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PREVALENCE OF UNDESCENDED TESTES (CRYPTORCHIDISM) FROM BIRTH TO SIX MONTHS IN BENIN CITY, NIGERIA

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ABSTRACT:

Although an undescended testes (UDT) is the most common developmental anomaly of the urogenital organ in males, they have often been regarded as mild malformation and as a consequence have been poorly reported despite its association with increased risk of infertility and testicular cancer in later life. In Nigeria, data on its prevalence is scarce. The objective of the study was to determine the prevalence rates of undescended testes at birth, 3 months and 6 months of age respectively. A prospective hospital-based cohort study was conducted to determine the prevalence rates of UDT at birth, 3 months and 6 months of age. The infants were examined at birth for UDT, using standardized technique. The infants who were identified at birth to have undescended testes were re-examined at the ages of 3 and 6 months respectively. To minimize inter-observer error, one physician examined all the infants. The gestational age, birth weight and birth position of each the neonates were recorded. The maternal age, parity, educational attainment and occupation of the parents were noted. The season in which each of the infants was born was recorded. At birth, 2.8% (39 of 1,394) of live-born male infants had undescended testes (UDT). This prevalence rate declined to 1.2% at the age of 3 months and 0.6% at the age of 6 months with an overall spontaneous testicular descent rate of 79.5% (31 of 39 cases). The prevalence rates were significantly elevated for low birth weight and preterm infants. The frequency of spontaneous descent of the testes was higher in both low birth weight and preterm infants compared to normal birth weight and full-term infants respectively. Comparing twin and non-twin infants, the prevalence of UDT was 3.8% (2 of 52) versus 2.8% (37 of 1,342); $p>0.05$. At birth, low birth weight and preterm infants had a significantly higher prevalence than their full-term as well as preterm counterparts with preterm infants having a greater tendency to achieve spontaneous descent of the testicles than full-term infants.

KEY WORDS: Undescended testes, cryptorchidism, testicular ascent, prevalence, Nigeria.
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INTRODUCTION:

At birth, undesended testes (UDT) or cryptorchidism is the most common developmental anomaly associated with the male external genitalia but it has often been regarded as mild malformation [1]. Despite the association of UDT with increased risk of infertility and testicular cancer in later life, it has not received sufficient attention [1,2]. Little has been published on the incidence and prevalence of UDT in Nigeria [3]. In addition, the presence of UDT at birth could point to the existence of serious endocrine or genetic disorder [4]. For instance, UDT has been linked to testosterone deficiency, complete androgen insensitivity syndrome, mixed gonadal dysgenesis and Klinefelter syndrome [4].

The process of testicular descent occurs in two phases (intra-abdominal, 8-15 weeks of gestation and inguino-scrotal, 28 weeks of gestation to birth) and is regulated by an interaction between hormonal and mechanical factors, such as testosterone, dihydrotestosterone, mullerian-inhibiting factor, the gubernaculums, intra-abdominal pressure, and the genitofemoral nerve [2,5]. Endocrine disruption of the function of the developmental genes, such as insulin-like factor 3 (INSL3) and homeobox (HOX) family have been linked to occurrence of cryptorchidism [5]. Usually, testicular descent is completed by the 35th week of gestation [5]. Therefore, most testes that are undescended at birth in preterm babies, descend spontaneously before the age of three months [6]. Although a variety of classification of UDT exists, the most useful is based on whether the testes are palpable or non-palpable on clinical examination [7]. Palpable undescended testes are either retractile, ectopic or truly undescended within the canal [7]. Non-palpable testes may be truly undescended (intra-canalicular or intra-abdominal) or are absent [7]. The consequences of UDT include infertility, testicular cancer, associated hernia, torsion of the cryptorchid testis, and the possible psychologic effects of an empty scrotum [2].

