JOURNAL OF THE ANATOMICAL SOCIETY OF INDIA 62 (2013) 157–165

Available online at www.sciencedirect.com

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Original Article

Fetal orbital and ocular biometry at different gestational ages

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ARTICLE INFO

Article history:
Received 15 November 2013
Accepted 17 December 2013

Keywords:
Fetal autopsy
Fetal eyeball
Fetal orbit
Fetal biometry

ABSTRACT

Introduction: Determination of orbital and ocular growth patterns in fetal life is necessary for early diagnosis of facial malformation syndromes. We aim to establish the normative data for growth of different ocular and orbital parameters. These parameters may also correlate with fetal anthropometry.

Methods: Fifty normal fetuses at different gestational ages were studied for anthropometric, orbital and ocular growth. The parameters measured included weight, height, biparietal diameter, depth and width of the orbit, interorbital distance, transverse and vertical corneal diameters, axial and transverse diameters of the eyeball and diameter of the lens. Normative values were determined for orbital and ocular parameters in fetuses of 11–36 gestational weeks.

Results: The orbital and the ocular parameters demonstrated significant positive correlation with age and biparietal diameter. However, the lens diameter did not show any significant correlation with either age or biparietal diameter. Among orbital parameters interorbital distance showed maximum correlation with biparietal diameter. The correlations of orbital and ocular parameters were better defined in males.

Conclusions: The gestational age specific normative data generated in this study may provide reference for comparing the growth of various orbital and ocular parameters and may aid in early diagnosis of fetal maldevelopment syndromes.

1. Introduction

Ocular growth during fetal life can be determined by biometric measurements of different ocular structures at various stages of intrauterine life. Wide availability and improvement in ultrasound technology has allowed prenatal measurements of different structures of eyeball as well as bony orbit. Normative data for ocular and orbital growth possibly has a correlation with fetal anthropometric growth. Therefore knowledge of normal growth patterns of the components of eyeball as well as different orbital parameters would help in determining the normal fetal growth and aid in early diagnosis of ophthalmic abnormalities.

Biometry is fundamental in definition of malformation syndromes. Most of the studies available in literature have utilized prenatal ultrasound for measurement of ocular and

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0003-2778/$ – see front matter
http://dx.doi.org/10.1016/j.jasi.2013.12.004

Table 1 – Correlations between gestational age, fetal weight, fetal height and fetal biparietal diameter.

		Age	Wt	Ht	BPD
Age	Pearson correlation	1	.506 (**)	.192	.507 (**)
	Sig. (2-tailed)		.003	.229	.000
	N	50	32	41	47
Wt	Pearson correlation	.506 (**)	1	.435 (*)	.270
	Sig. (2-tailed)	.003		.014	.135
	N	32	32	31	32
Ht	Pearson Correlation	.192	.435 (*)	1	.149
	Sig. (2-tailed)	.229	.014		.354
	N	41	31	41	41
BPD	Pearson correlation	.507 (**)	.270	.149	1
	Sig. (2-tailed)	.000	.135	.354	
	N	47	32	41	47

**Correlation is significant at the .01 level (2-tailed).
*Correlation is significant at the .05 level (2-tailed).
Age – gestational age in weeks, wt – weight, ht – height, BPD – biparietal diameter.

Table 2 – Mean values of the orbital, ocular and anthropometric data.

