 0.22 \times X + 0.00405 \times X^2$. R^2= 0.859.
3. $Y = 20.71 – 0.74 \times X + 0.03 \times X^2 – 0.000205 \times X^3$. R^2= 0.861.

Regression analysis between BOD and BPD has been made, correlation coefficient (r = 0.935. r^2 = 0.8743, Standard deviation of residuals from line = 6.274). P< 0.0001. The relation between BOD and BPD could be expressed by the following equation formulae:

1. $Y = 0.09 + 1.54 \times X$. When Y is BPD, X is BOD; R= 0.935, R^2= 0.874, Standard deviation ±6.3 mm.
2. $Y = 2.72 + 1.41 \times X + 0.0017 \times X^2$. R^2= 0.872.
3. $Y = 42.38 – 1.89 \times X + 0.09 \times X^2 – 0.000706 \times X^3$. R^2 = 0.875.

Correlation coefficient (r = 0.8792. r^2 = 0.773, Standard deviation = 18.463 and the P value < 0.0001). The following equations could express the linear relationship between BOD and HC:

1. $Y = 27.41 + 4.76 \times X$. When Y is HC, X is BOD; R= 0.879, R^2= 0.773, Standard deviation ±18.5mm.
2. $Y = 64.5 + 2.56 \times X + 0.03 \times X^2$. R^2= 0.772.
3. $Y = 250 – 13.46 \times X + 0.47 \times X^2 – 0.00391 \times X^3$. R^2 = 0.780.

Regarding regression analysis between BOD and FL Correlation coefficient (r = 0.9386. r^2 = 0.8810. Standard deviation = 5.341). The P value < 0.0001, considered extremely significant. Linearity between BOD and FL could be expressed by the following equation formulae:

1. $Y = 1.37 \times X – 12.26$. When Y is FL, X is BOD; R= 0.939, R^2= 0.881, Standard deviation ±5.3mm.
2. $Y = 1.2 \times X + 0.00211 \times X^2 – 8.95$. R^2= 0.878.
3. $Y = 31.9 – 2.15 \times X + 0.09 \times X^2 – 0.000702 \times X^3$. R^2= 0.882.

Linear regression with 95% confidence interval between BOD and AC has been made; correlation coefficient (r = 0.7012. r^2 = 0.4916. Standard deviation = 21.876). The P value < 0.0001, considered extremely significant. This result obtained from

ANOVA figure 4.9. Relation between BOD and AC could be expressed by the following equation formulae:

1. $Y = 79.07 + 3.52 \times X$. When Y is AC, X is BOD; R= 0.701, R^2= 0.492, Standard deviation ±21.9.
2. $Y = 212 – 1.74 \times X + 0.05 \times X^2$. R^2= 0.492.
3. $Y = 1250 – 65.25 \times X + 1.33 \times X^2 – 0.00848 \times X^3$. R^2 = 0.505.

Regression analysis between BOD and FW has been made, correlation coefficient (r= 0.8007. r^2 = 0.6412, Standard deviation = 463.04). The P value was < 0.0001, considered extremely significant. Linearity between BOD and FW can be expressed by the following equation formulae:

1. $Y = 58.43 \times X – 1310$. When Y is FW, X is BOD; R= 0.800, R^2 = 0.641.
2. $Y = 819 – 52.47 \times X + 1.35 \times X^2$. R^2 = 0.687.
3. $Y = 1370 – 97.97 \times X + 2.53 \times X^2 – 0.00963 \times X^3$. R^2 = 0.687.

Regression analysis expressed by scatter plot for different fetal biometrics as shown in figure 2.