The prevalence of UDT at birth varies from 1.6% to 9.0% among male infants [7,8]. Different prevalence rates have been reported from different countries. For instance, at birth, 2.4 -9.0% in Denmark [9,10], 2.4% in Finland [9], 3.7% in USA [11], 5.9% in United Kingdom [12], 4.8% in Malaysia [13] and 5.7% in Lithuania [14]. However, many of these studies did not state the case definition and the examination techniques employed in their study [9,10,14]. It is well established that in epidemiological studies standardized diagnostic criteria and examination techniques are required to obtain reliable data [1,15]. Approximately, two-third of infants with UDT at

birth will have descent of the testicles into the scrotum by the age of 6 months [6]. In most cases, the UDT descend spontaneously during the first 3 months of life with the incidence of UDT dropping from 1.5% to 0.8% between the ages of 3 and 12 months [8,,11,14]. If the testes have not descended by the age of six months, spontaneous descent occurs only very rarely, indicating that the strategy of watchful waiting after the age of six months is no longer recommended [11,16]. It is estimated that 6% to 7% of siblings of boys with UDT may have similar problem with testicular position and descent, indicating that the presence of UDT in one infant could serve as a window for identifying other male siblings with similar clinical conditions [9,14]. Estimates indicate that the heritability of cryptorchidism in first degree relatives is 0.67 [16]. In Nigeria, data on the prevalence and incidence of cryptorchidism is scarce. Although in a recent study in Nigeria the prevalence of UDT was 0.82% among primary school children, the question of its prevalence at birth still remains unanswered [3]. A research of the literature did not reveal a Nigerian study on the prevalence and incidence UDT from birth to the first six month of life. This lack of published data prompted us to conduct this study.

The purpose of the present study was to determine the prevalence rates of UDT at birth, at 3 months and 6 months of age.

PATIENTS AND METHODS:

In this prospective hospital-based cohort study, a total of 1,394 consecutive live-born male neonates delivered between 1st January, 2010 and 31st December, 2011 at St Philomena Catholic Hospital (SPCH), Benin City were examined at birth for testicular position, using standard techniques [15]. The examination took place in the postnatal ward at room temperature with the neonate lying in supine position. The testicular examination of the infant involved a two-handed technique. The examining hand is gently swept along the inguinal canal, starting at the superior-lateral extent of inguinal canal. A true undescended or inguinal testicle will be felt to “pop” under the examiner’s fingers during this maneuver. A retractile testicle will be felt by the opposite hand as it is manipulated into the scrotum. The ectopic testicle will immediately spring out of the scrotum when it is released whereas the retractile testis will remain in the scrotum. The position of the testis was recorded after its manipulation to the most distal position along the normal pathway of anatomical descent without forced traction. In this study, the position of the each testis was categorized into two major group as normal (if they were either normal scrotal or normal retractile) or undescended.

The undescended group was sub-classified into prescrotal (if they were high scrotal or suprascrotal), inguinal or non-palpable testes

[17]. Where a testis cannot be palpated in the inguinal canal or the scrotum or in ectopic sites such as the femoral region or perineum, evaluation for non-palpable testis was initiated, including inviting the urologist. The laterality of the UDT was recorded (right, left, or bilateral). All the examination for testicular position was performed by one specialist paediatrician to minimize inter-observer errors. Infants who were identified at birth as having UDT were re-examined at the ages of 3 and 6 months. The birth weight and birth order of each of the neonates was recorded. The gestational age was assessed using as an appropriate antenatal ultrasonography report performed between 18 and 20 weeks of gestation, data on last menstrual period or Dubowitz score [18] postnatally. Infants born before 37 completed weeks of gestation were considered preterm. A small-for-gestational age infant was defined as that whose birth weight for gestational age was below the 10th percentile. Any testis that could not be manipulated into a stable scrotal position was considered undescended. The maternal age and parity were also recorded. The socio-economic status of the parents was determined using the classification suggested by Ogunlesi et al [19].This was determined by combining the highest educational attainment, occupation and income of the parents (based on the mean income of each educational qualification and occupation). In this Social Classification System, classes I and II represent high social class, class III represents middle social class while classes IV and V represent low social class. In this way, the women were categorized into high, middle and low socio-economic groups. The deliveries were recorded according to the month and year of delivery to allow for assessment of influence of season. The season was categorized into two; dry season (November to April) and wet season (May to October). The infants were examined for the presence of other congenital malformation of the genitalia, particularly hydrocoele and hypospadias.

Ethical clearance and approval for the study were obtained from the appropriate hospital authority. Permission to examine the infants was obtained from the parents after explaining the purpose and the potential benefits of the study to them. The data was analyzed using SPSS for Windows version 11.0 (Chicago, IL USA). Where applicable and appropriate, descriptive statistics such as frequencies, means, odd ratios, standard deviations, confidence intervals, percentages were used to describe all the variables.