Age		DO	WO	IOD	CTD	CA	EBA	EBT	LD	Wt	Ht	BPD
11	Mean				.07	.07						.70
	S.D.				.	.						.
12	Mean	.41	.35	.81	.17	.80	.37	.30	.17	12.00	8.00	1.39
	S.D.	.	.	.	.	.	.	.	.	.	.	.
14	Mean	.70	.59	1.00	.40	.39	.42	.40	1.075	28.00	11.61	2.04
	S.D.	.10	.03	.00	.03	.03	.12	.08	1.09	17.35	1.51	.37
16	Mean	.78	.70	.97	.30	.30	.58	.55	.22	68.50	12.85	2.39
	S.D.	.24	.28	.49	.00	.00	.28	.35	.16	6.89	4.74	1.12
17	Mean	1.25	.95	1.66	.50	.47	.95	.66	.35	169.00	23.00	3.15
	S.D.	.00	.07	.34	.00	.046	.64	.19	.07	.	.	.49
18	Mean	1.15	1.07	1.90	.48	.50	.80	.83	.34	236.20	21.03	5.04
	S.D.	.22	.33	.19	.068	.087	.085	.037	.045	86.92	4.11	3.51
19	Mean	1.30	.86	1.80	.49	.47	.92	.96	.34	363.67	21.48	3.73
	S.D.	.56	.12	.48	.04	.09	.44	.48	.09	171.27	4.64	.83
20	Mean	.96	.90	1.56	.51	.50	1.00	.95	.46	224.00	21.15	3.90
	S.D.	.20	.12	.49	.06	.05	.15	.21	.21	59.90	4.31	.69
21	Mean	1.54	1.14	1.91	.66	.63	.85	.81	.38	334.67	25.85	4.57
	S.D.	.33	.19	.66	.21	.25	.15	.22	.05	33.85	2.97	.29
22	Mean	1.65	1.90	1.75	.60	.60	.95	.92	.30	675.00	26.30	4.30
	S.D.	.	.	.	.	.		.	.	.	.	.
23	Mean	1.67	1.10	2.66	.69	.67	1.05	1.06	.40	348.50	105.15	5.20
	S.D.	.28	.11	.19	.08	.09	.05	.05	.02	307.04	152.66	.72
24	Mean	1.87	1.24		.61	.58	1.10	1.07	.45		24.92	5.16
	S.D.	.14	.07		.09	.03	.13	.08	.03		2.51	.34
26	Mean	1.98	1.39	2.53	.80	.81	1.29	1.29	.52	919.00	31.75	6.15
	S.D.	.44	.16	.12	.00	.06	.07	.17	.01	.	1.06	.21
27	Mean	2.10	1.30		.70	.70	1.20	.80	.30			
	S.D.	.	.		.	.	.	.	.			
28	Mean	1.27	.81	1.70	.52	.48	.89	.88	.38	135.00	18.80	4.14
	S.D.	.41	.05	.71	.17	.14	.32	.36	.07	.	6.64	.91
29	Mean	1.58	1.15	2.60	.68	.67	1.10	1.10	.50			5.32
	S.D.	.	.	.	.	.	.	.	.			.
32	Mean	1.47	1.00	2.50	.50	.50	1.00	.95		700.00	35.70	5.00
	S.D.	.	.	.	.	.	.	.	.	.	.	.
36	Mean	1.79	1.42	3.18	1.02	1.03	1.60	1.38	.53	268.00	46.00	8.50
	S.D.	.	.	.	.	.	.	.	.	.	.	.

Age – gestational age in weeks, DO – depth of orbit, WO – width of orbit, IOD – interorbital distance, CTD – transverse diameter of cornea, CA – vertical diameter of cornea, EBA – axial diameter of eyeball, EBT – equatorial diameter of eyeball, LD – lens diameter, Wt – weight, Ht – height and BPD – biparietal diameter.

orbital diameter.[1–5] More recently magnetic resonance imaging (MRI) of the fetal eyes has been used to derive normal growth charts.[6] Measurement of various ocular and orbital parameters directly from fetuses at various gestational ages is probably the most direct method of biometric and morphological assessment.

It is important to be able to detect fetal eye abnormalities associated with various genetic diseases at an early stage. It is now possible to evaluate the intra ocular and orbital details early in the second trimester. Thus availability of normal data for these parameters at different gestational ages can provide baseline for the early detection of deviation from the normal.[7,8]

Several studies have evaluated the dimensions of fetal orbit and lens at different gestational ages in various population groups. Many of these studies included fetuses in mid to late gestation.[1–3] There are only a few studies evaluating growth patterns of other intra ocular structures and their correlation with corresponding orbital growth parameters.[4,9,10] As these values may have racial and ethnic variations, it is necessary to define the normative growth patterns for different population groups.

The present study was undertaken to establish the normative data for growth of different ocular and orbital parameters and their correlation with fetal anthropometry in North–West Indian population.

2. Material and methods

This study was conducted on fifty normal fetuses received for routine fetal autopsy. Ethical clearance was taken from the institutional ethical committee. The fetuses were obtained from both therapeutic and spontaneous abortions. They were preserved in 4% formaldehyde solution right after the delivery. Malformed fetuses with cranio-facial or ocular abnormalities, chromosomal disorders, or neurological defects that could affect cranial or orbitofacial or ocular growth were excluded from the study.

Fifty fetuses, 23 males and 27 females were included in the study. Gestational age was determined, based on last menstrual period, confirmed by the first trimester and/or the early second trimester ultrasound examination. The available fetuses were divided into 18 groups according to the gestational age in weeks, ranging from 11th to 36th weeks of intrauterine life with no representation for the 13th, 15th, 25th, 30th, 31st and 33rd to 35th weeks of intrauterine life. Measurements were done with the help of sliding vernier calipers with an estimated precision of .02 mm. Parameters were taken twice and mean of both the values was used. All the measurements were done by a single person. Following parameters were studied:

