Testicular volume of healthy term neonates: Determination of normative values among Igbo babies in South-Eastern Nigeria

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Abstract

Background: Testicular volume (TV) in neonates has some predictive values of clinical importance. Establishing the normal values of TV among term newborn males of every population is important as differences exist among different populations. Much is not known on TV among Igbo newborns.

Aim: The aim of this study was to determine the normative values of TV in apparently healthy term Igbo newborn males in Enugu, South-Eastern Nigeria and its relationship with gestational age (GA), birth weight (BW), and birth length (BL).

Subjects and Methods: This was a hospital-based, cross-sectional and descriptive study. Eight hundred and eleven apparently healthy term Igbo male neonates within the first 3 days of life were studied. The TV was measured with Prader Orchidometer (ZKL-135-H), ESP Model. Smoothed centiles (3–97th percentile values) for TV by GA were determined. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17.0 (Chicago). $P < 0.05$ were regarded as statistically significant.

Results: The mean TV was 1.74 ± 0.62 ml ranging from 1 to 3 ml. The TV increased with increasing GA ($P = 0.00$). Pearson's correlation test between TV and birth length ($r = 0.301$, $P = 0.001$), as well as with BW ($r = 0.247$, $P = 0.001$) were significant. A linear regression demonstrated correlation between TV and birth length ($P = 0.0001$, $r^2 = 0.091$).

Conclusion: The mean TV among male Igbo newborn is 1.74 ± 0.62 ml. Also, the first smoothed percentile values for TV by GA for Nigerian Igbo babies is created.

Key words: Gestational age, Igbo babies, smoothed percentile, testicular volume

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Introduction

The presence of the testes determining region of the Y-chromosomes is the key turning point in the gonadal differentiation into testes.[1] Testicular volume (TV) is largely a reflection of spermatogenesis with over 80% of the testicular mass consisting of seminiferous tubules while Leydig's cells make up the remaining 20%.[1-4] Since testicular size is more closely related to spermatogenic activity than Leydig cell function, TV may reflect sperm production and male fertility in the future.[3] The volume of the testes at birth have some predictive values of clinical

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importance.[5] It has been observed that Danish men have a 4-fold higher incidence of testicular cancer and poor semen quality than the Finnish men do.[6] This was attributable to the smaller testicular size of Danish boys at birth and throughout infancy than the Finnish boys.[6] In addition, determination of the normal TV is necessary since the fetal testes secrete testosterone that is required for virilization of the male newborn and continued penile growth.[7] Defect of androgen production and genital development in the male are closely related to TV at birth.[1] Therefore, TV assessment at birth is important in early detection of disorders of sex development such as disorders of gonadal development and/or androgen synthesis.

There are different methods of measuring TV such as orchidometery, ultrasonography, water displacement, and use of calipers and rulers.[8] The Orchidometer is the most widely used and it has different types such as Prader, Tukihara-punched ring, Rochester and Seager.[9,10] However, Prader orchidometer is the most popular, and it consists of a string of twelve numbered wooden or plastic beads of increasing size from about 1 to 25 ml in width. The beads are compared with the testicles, and the volume of the bead that matches most closely in size, is read off in ml.[10-12] Although Prader orchidometer is more practical, inexpensive, and less time-consuming, it tends to overestimate the TV, especially in small testes as it measures not only the testes but also the epididymis as well as the scrotal skin.[12-15] Furthermore, the smallest bead in Prader orchidometer is 1 ml, making it impossible to get values <1 ml.[12-14]

On the other hand, ultrasonography is done by careful measurement of the testes in longitudinal and transverse planes to obtain the length, width, height, and the TV is then calculated using various formulae. These formulae include Lambert's formula $0.71 \times L \times W \times H$,[16] $\pi/6$ (LWH) $\times$ 0.52 and prolate formula (LW) 0.52.[16] Several studies that have compared orchidometery and ultrasonography[8,9] concluded that ultrasound (US) measured volume is more precise showed low variability and correlated well with true TV, and thus, should be regarded as gold standard. However, the above studies[9,16] still found a strong linear positive correlation ($r^2 = 0.96$) between orchidometer and US measured volume, thus, the Prader orchidometer was used in this study.