RESULTS:

During the two-year study period there were 2,688 deliveries, resulting in 2,741 live-born babies (1,394 males and 1,347 females); giving an overall male-to-female ratio of 1.03:1. Of the 2,688 women who delivered, 53 (2.0%) had twins with gender-pair distribution of 20(37.7%) different-gender, 17 (32.1%) female same-

gender and the remaining 16 (30.2%) male same-gender pairs.

Fifty two (3.7%) of the 1,394 males were derived from the twin deliveries. Among a total of 1,394 male live-born infants, 39(2.80%; 95% Confidence Interval, CI= 2.75-2.85) had undescended testes (UDT) or cryptorchidism at birth. The testes were palpable in 89.7% (35 of 39 cases) and non-palpable in 10.3% (4 of 39 cases). At the age of 3 months, the testes remained undescended in 17(43.6%) of the 39 babies identified at birth. In eight (20.5%) of the 39 cases, the undescended testes persisted till the age of six months.

Table 1 shows that 56.4% (22 of 39 cases) of the infants with UDT at birth had descent of the testicles into the scrotum by the age of 3 months while an additional 23.1%(9 of 39 of cases) had descent of the testicles into the scrotum at the age of 6 months, giving an overall spontaneous descent rate of 79.5% (31 of 39 cases).

Table 1: Prevalence of undescended testes (cryptorchidism) at birth, 3 months and 6 months of age

Age	Study population	Number with UDT	Prevalence (%)	95% CI
At birth	1,394	39	2.80	2.75-2.85
At 3 months	1,394	17	1.22	1.16-1.24
At 6 months	1,394	8	0.57	0.55-0.59

UDT = Undescended testes

Table 2: Prevalence of undescended testes (cryptorchidism) at birth according to birth weight and gestational age

Variable	Number (%)	Prevalence: N (%)	Odd ratio (95% CI)
Birth weight < 2500g	190 (13.6)	14 (7.4)	0.08
Birth weight ≥2500g	1204 (86.4)	25 (2.1)	(0.04-0.14)
Gestational age <37 weeks	166 (11.9)	11 (6.6)	2.90
Gestational age ≥37 weeks	1228 (88.1)	29 (2.4)	(1.44-5.99)
Small-for-gestational age	77 (5.5)	3 (3.9)	1.40
Appropriate-for-gestational age	1317 (94.5)	36 (2.7)	(0.43-4.79)

Table 3: Distribution of testicular descent at 3 and 6 months of age among infants with undescended testes (cryptorchidism) detected at birth

Variable	Testicular descent at 3 months of age (n=22) No (%)	Testicular descent at 6 months of age (n=31) No (%)
Birth weight < 2500g	14(63.6)	19(61.3)
Birth weight ≥2500g	8(36.4)	12(38.7)
Gestational age < 37 weeks	18(81.8)	22(71.0)
Gestational age ≥37 weeks	4(18.2)	9(29.0)
Small-for-gestational age	1(4.5)	2(6.5)
Appropriate-for-gestational age	21(95.5)	29(93.5)

As shown in Table 2, low birth weight (birth weight < 2500g) and prematurity (gestational age < 37 weeks) were the significant risk factors associated with undescended testes. Comparing twin and non-twin infants, the prevalence of UDT was 3.85% (2 of 52) versus 2.76% (37 of 1,342); Z-statistic = 0.372, p>0.05. The frequency of low birth weight (birth weight < 2,500g) was 46.2% (24 of 52) in twins and 8.0% (107 of 1,342) in singletons. The frequency of preterm delivery was 51.9% (27 of 52) in twins and 11.9% (160 of 1,342) in singletons.

As depicted in Table 3, the frequency of spontaneous descent of the testes was higher in both low birth weight and preterm infants compared to normal birth weight and full-term infants respectively.