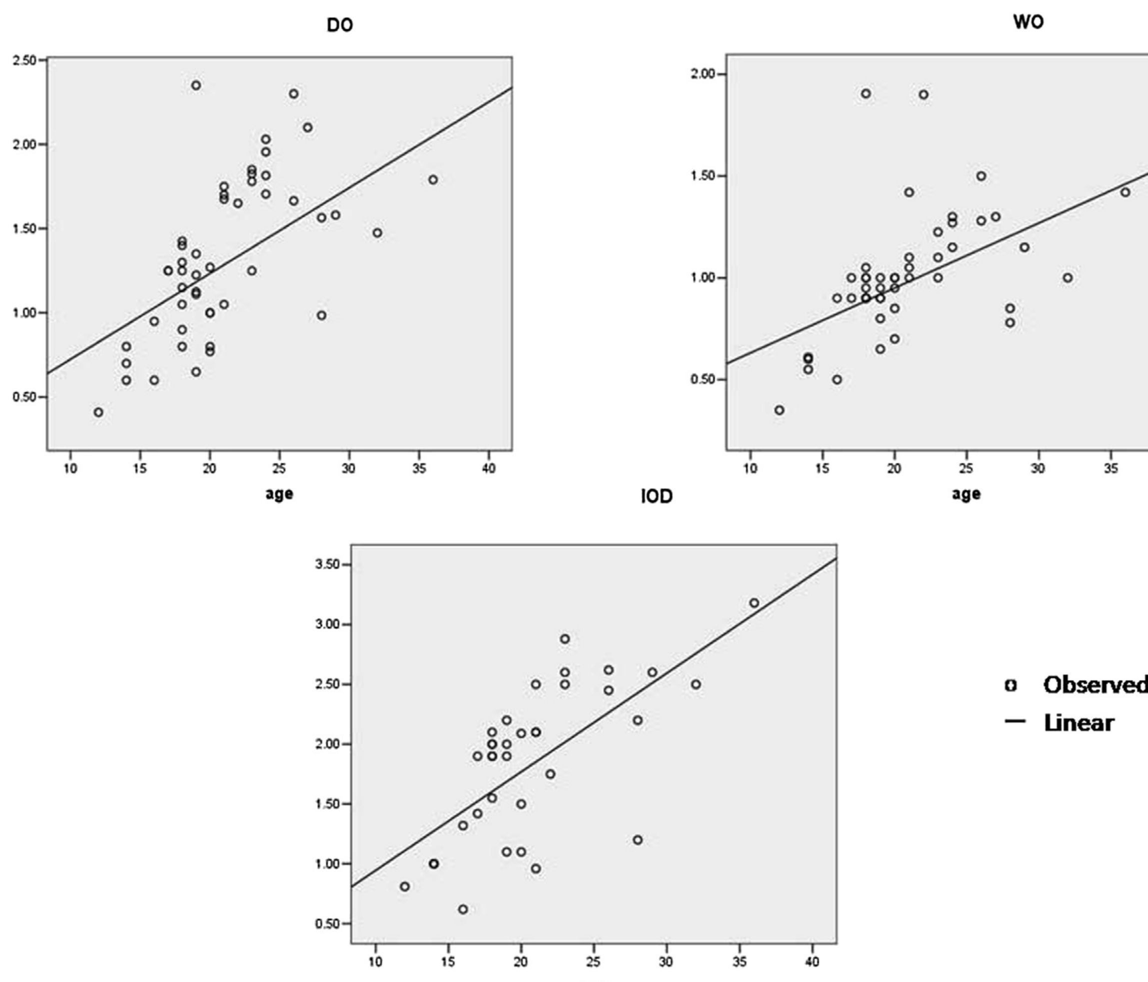

Fig. 1 – Relationships between orbital depth (DO), orbital width (WO), interorbital distance (IOD) and gestational age.

A. Anthropometric measurements:
   1. Gestational age in weeks
   2. Height (Crown heel length)
   3. Biparietal diameter (BPD)
B. Orbital measurements:
   4. Depth of orbit (DO): distance between the center of the orbit at the level of the orbital rim and apex of the orbit
   5. Width of orbit (WO): maximum transverse distance measured between the right and the left orbital margin
   6. Interorbital distance (IOD): transverse distance between the centers of the two orbits
C. Ocular measurements:
a. Corneal parameters:
   7. Transverse diameter (CTD): distance measured between the two points situated at 3'o clock and 9'o clock positions on the cornea
   8. Vertical diameter (CA): Distance measured between the two points situated at 12'o clock and 6'o clock positions on the cornea
b. Eyeball parameters:
   9. Axial diameter (EBA): anterior–posterior diameter of the eyeball.
   10. Equatorial diameter (EBT): transverse diameter of the eyeball.
c. Lens parameters:
   11. Diameter (LD) of the lens.

Anthropometric data was noted first. All the ocular parameters were taken in the enucleated eye except for the corneal diameters, which were taken before the enucleation. After measuring the eyeball an equatorial cut was given in the eyeball just behind the limbus. The lens was delivered through this cut by gentle pressure and its diameter was recorded. Then the depth and the width of the orbit were measured followed by the interorbital distance.