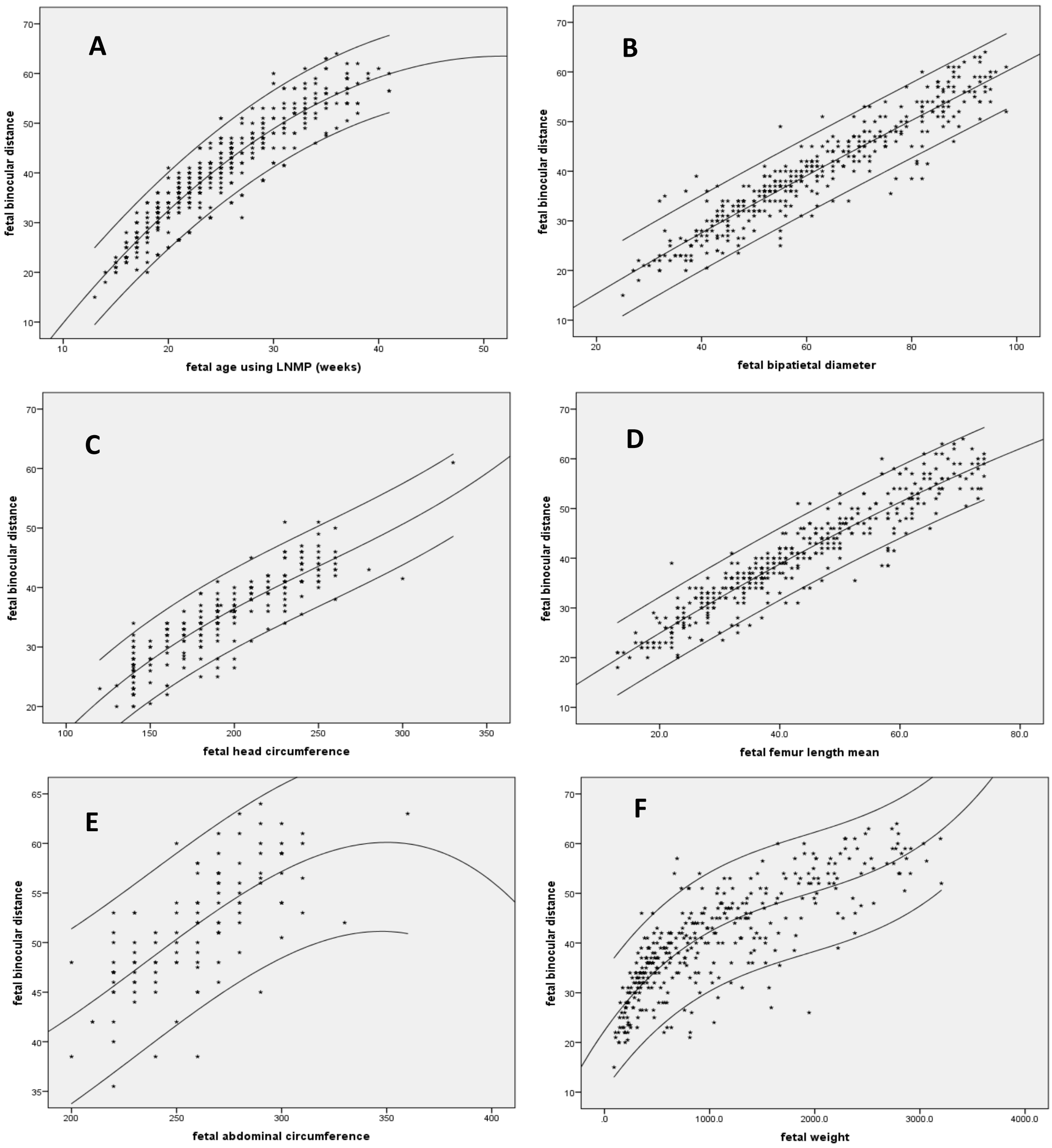

Fig (2): Scatter plot graph showing linear relationship between BOD with GA (A), BPD (B), HC (C), FL (D), AC (E) and FW (F).

Maternal information such as maternal age, weight, height and BMI has been taken as shown in table (3).

Table 3: Descriptive statistics regarding maternal age, weight, height and BMI.

Anthropometric data	Minimum	Maximum	Mean	Std. Deviation
Maternal age (Years).	16	44	27.21	5.486
Maternal height (Meter).	1.46	1.87	1.6487	.07467
Maternal weight (KGs).	44	104	70.79	11.608
Maternal BMI	16	42	26.07	3.821

Regarding correlation between BOD and maternal information such as age, height, weight, BMI, parity, socioeconomic status, occupation, residence city and state, tribe and state of origin, independent samples nonparametric tests have been made with significance level of 0.05 and 95% confidence interval level. Correlation between BOD and tribe was significant (P=0.023), while other parameters appeared to be insignificant regarding BOD. Significant difference found regarding fetal (P=0.021).

Discussion

The present study showed linear growth of fetal BOD from 14-41 weeks of gestation. The mean values of BOD at various points in gestation were agreed relatively well with the values reported by previous works elsewhere. Guariglia and Rosati [18] studied 923 normal singleton pregnancies, from 11 to 16 weeks of gestation using transvaginal high resolution ultrasound technique,mean values estimated by Guariglia and Rosati slightly larger than results of present study, transabdominal technique has been employed in the present study. Predicted mean values of BOD slightly larger than results obtained by Sukonpan and Phupong [6], whom constructed reference, ranges for BOD during 15-40 weeks gestation in 602 normal pregnant women, transabdominal ultrasound technique was used in both studies. Martins' sliding calipers were used by Rajlakshmi [19]to evaluate BOD in 64 fetal autopsies, and Denis *et al.*[2] examined 205 fetuses came from both therapeutic and spontaneous abortions,these studies made groups for GA including two or more weeks' groups. The present study results for mean values of BOD was totally agreed with Denis *et al.*[2] and also agreed with Rajlakshmi [19] except for the last 9 weeks of gestation which the mean values of BOD were slightly smaller in the present study. Tongsong*et al.*[7] correlate fetal BOD and menstrual age by cross-sectional analysis of 555 normal fetuses (14-40 weeks) using real-time sonography. The mean values estimated by Tongsong*et al.*[7] seemed to be similar as compared to the present study. Although studies of the different techniques and different sample size that used to evaluate BOD, there are no comparable differences in BOD mean values.