The normal TV in neonates varies from 0.27 to 2.5 ml[8,9,12,14,15,17-22] with an average of 1 ml.[17] These reference values were derived from previous studies.[11,12,14,15,18-22] Chin *et al.*[18] in Taiwan, in 1998, measured the normal TV in 430 Taiwanese neonates using Prader orchidometer and reported the TV as 1.35 ± 0.3 ml. Similarly, Matsuo *et al.* in 2000[19] carried out a study in Japanese boys and recorded 1.2 ml as the TV in the neonatal period. Main *et al.*[6] measured the TV of Finnish and Danish newborn boys using ultrasonography and reported 0.98 ml and 0.95 ml, respectively. This is similar to Preiksa *et al.*[22] findings in 2009, in Lithuania, who reported an average of 0.9 ± 0.3 ml in 712 healthy newborn males. The above results suggest evidence of TV in some variations in the measurement of mean TV among the different population.

The Igbo people, are an ethnic group of South-Eastern Nigeria and constitute one of the largest ethnic groups in Africa.[23,24] They have a unique cultural heritage and studies suggest a link between the influence of some environmental factors on TV. For instance, exposure to phthalates can interfere with the stage of proliferation of Sertoli cells in fetal and early postnatal life.[5] However, no consensus has been reached on the influence of race or ethnicity on infant TV.[13,20,21] Although several studies[13,19,20] have been done on TV among different countries worldwide, the emphasis was mainly on the different methods of measurements rather than differences based on racial or ethnic background. However, Kuijper e*t al.*[13] in Amsterdam studied a multi-ethnic group of Caucasians, Asians, Mediterranean, and Africans living there, and found no difference between the various ethnic groups. On the other hand, Main *et al*.[6] reported a larger testis size in Finnish neonates compared to Danish boys. Although the phenomena could be due to the genetic difference between the two countries, it may also reflect an adverse environmental influence on testicular development.[6]

There is a dearth of data on TV in Nigerian baby boys. The reference values currently in use were done in Caucasians and may not be applicable to our clime. There is need to have a baseline data of TV of Igbo boys and how it compares with other published works These normative values aims to create baseline data that will serve as a guide to clinicians in appropriate assessment of TV among newborns in the Igbo population and Nigeria at large.

Subjects and Methods

The study was hospital-based involving two Tertiary and one Secondary Hospitals in Enugu. Enugu is the capital city of Enugu State in South-Eastern, Nigeria located at 6° 27' 9.6" N, 7° 30' 37.2".[23] It is largely populated by members of Igbo ethnic group. The city has a hilly geography with a population of 722,664.[23] It has a tropical savannah climate with a mean daily temperature of 26.7°C and average annual rainfall of 2000 mm.

These hospitals, included, University of Nigeria Teaching Hospital (UNTH), Enugu State University Teaching Hospital (ESUTH), and Mother of Christ Specialist Hospital (MCSH). These hospitals were purposively chosen because they enjoy very high patronage of patients, and combined average annual delivery is 1133.3 babies. All measurements were carried out in the labor wards and lying-in wards of these hospitals.

Study design

This was a cross-sectional and descriptive study, and subjects were enrolled consecutively within the first 72 h of life. Enrolled subjects were apparently healthy term male neonates with appropriate weight and whose parents are of Igbo extraction. A term baby is, one delivered from 37 completed weeks to 42 weeks of gestation. While, an apparently healthy baby with an appropriate weight is a baby who appears to be well with a normal weight, that is, between 2.5 and 3.99 kg.[1]

Neonates with ambiguous genitalia or suspected endocrine disorder were excluded from the study. Also, excluded from the study were babies with undescended testes and hydrocele, babies with dysmorphism or multiple congenital abnormalities, and neonates <2.5 kg and more than 4.0 kg. Neonates of nonconsenting mothers or babies from parents of non-Igbo extraction were also excluded from the study.

Ethical considerations

Ethical approval was obtained from the Health Research and Ethics Committee of UNTH, ESUTH, and MCSH. Informed written consent was obtained from the parent/guardian of each subject after delivery. Details of the study were explained to the parents, and only those who gave consent were included in the study.