Data was grouped into anthropometric, orbital and ocular groups. Correlations were tested among all parameters by computing paired correlation coefficients. The growth of orbital and ocular parameters versus gestational age, crown heel length and biparietal diameter was studied by simple linear and multiple polynomial regression analysis.

3. Results

A total of 50 fetuses were studied out of which 27 were females. The gestational age in weeks was plotted against variables like weight, height and biparietal diameter (BPD) (Table 1). There was a significant correlation between increase in the gestational age and the corresponding increase in weight and BPD. BPD was found to correlate maximally with age ($p < .000$). The height and weight did not correlate with BPD. Therefore in further analysis age and BPD were the parameters against which various orbital and ocular parameters were compared.

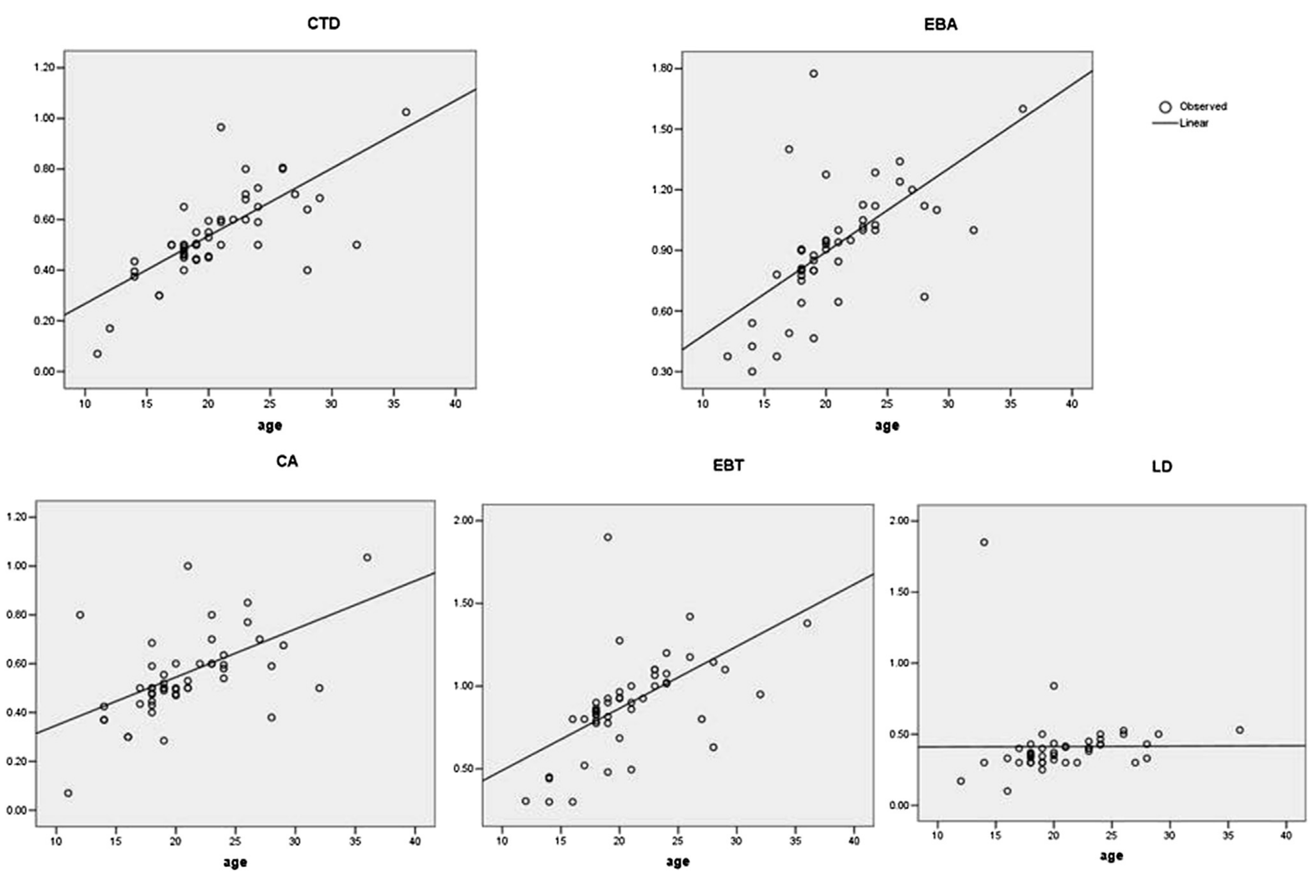

Fig. 2 – Relationships between transverse diameter of cornea (CTD), vertical diameter of cornea (CA), axial diameter of eyeball (EBA), transverse diameter of eyeball (EBT), Lens diameter (LD) and gestational age.