Correlation coefficient (r= 0.925, P < 0.0001) in this study at the rang of Rajlakshmi [19], Tongsong*et al.*[7] and Denis *et al.*[2], whenRosati *et al.*[21] (r=0.813) slightly lower.However, the best correlation was obtained by Pommier *et al.*[20] and Trout *et al.*[8], (r=0.962 and 0.960) respectively. Bear in mind that all of the mentioned values are significant and strongly correlated to GA.

The present study constructed linear function for predicting menstrual age from BOD (r^2 linear = 0.855, P= 0.0003) which completely agreed with Rajlakshmi [19] who constructed linear equation to calculate GA from BOD, (P = 0.05, r^2 = 0.860). Furthermore, Sukonpan and Phupong [6] calculated BOD from GA, (P = 0.0001, r^2 = 0.953). In addition, Denis *et al.*[2] also calculated BOD from GA, (P = 0.001, r^2 = 0.88).

BOD is effective tool to predict menstrual age with a correct standard error. In the present study quadratic equation has been calculated (r^2 = 0.859, P= 0.0003). Tongsong *et al.*[7] found linear quadratic function for predicting menstrual age from BOD (P = 0.000, r^2 = 0.941). Moreover, BOD also can be calculated by using quadratic function from GA, which was reported by Tongsong *et al.*[7] (r^2 = 0.947, P = 0.000), Denis *et al.*[2] (r^2 = 0.88, P < 0.001) and Jacquemyn *et al.*[23]. Furthermore, our study constructed cubic equation to estimate GA from BOD (r^2 = 0.861, P= 0.0003).

In this study the best correlation regarding common fetal biometric parameters (GA, BPD, HC, FL, AC and FW) was observed between BOD and FL (r=0.939), then BOD and BPD (r=0.935), and correlation between BOD and GA (r=0.925). Hereby, the BOD canused for prediction of FL and BPD in addition to GA estimation. However, GA/BOD ratio remained roughly constant. Furthermore, FL/BOD ratio also remained constant throughout gestation, thus BOD almost nearly equal to FL throughout gestation.

Regression analysis between BOD and BPD has been made in the present study ($r^2 = 0.874$, $P < 0.0001$). Mayden *et al.*[14] reported close relation between BOD and BPD, also a linear growth function between BPD and BOD has been reported by Sukonpan and Phupong [6]($r^2 = 0.965$; $P < 0.0001$). In the present study, rather than BPD, linear correlations have been found between BOD and HC ($r^2 = 0.773$, $P < 0.0001$), FL ($r^2 = 0.881$, $P < 0.0001$), AC ($r^2 = 0.492$, $P < 0.0001$) and FW ($r^2 = 0.641$, $P < 0.0001$); thus pointing possibility to calculate BOD from other fetal biometric parameters and vice versa.

The present study reported significant difference regarding BOD throughout different tribes in Sudan ($P = 0.023$).This finding disagreed with Salpou *et al.*[22], who reported that ethnic significant differences between mothers are not reflected in fetal biometry. while a statistically significant difference for BOD was reported by Jacquemyn *et al.*[23] between Moroccan versus Belgian and Turkish fetuses, which agreed with our results regarding ethnic variations.

Significant correlation regarding BOD throughout fetal sex ($P = 0.021$) reported by the present study, this disagreed with Denis et al.(2) whom reported that sex has no detectable effect on orbital biometry. Consequently our findings agreed with Gupta et al.(28) who reported that orbital measurements better defined in males. However, the clinical value of determination of fetal sex by ultrasound is to minimize invasive testing in pregnancies at risk of sex-linked genetic abnormalities(30).Moreover, there is a sex-specific growth pattern for each of the individual fetal biometric indices, as reflected in the ratios of the various indices (31). Sex-related differences in prenatal BPD, HC and AC measurements were established (32); adding new parameters such as BOD is necessary to maximize of fetal sex-related biometric parameters.

Limitations of the Study

Funding

Conflict of Interests

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