Data collection

Information obtained from the history and physical examinations were entered into a purpose-designed proforma. Subjects were consecutively enrolled from both the labor ward and lying-in ward. The mothers were interviewed to obtain bio data such as age, sex, and tribe of parents. Antenatal history and condition of each infant were obtained from the mothers and hospital records. A general examination was done for each neonate to determine the gender and other features of inclusion and exclusion criteria.

Gestational age (GA) was calculated to the completed weeks and was determined from the maternal last menstrual period. The gestation of each neonate was also assessed using the new Ballard score.[25]

Measurements

All measurements were done by the researchers. To validate the accuracy and ensure the measurements, a pilot study was conducted, and 30 babies were measured. The interobserver and intraobserver differences were not statistically significant (kappa analysis was 0.96 and Cronbach's alpha = 0.97).

The birth length (BL) was measured to the nearest 0.1 cm using an infantometer (Seca), model: 210182109. Birth weight (BW) of all subjects was weighed naked on a digital weighing scale (Seca, Vogel and Halke) sensitive to the nearest 10 g.

Measurement of testicular volume

TV was measured with a Prader orchidometer (ZKL-135-H), ESP Model. It has a sensitivity of <50%. The Prader orchidometer consists of 12 ellipsoid testis models graded from 1 to 25 ml (1–6, 8, 10, 12, 15, 20, and 25 ml) against which each testis was compared. The scrotal skin was stretched over the testis in a warm room, and the beads were compared by visual inspection with the testes. The volume of the bead that matches most closely was read off in ml. Both the right and left testes were measured. A testis size that was in - between two standard ellipsoid volumes was determined by calculating the mean between the larger and the smaller ellipsoid sizes.[5]

Data analysis

All the data obtained were recorded and analyzed using the Statistical Package for Social Sciences (SPSS) software version 17.0 (Chicago). Data were presented in prose, tables, figures, and graphs. The means, standard deviations, and 95% confidence intervals of the continuous variables (TV, BW, and BL) were reported. The smoothed centiles (3–97th percentile values) for TV by GA were calculated. Pearson correlation coefficient (r) and linear regression analyses were conducted to express the relationship between TV and GA and BW and BL. $P < 0.05$ was regarded as statistically significant.

Results

The study lasted 6 months; from April to September 2012. Eight hundred and eleven neonates were studied. 146 neonates were from UNTH, 284 from MCSH, while 381 newborns were from ESUTH. The minimum GA was 37 weeks, while the maximum was 42 weeks with mean GA of 39.17 weeks ± 1.24. However, the majority of the subjects were delivered between 38 and 40 weeks of gestation [Tables 1 and 2].

The minimum BW was 2.5 kg while the maximum was 4.0 kg with mean BW weight of 3.36 ± 0.42 kg. The majority of the patients weighed between 3.0 and 3.5 kg.

The majority of the subjects had a birth length between 49.1 and 51.0 cm, with a range of 45–55 cm and mean value of 51.12 cm. ±2.03 cm [Tables 2-4].

Table 1: Characteristics of variables

Variables	Mean±SD	Range
GA (weeks)	39.17±1.24	37-42
BW (kg)	3.36±0.42	2.5-4
Birth length (cm)	51.12±2.03	45-55
TV (ml)	1.74±0.62	1-3

GA=Gestational age; BW=Birth weight; TV=Testicular volume; SD=Standard deviation

Table 2: Distribution of BW (kg) of subjects

BW (kg)	Frequency (*n*)	Percentage
2.500-2.749	72	8.9
2.750-2.999	72	8.9
3.000-3.249	195	24.0
3.250-3.499	97	12.0
3.500-3.749	189	23.3
3.750-4.000	186	22.9

Range=2.5-4.0 kg; 95% CI=3.33-3.39 kg. CI=Confidence interval; BW=Birth weight

Table 3: Distribution of body length (cm)