The mean values of orbital and ocular parameters on the right and the left side were calculated for each gestational age group. A paired sample correlation test with 95% confidence interval was done which demonstrated that there was no statistically significant difference in any of these parameters between the right and the left sides. For further analysis of the results the combined means of the right and left values was used. Means of all the parameters studied are given in Table 2.

Orbital parameters

Using linear regression analysis with age as an independent variable, the increase in the depth of orbit (DO), width of orbit (WO) and the interorbital distance (IOD) were correlated with the increase in gestational age. There was significant correlation between age and all the three orbital parameters ($r = .448–.684$, $p < .001$) (Fig. 1). The increase in the DO, WO and IOD also correlated well with each other ($r = .637–.783$, $p < .000$). Similarly significant correlation was found in increase in BPD and the corresponding increases in DO, WO and IOD (Fig. 3). IOD showed the best correlation with the BPD ($r = .496$, $p < .002$).

All these orbital parameters were tabulated separately for males and females. Correlation was calculated in both the sexes' separately. Among males there was a good correlation between all the orbital parameters with age as well as with the BPD. Among females increase in the gestational age correlated significantly with DO ($r = .587$, $p < .002$) and to some extent with the IOD ($r = .501$, $p < .024$) but there was no statistically significant correlation between the gestational age and the WO ($r = .261$, $p < .197$). When the growth of the BPD was plotted against the orbital parameters in the females no statistically significant correlation was found ($r = .170–.307$, $p > .01$). However the three orbital parameters correlated well among themselves ($r = .664–.842$, $p < .000$).

Ocular parameters

The corneal transverse (CTD) and vertical (CA) diameters, the axial and transverse diameters of the eyeball (EBA & EBT) and the lens diameter (LD) in all the fetuses were measured and grouped according to the gestational age. Linear regression analysis demonstrated good correlation between the gestational age and the CTD, CA, EBA and EBT ($r = .561–.714$,