The overall mean maternal age and parity in this general obstetric population was 27.8±4.6 years and 1.5±1.2 respectively. When the mean maternal age of infants with UDT was compared with that of infants without UDT, it was 28.2±4.4 years versus 28.6±4.7 years t=0.780 p>0.05. Comparing the mean maternal parity of infants with UDT and infants without UDT, it was 1.5±1.4 versus 1.4±1.6 t= 0.438 p>0.05. Among the 1,394 male live-born infants, 701(50.3%) were born during the dry season while the remaining 693(49.7%) were born during the wet season. Of the 39 infants with UDT at birth, 21(53.8%) were born during the dry season while the remaining 18(46.2%) were born during the wet season. Comparing the prevalence of UDT during the dry and wet seasons, it was 3.0% (21 of 701 infants) versus 2.6 % (18 of 693 infants) X^2 =0.203 p>0.05. The distribution of socioeconomic status (SES) of this general obstetric population was as follows: high SES 20.0% (538 of 2,688 mothers), middle SES 25.0% (672 of 2,688 mothers) and low SES 45.0% (1,433 of 2,688 mothers) respectively. The prevalence of delivery of infants with UDT according to SES was as follows: high 1.7 % (9 of 538 mothers),

middle 1.9% (13 of 672 mothers), and low 1.2% (17 of 1,433 mothers).

Of the 35 infants with palpable UDT, 18(51.4%) were prescrotal (high scrotal or suprascrotal), 17(48.6%) were inguinal (variously located along the inguinal canal), and none was ectopic. In 65.7% (23 of 35 unilateral cases) it was on the right side while in 34.3% (12 of 35 unilateral cases) it was on the left side. Only in one (2.6%) of the 39 cases of UDT was it bilateral and non-palpable with a normal renal ultrasound scan result. The patient with bilateral non-palpable testes was a low birth weight infant and did not have clinical features suggestive of Prune belly syndrome, ambiguous genitalia or Prader-Willi syndrome and was referred to the Paediatric Surgeon/Urologist for further investigation.

DISCUSSION:

The prevalence (2.8%) of UDT, at birth, being reported here is comparable to 2.4% separately reported from Finland and Denmark [9,10] but lower than the 3.7%, 4.8%, 5.7% and 5.9% reported from the USA, United Kingdom , Lithuania and Malaysia respectively [11-14]. This finding is not surprising as it reflects the known variability in prevalence rates from different countries. This country-to-country variability in prevalence has been attributed to genetic factors as well as environmental factors like the endocrine disruptors and lifestyle (cigarette smoking and alcohol consumption during pregnancy) [7,20]. On the other hand, the case definition, the population characteristics and the examination technique used in a given study may influence the observed prevalence in that study [21], making comparison of prevalence rates between studies difficult.

At the age of three months, the prevalence of UDT in the present study was 1.2% which was lower than the 1.9% and 2.4% found in Denmark and in the United Kingdom respectively [9,12] but slightly higher than 1.0% found separately in Finland and USA [10,9]. In another study in Oxford by the John Radcliffe Hospital Study Group (1984-1988) in which they examined a cohort of 7,500 consecutive newborn boys the prevalence at birth was 4.1% but dropped to 1.6% at the age of three months [22]. As in other studies [10,11], majority of the spontaneous descent of the testis in infants with UDT occurred in the first three months of life. This drop in prevalence of UDT by the age of 3 months has been attributed to short-term postnatal endogenous testosterone secretion [23].

In the present study, the prevalence of UDT dropped further to 0.6% at 6-month assessment. Considering the dynamics of testicular descent, the significance of the prevalence at 6-month assessment is that the figure might represent the true birth prevalence of cryptorchidism. A similar view was also expressed by Abdullah et al [24] who reviewed the prevalence of cryptorchidism and

hypospadias in northern England, using data derived from northern region hospital episodes statistics (HES) (1993-2000). This view is based on the knowledge that after the age of 6 months spontaneous testicular descent is unlikely [4].Comparison with previous studies was not possible because they did not report on 6-month assessment [5,7,8]. However, in a study in southern Nigeria, the prevalence of cryptorchidism among primary school children aged 5 to 13 years was 0.82% [3]. This prevalence is higher than the 0.6% observed at the age of 6 months in the present study. The observed difference is intriguing in that it might, at least indirectly, represent the prevalence of testicular ascent (acquired cryptorchidism) among children in southern Nigeria. There is absolutely no published data on prevalence of testicular ascent in Nigeria. Testicular ascent (acquired cryptorchidism) is a well-documented phenomenon [15]. Our data indicated that the UDT persisted in 20.5% of cases after 6 months. This finding is comparable to 23.5% reported by Thong et al [11]. The explanation for the persistence of UDT in some cases may be found in the report of Ferlin et al [25]. In that study, they reported that boys with persistent cryptorchidism had a 17-fold greater odd of having a genetic alteration such as Klinefelter syndrome or mutation in the INSL3 receptor genes. However, such a conclusion cannot be derived from the present study as it was not designed to assess the reason for persistence of cryptorchidism beyond the age of 6 months.