Body length (cm)	Frequency	Percentage
≤47	25	3.1
47.1-49.0	99	12.2
49.1-51.0	331	40.9
51.1-53.0	239	29.5
53.1-55.0	117	14.4

Range=45.0-55.0 cm; 95% CI=51.06-51.31 cm. CI=Confidence interval

Table 4: The mean BW, BL, and TV at various GAs

GA (weeks)	Frequency	Mean BW kg (±SD)	Mean BL cm (±SD)	Mean TV ml (±SD)
37	115	3.03 (0.42)	49.49 (1.8)	1.34 (0.53)
38	93	3.3 (0.42)	51.21 (1.9)	1.71 (0.59)
39	190	3.4 (0.44)	51.22 (1.9)	1.81 (0.64)
40	212	3.40 (0.38)	51.63 (1.8)	1.78 (0.57)
41	121	3.49 (0.41)	51.63 (2.0)	1.88 (0.64)
42	80	3.54 (0.30)	51.75 (1.8)	1.88 (0.55)
		P=0.00	*P*=0.00	*P*=0.00

TV=Testicular volume; GAs=Gestational ages; BW=Birth weight; SD=Standard deviation; BL=Birth length

The mean TV was 1.74 ± 0.62 ml with a range of 1–3 ml and the 95% confidence interval around the mean was 1.698–1.783 ml. There is significant statistical differences in the TV with the increasing GA ($P = 0.00$) see nomogram in Table 5.

The smoothed percentiles for TV by GA were calculated and shown in Table 6. There was no observed difference in TV for each GA below the 10th percentile. The 50th percentile corresponded to the median value of TV for each GA. Their corresponding values at 37, 38, 39, 40, 41, and 42 weeks were 1.48 ml, 1.59 ml, 1.70 ml, 1.81 ml, 1.92 ml, and 2.03 ml, respectively [Table 6].

Pearson's correlation test showed a statistically significant correlation between TV and birth length ($r = 0.301$, $P = 0.001$) as well as in body weight ($r = 0.247$, $P = 0.001$) [Table 7].

Linear regression analysis showed a significant correlation between the TV and birth length ($P = 0.0001$, $r^2 = 0.091$) [Figure 1].

Table 5: Distribution of TV (ml) of subjects

TV (ml)	Frequency	Percentage
1-1.50	354	43.6
1.51-2.00	282	34.8
2.01-2.50	114	14.1
2.51-3.00	61	7.5

Range=1-3 ml; 95% CI=1.698-1.783 ml. TV=Testicular volume; CI=Confidence interval

Table 6: Percentiles for TV (ml) by GA (weeks)

Gestation weeks	Percentiles								
	3	5	10	25	50	75	90	95	97
37	1.00	1.00	1.00	1.00	1.48	2.00	2.33	2.61	2.74
38	1.00	1.00	1.00	1.08	1.59	2.06	2.43	2.69	2.81
39	1.00	1.00	1.00	1.16	1.70	2.12	2.53	2.77	2.88
40	1.00	1.00	1.00	1.24	1.81	2.18	2.63	2.85	2.95
41	1.00	1.00	1.00	1.32	1.92	2.24	2.73	2.93	3.02
42	1.00	1.00	1.00	1.40	2.03	2.30	2.83	3.00	3.09

TV=Testicular volume; GA=Gestational age

Table 7: Pearson's correlation between TV with growth parameters of BW and birth length

Correlation (*r*)	TV	
	r	*P*
BW	0.247	0.001
Birth length	0.301	0.001

TV=Testicular volume; BW=Birth weight

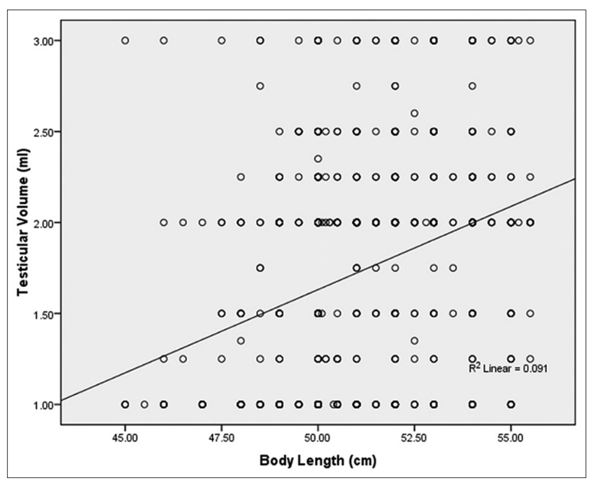

Figure 1: Linear regression showing the correlation between testicular volume and birth length