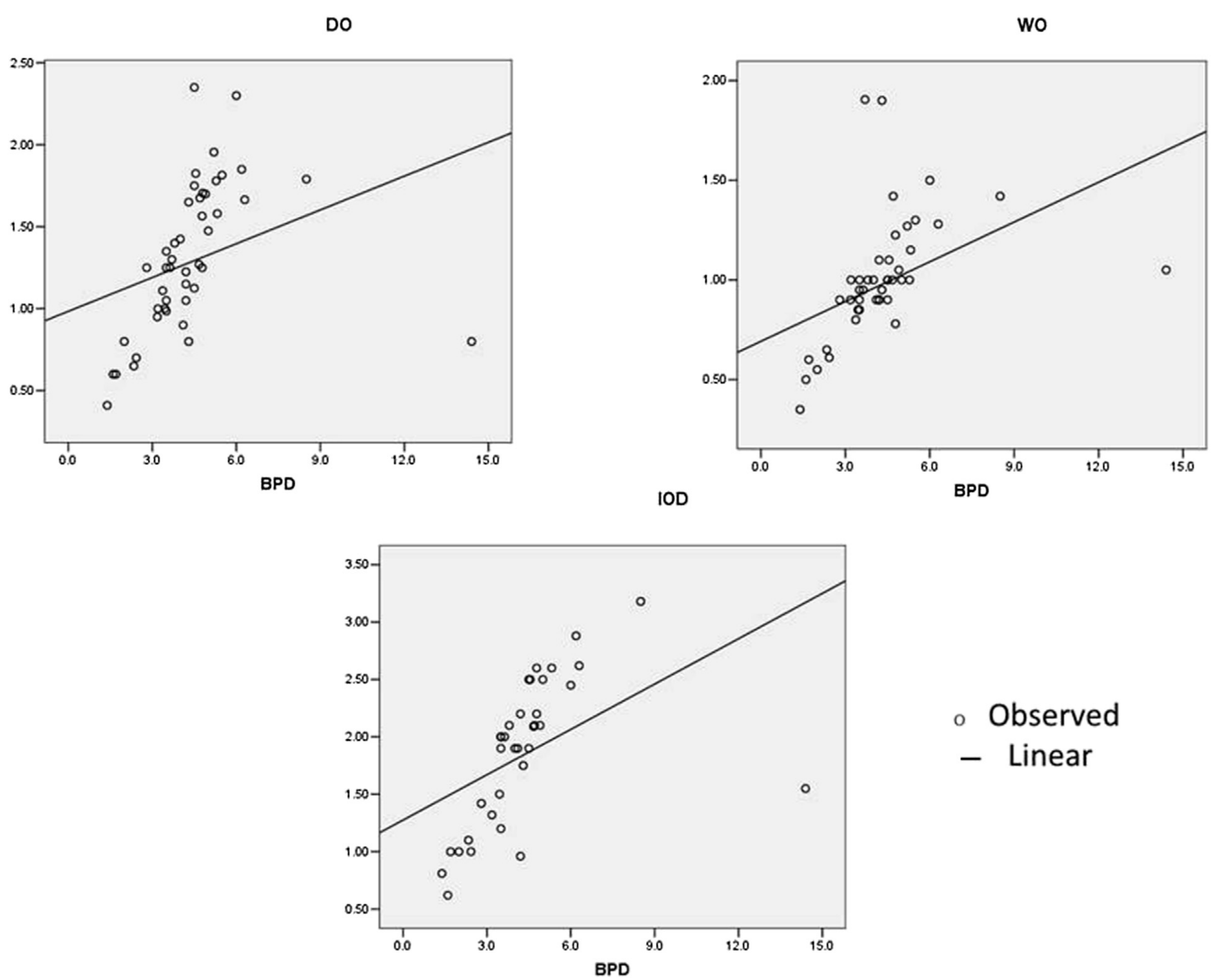

Fig. 3 – Relationships between orbital depth (DO), orbital width (WO), interorbital distance (IOD) and biparietal diameter (BPD).

$p < .000$) but there was no correlation between LD and the gestational age ($r = .005$, $p = .973$) (Fig. 2). Similarly all ocular parameters except the diameter of the lens, showed good correlation between themselves in their growth pattern.

The BPD had statistically significant correlation with the CTD, CA, EBA and EBT ($r = .438–.530$, $p < .01$) but not with the LD ($r = -0.027$, $p = .866$) (Fig. 4).

The parameters were analyzed for males and females separately. Among males, similar correlation was seen between the gestational age and all the ocular parameters as mentioned above but with the following exceptions: the CA did not show significant correlation with the EBA, EBT and LD. However in females the age did not have significant correlation with CTD, CA and LD. The various ocular parameters in females did not show as significant a correlation as was seen in males or in the combined group. The BPD also showed good correlation with the CTD, CA, EBA and EBT in males but not in females. As in the combined group LD did not show significant correlation with any of the parameters in both the sexes.

4. Discussion

In the present study we have established normative values for orbital and ocular parameters in fetuses of gestational age, ranging from 11th to 36th week. As this study encompasses all three trimesters of pregnancy, this should be helpful in comparing the antenatal ultrasound data with the expected normative value for the gestational age.

The means of various orbital and ocular parameters measured in the study were found to be similar to the values reported by the other authors.[11–13] As has been reported in these studies, we also found that gestational age and BPD correlated well with corresponding growth of the orbit and eyeball. Since BPD is one of the commonest and easily measurable dimensions during fetal ultrasound, this along with the gestational age can prove to be a reliable constant against which the growth of the chosen orbital and ocular parameters can be plotted to establish nomograms for a particular population group.

The growth of all the orbital parameters studied showed good correlation with age and the BPD as well as with each other. The interorbital distance (IOD) demonstrated maximal correlation with BPD in linear regression analysis. This seems reasonable as IOD is a function of the growth of the frontal bone, which is a part of calvaria and therefore corresponds to the increase in the BPD.

The ocular parameters i.e. the cornea, eyeball and lens dimensions were also correlated to the gestational age and BPD. Although the corneal and eyeball dimensions had good correlation with age as well as with the BPD, the lens diameter did not show any correlation with either age or the BPD. Correlations were better demonstrated in males as compared to females for ocular parameters. However since number of fetuses in each age group were small for each sex, it would be preferable to study more fetuses to come to definitive conclusions regarding gender based differences.

We have also derived nomograms of the means and 95% confidence interval (C.I.) for the various orbital and ocular