Data from the present study revealed that the prevalence of UDT was significantly elevated for low birth weight (LBW) and preterm infants. This finding is in consonance with the report of previous studies [8,9] . One possible explanation in the case of preterm infants is that the infant may not have achieved full descent of the testes before delivery. Testicular descent is usually completed at 35 weeks of gestation [6]. A similar argument holds true for LBW infants as many of them were preterm. In addition, Abdullah et al [24] in their report suggested that fetal androgen dysfunction might play a role in the aetiologic link between LBW and the occurrence of cryptorchidism. Although twin gestation is associated with increased frequency of delivery of LBW and preterm infants, the risk of UDT does not appear to be higher in twins compared to singletons. A study in Denmark has reported a similar finding [8]. The reason for the lack of significant bearing between twins and frequency of UDT despite the established higher incidence of LBW and preterm infants in twin gestations is not clear. The social class, maternal age, parity, mode of delivery and the season in which a baby is born had no bearing with the frequency of occurrence of UDT in the present study. This finding is largely similar that reported in previous studies [8,10,12]. In contrast, Berkowitz et al [26] reported a positive correlation between the mode of delivery (Caeserean section) and the season in which a baby was born with frequency of UDT. In that

study, the frequency of UDT was found to be higher between September and November as well as between March and May. The reason for this opposite finding between our study and that of Berkowitz et al [26] is not clear.

In the present study, some laterality in occurrence of UDT was demonstrated. The frequency of right-sided UDT was higher than left-sided UDT. This observation is in consonance with the report of previous studies [27]. In only 2.6% of cases were UDT bilateral in the present study. This is lower than the 8.5% prevalence rate of bilateral UDT reported by Boisen et al [9]. The difference may be a reflection of the higher frequency of abnormal testicular function reported among Danish men [9]. Such an increased frequency of abnormal testicular function has not been reported among Nigerian men. There is no readily available explanation for the observed laterality in UDT in the present study. The only infant with bilateral UDT had a non-palpable type, indicating the need to exclude bilateral anorchia. Bilateral anorchia is characterized by elevated Lutenizing hormone and Follicle stimulating hormone, absence of detectable Mullerian inhibiting substance and inhibin B. A rise in serum testosterone level following βHCG stimulation reflects the presence of functioning testicular tissue. However, we were unable to differentiate between bilateral cryptorchidism and bilateral anorchia because of poor laboratory facility for measuring these biochemical parameters. This scenario depicts one of the challenges experienced in the practice of paediatric endocrinology in a developing country. However, in keeping with the current consensus statement on management of UDT, the parents of all infants with UDT were informed of the findings, while those infants whose testes remained undescended at the age of six months were referred to the Paediatric Surgeon/Urologist. For those infants with UDT at birth who achieved spontaneous descent of the testicles by the 6-month assessment (or were classified as retractile testes), the parents were advised that annual follow-up will be needed throughout childhood because there is a significant risk for re-ascent [7].

One limitation of the present study is that it is based on data from only one hospital. A multicentre study in future will ensure a larger and a more representative study sample, allowing for generalization of the conclusion as it relates to the country (Nigeria). This is important, given that different prevalence rates have been reported from different countries [10-14]. On the other hand, different prevalence rates have also been observed within the same country [1,27], making the present study relevant because it provided a prevalence rate from one of the regions of Nigeria. Hopefully, the data from the present study will encourage clinicians to examine and document in details the external genitalia findings during a routine newborn physical examination, thereby improving the standard of clinical practice in

Nigeria. UDT should normally be diagnosed during the routine newborn examination as its recognition at this time is an important step in preventing adverse consequences [15].

CONCLUSION:

In conclusion, at birth, low birth weight and preterm infants had a significantly higher prevalence than their full-term as well as preterm counterparts with preterm infants having a greater tendency to achieve spontaneous descent of the testicles than full-term infants.

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