Discussion

Adequate spermatogenesis is presumed to be possible only in a testis of normal or nearly normal volume.[25] Although TV measurements are considered important for assessing spermatogenesis, a cut-off value for the TV that would ordinarily ensure normal testicular function has not been established.

The mean TV (1.74 ml) in this study was similar to the TV (1.73 ml) documented by Semiz *et al*.[26] in Turkey but slightly higher than the findings of Chin *et al*.[18] in Taiwan (1.35 ml), as well as Matsuo *et al*.[19] in Japan (1.2 ml) and Béres *et al*.[20] in Hungary. However, it was relatively lower than the TV of 2.4 ml reported by Ting and Wu[27] in Malaysia. There are appreciable differences in the values of TV reported by the aforementioned studies though they all used Prader orchidometer for measurement but for Béres *et al.* who used Hymie's testometer. The differences can be explained by the lack of precision and low sensitivity associated with Prader orchidometer. On the other hand, TV reported in this study was much higher than the values of US measured TV, reported in some studies.[13,21] The observed significant differences could be explained by the lack of standardization in the methodologies. However, racial and ethnic influence cannot be ruled out entirely.

Furthermore, the true TV is only slightly overestimated by US when compared to orchidometer.[28] It is unknown whether the reliability of the Prader orchidometer is age dependent.[3] It is also noted that the orchidometer measures the epididymis as well as the scrotal skin, and, as a result, it tends to slightly overestimate TV, especially in small testes, in which the epididymis is large in comparison to the total TV. Notwithstanding, because of its practical use, the Prader orchidometer is one of the main instruments in the analysis of TV. However, because of its accuracy in the follow-up of testicular growth, US has an additional role in the development of puberty.[13]

It is important to note that few studies comparing the orchidometer and US found that both methods correlated well.[2,12,21,29]

We also noted a statistically significant positive correlation between TV and GA.

This positive correlation between TV and GA is also noted by Malas *et al*.[30] He noted that this increase in TV and GA is traceable to the fact that laminar propia (fibroblast-like and myoid-like type) in the testis and the interstitial tissue become more mature and regular and had a well-organized structure with progress of GA. He also opined that in the third trimester, the lumen in the seminiferous tubules and the testes became more regular and clear, and the interstitial tissue had a clear appearance.[30]

From the above findings, it becomes meaningful to evaluate and calculate the individual expected values for TV of term newborns that this sample represents. However, the nature of these correlations on a much more comprehensive scale can only be understood via the contribution of future studies by various centers around the world on TV of newborn males.

This increase of TV and GA was also buttressed by Cicognani *et al*.[31] He noted that small age subjects have pituitary-gonadal axis function that tends toward hypogonadism. Disruption of the exocrine function in babies with smaller testicular size is a possible reason for this.

We also noted increase in TV with BW in this study. This was also corroborated by Semiz *et al*.[26] Hormonal changes and maturity of the pituitary hypothalamic axis as GA progresses, could explain these changes.[26]

We noted, in this study, a positive correlation between birth length and TV. Also, a linear regression between TV and body length showed a statistically significant correlation (P = 0.0001 r^2 = 0.091), implying that 0.9% of variations are explained by a body length. However, this was refuted by Sutan-Assin *et al*. who noted no correlation. The difference between our finding and that of Sutan-Assin could be due to the smaller sample size used. Racial and geographical differences could also be contributory.[32]

Conclusion

The mean TV of Igbo babies was 1.74 ± 0.62 ml with the first set of smoothed percentiles generated and our findings indicate some variations from studies from other populations. This study has also shown a positive correlation between TV and GA and BW and birth length.

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Conflicts of interest
There are no conflicts of interest.

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