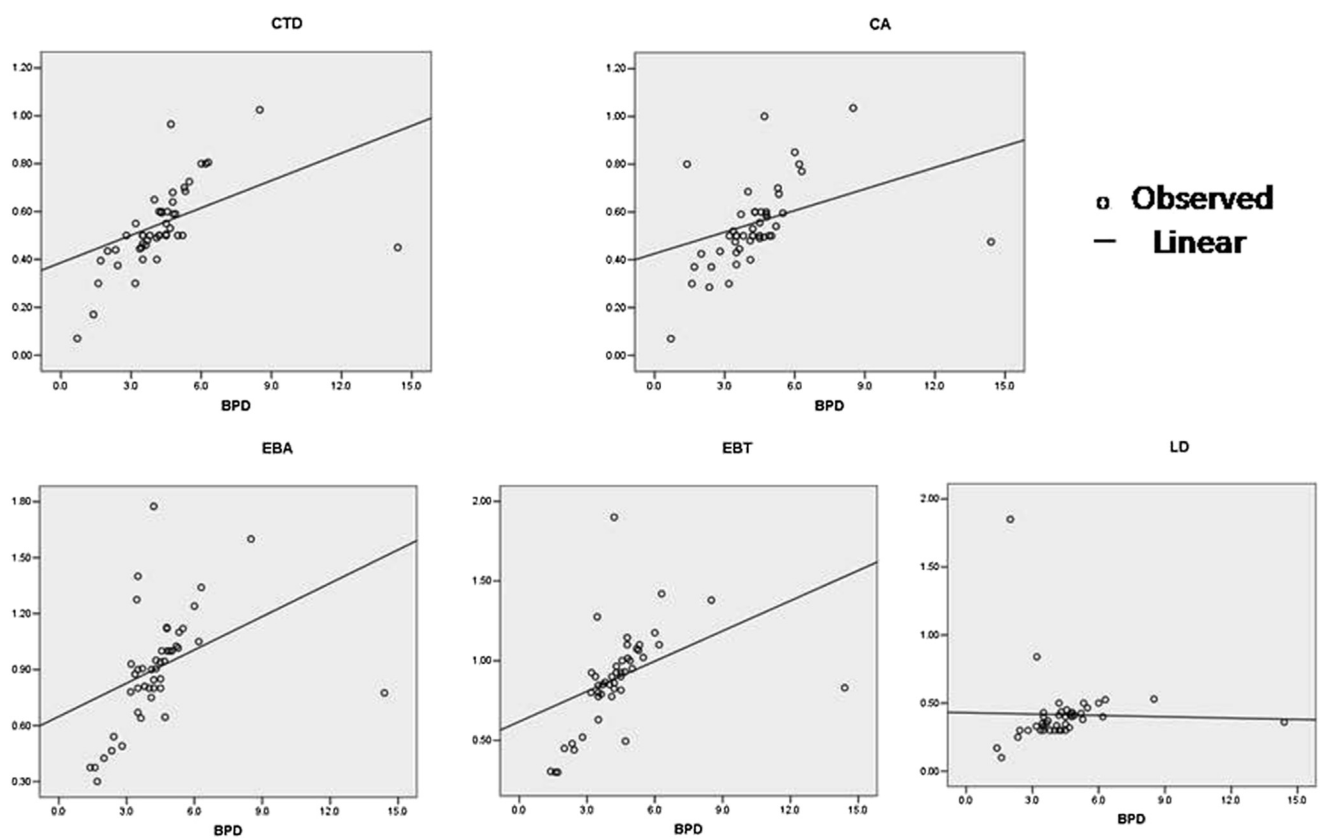

Fig. 4 – Relationships between transverse diameter of cornea (CTD), vertical diameter of cornea (CA), axial diameter of eyeball (EBA), transverse diameter of eyeball (EBT), lens diameter (LD) and biparietal diameter (BPD).

Table 3 – 95% confidence interval for all orbital and ocular parameters at different gestational ages.

GA	DO	WO	IOD	CTD	CA	EBA	EBT	LD
	A	A	A	A	A	A	A	A
	B	B	B	B	B	B	B	B
11	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
12	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
14	.4516	.5068	1.0000	.3258	.3095	.1235	.1883	−8.7723
	.9484	.6665	1.0000	.4776	.4672	.7198	.6050	10.9223
16	−1.4486	−1.8412	−3.4772	.3000	.3000	−1.9955	−2.6266	−1.2462
	2.9986	3.2412	5.4172	.3000	.3000	3.1505	3.7266	1.6762
17	1.2500	.3147	−1.3895	.5000	.0545	−4.8363	−1.1189	−2853
	1.2500	1.5853	4.7095	.5000	.8805	6.7263	2.4389	.9853
18	.9685	.7915	1.7081	.4360	.4333	.7428	.8077	.3054
	1.3503	1.3597	2.1086	.5407	.5678	.8750	.8657	.3808
19	.7080	.7353	1.0314	.4466	.3743	.4645	.4573	.2553
	1.8953	.9980	2.5686	.5334	.5757	1.3905	1.4743	.4431
20	.7191	.7417	.3262	.4383	.4422	.8096	.6949	.1961
	1.2169	1.0583	2.8005	.5937	.5738	1.1924	1.2171	.7299
21	1.0176	.8410	.8584	.3363	.2420	.6103	.4629	.2948
	2.0699	1.4440	2.9716	.9912	1.0230	1.1047	1.1646	.4727
22	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
23	1.2217	.8283	2.1707	.5641	.5227	.9588	.9912	.3600
	2.1308	1.3884	3.1493	.8259	.8273	1.1362	1.1413	.4550
24	1.6458	1.0428	.	.4648	.5250	.9020	.9405	.3995
	2.1067	1.4372	.	.7677	.6500	1.3130	1.2145	.5105
26	−2.0517	−0077	1.4550	.7707	.3018	.6547	−2590	.3537
	6.0167	2.7877	3.6150	.8343	1.3182	1.9253	2.8540	.6713
27	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
28	−2.4098	.3703	−4.6531	−1.0047	−8492	−1.9639	−2.3843	−2553
	4.9598	1.2597	8.0531	2.0447	1.8192	3.7539	4.1593	1.0153
29	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
32	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.
36	.	.	.	.	.	.	.	.
	.	.	.	.	.	.	.	.

(A – upper boundary, B – lower boundary).
DO – depth of orbit, WO – width of orbit, IOD – interorbital distance, CTD – transverse diameter of cornea, CA – vertical diameter of cornea, EBA – axial diameter of eyeball, EBT – equatorial diameter of eyeball and LD – lens diameter.

parameters studied (Tables 2 and 3). A linear growth function was observed for all the parameters studied but the diameter of lens did not correlate well with the age, BPD and the other parameters studied. However other authors have found good correlation between age and lens diameter.[4,5] The discrepancy in growth of the lens as compared to the other ocular and orbital parameters is difficult to explain. It is possible that the lens grows early in the first trimester and then its diameter remains static for rest of the intrauterine life.

Polynomial regression models for the orbital and ocular parameters against gestational age in normal fetuses were prepared (Table 4). Polynomial regression analysis

Table 4 – Polynomial regression analysis of the orbital and ocular parameters with age as an independent variable.

	DO	WO	IOD	CTD	CA	EBA	EBT	LD
Linear (r2)	.375	.238	.467	.510	.321	.376	.315	.000
Quadratic (r2)	.490	.337	.501	.559	.321	.413	.394	.026
Cubic (r2)	.490	.378	.531	.605	.331	.457	.440	.037
Power (r2)	.476	.377	.449	.550	.349	.463	.426	.065

DO – depth of orbit, WO – width of orbit, IOD – interorbital distance, CTD – transverse diameter of cornea, CA – vertical diameter of cornea, EBA – axial diameter of eyeball, EBT – equatorial diameter of eyeball and LD – lens diameter.

Table 5 – Table depicting the quantum of increase in each parameter with unit increase in gestational age (per week).

Index[a]	Change statistics				
	R Square change	F change	df1	df2	Sig. F change
BPD	.258	15.609	1	45	.000
IOD	.467	29.842	1	34	.000
DO	.375	27.623	1	46	.000
WO	.238	13.746	1	44	.001
CTD	.510	49.981	1	48	.000
CA	.321	22.680	1	48	.000
EBA	.376	28.262	1	47	.000
EBT	.315	21.584	1	47	.000
LD	.000	.001	1	44	.973

Predictors: (constant), age.
[a] BPD – biparietal diameter, IOD – interorbital distance, DO – depth of orbit, WO – width of orbit, CTD – transverse diameter of cornea, CA – vertical diameter of cornea, EBA – axial diameter of eyeball, EBT – equatorial diameter of eyeball and LD – lens diameter.

demonstrated that the r^2 values were higher in the quadratic (second degree) and cubic (third degree) models. Therefore the second and third degree models probably best describe the growth of each parameter. An attempt was made to study the quantitative growth of each parameter with gestational age (Table 5). Quantitatively among the orbital data, IOD showed maximum r^2 change while in the ocular group; the CTD (corneal transverse diameter) had the maximum r^2 change with the increase in gestational age. As noted earlier, lens diameter did not show any change in r^2 across all age groups.

This study has demonstrated that orbital and ocular growth patterns show good correlation with each other and with age and the BPD but not with the fetal height and weight. A major limitation of this study is small number of fetuses in each gestational age group.

Orbital distances and measurements have been reported to correlate closely to BPD.[14] This fact has been used to predict the gestational age from normograms of orbital diameters. This is especially useful in cases where the BPD cannot be easily measured abnormal fetal head position.

Many authors have studied the growth of fetal orbit, eyeball and lens and have used these parameters for prenatal diagnosing and dating in different population groups.[1,4,5,8–10,15–19] There is also a need for a working knowledge of normal ocular measurements. Syndromes involving the eyes can go unrecognized without a thorough and a systematic approach. The ocular abnormalities may be a part of congenital syndromes such as Trisomy 13, Trisomy 21, Walker–Warburg syndrome, Fraser–Cryptophthalmos syndrome or a brain anomaly such as holoprosencephaly.[20] Ocular and orbital congenital malformations are also known to be associated with Patent ductus arteriosus, aplasia of corpus callosum, Talipes equinovarus, crpto-orchism, micro-otia etc.[21] Detection of ocular abnormalities can often be a critical step in clinching a diagnosis in fetal dysmorphology. The present study is possibly the first to be done for the North–West Indian population.

5. Conclusion

Most of the present day studies are based upon ultrasound or MRI derived data. Fetal studies provide the most direct and possibly accurate biometric data against which measurements obtained through various imaging modalities should be compared. Therefore the data generated in this study can serve as a reference for antenatal diagnosis of orbital and ocular malformations as well as for early detection of fetal maldevelopment syndromes.

Conflicts of interest

All authors have none to declare.

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