

# Germ Cell Tumours in Children: A Twenty-year Retrospective Study (January 1988 - December 2007) in Ibadan, South-West Nigeria

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## ABSTRACT

**Background:** *There is a significant lack of studies of germ cell neoplasms in the paediatric age group from Nigeria and other parts of Africa.*

**Objectives:** *The aim of this study was to determine the histological pattern of paediatric germ cell tumours in Ibadan, Nigeria.*

**Method:** *This is a retrospective study of cases of germ cell neoplasms histologically diagnosed at the Department of Pathology, University College Hospital (UCH), Ibadan between January 1988 and December 2007 among children aged 0-14 years. Haematoxylin and eosin stained slides were reviewed and where necessary, the paraffin blocks were recut and stained. The World Health Organization Histological Classification of paediatric germ cell tumours of 2004 was used in this study.*

**Result:** *Paediatric germ cell tumours comprised 0.05% of all surgical pathology specimens in the study period. There were 10 (25.6%) male and 29 (73.4%) female patients, giving a male to female gender ratio of 1:2.9. Extragenadal germ cell tumours constituted 25 (64.1%) and gonadal germ cell tumours 14 (35.9%) cases. Benign neoplasms accounted for 26 (66.7%) and malignant neoplasms accounted for 13 (33.3%) cases. Thirty-one (79.5%) of the 39 cases were teratomas, 7 (17.9%) were yolk sac tumours and one (2.6%) was a mixed germ cell tumour. The most common sites were the ovary (33.3%), sacrococcygeal region (20.5%) and neck (10.3%). There was a bimodal age distribution, with a first peak in infancy and a second peak between >5-10 years of age.*

**Conclusion:** *In view of the paucity of studies on germ cell tumours from Nigeria and other parts of Africa, further studies of this unique group of neoplasms are required in order to validate the findings of this study.*

**Keywords:** *Germ cell tumours, Children, Pathology, Nigeria.*

## INTRODUCTION

Germ cells are progenitors of the gamete found in the gonads. The ovaries and testes are paired organs. The ovaries are located on the sides of the uterus close to the lateral wall while the testes are suspended by the spermatic cord and are housed within the scrotum<sup>1</sup>.

A substantial proportion of germ cell tumours have benign rather than malignant behaviour with diversity in biology and histologic heterogeneity<sup>2</sup>. They originate in primordial germ cells within the yolk sac endoderm, which may subsequently undergo germinomatous or embryonic differentiation. At about four weeks gestation, the primordial germ cells are initially detectable in the yolk sac of the embryo, and their route of migration during embryogenesis from the yolk sac to either the testes or ovaries may account for the primarily midline location of most extragonadal germ cell tumours<sup>2</sup>. Extragenadal germ cell neoplasms manifest when germ cells fail to reach their final destination and develop as tumours. In the International Classification of Childhood Cancer (ICCC), germ cell tumours are grouped together with trophoblastic and other gonadal neoplasms<sup>3</sup>. Extragenadal germ cell neoplasms account for 2% to 3% of childhood cancers<sup>4</sup>.

It is essential for a proper understanding of the incidence patterns for germ cell tumours of children to note that germ cell tumours of infancy and early childhood are biologically distinct from those that arise in older children. The ICCC provides the basis for understanding the incidence patterns and trends of germ cell tumours in children in their categorization of germ cell tumours<sup>3</sup>.

Apart from case reports and sporadic reviews of teratomas, there is a significant lack of studies of germ cell neoplasms in the paediatric age group from Nigeria and other parts of Africa. However, in United States of America (USA) for example, each year, approximately 900 children and adolescents younger than 20 years of age are diagnosed with germ cell tumours<sup>2</sup>, and germ cell tumours are known to represent 3.5% of cancer diagnoses for children younger than 15 years<sup>2</sup>.

Considering the differences in the pattern of occurrence of germ cell tumours in childhood from Caucasian studies and the absence of any corresponding studies from Africa, therefore, the aim of this study is to determine the histological pattern of germ cell tumours among the paediatric age group in Ibadan, Nigeria.

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## MATERIALS AND METHODS

All surgical specimens of paediatric germ cell tumours received in the Department of Pathology, University College Hospital Ibadan between January 1988 and December 2007 constituted the materials for the study. Only germ cell tumours from children aged 0-14 years were included in this study, in line with the recommendations of the World Health Organization (WHO) and International Agency for Research on Cancer<sup>5</sup>.

The age, sex and original histopathological diagnosis were obtained from the surgical daybook and original request cards in the archives of the Pathology Department. The case notes of the patients were retrieved and possible associated factors such as cryptorchidism in the case of testicular neoplasms and other congenital malformations were sought.

Histopathological slides from the cases were reviewed and reclassified where necessary to determine the histological type. The 2004 WHO classification outlined by Eble et al.<sup>6</sup> for testicular germ cell tumours was adopted. If the slides were unavailable, freshly cut-paraffin embedded sections were prepared.

Cases excluded include those in which the demographic data were absent and in which both the histology slides and blocks could not be retrieved. The data obtained was subjected to statistical analysis using the SPSS software (version 17). Ethical clearance for the study was obtained from the joint University of Ibadan- University College Hospital Ethical review committee.

## RESULTS

### General Findings

The total number of paediatric germ cell tumours received in the Department of Pathology, University College Hospital during the 20-year period of the study was 39 cases. During this period, a total number of 74,045 surgical pathology specimens were received in the department. Thus, paediatric germ cell tumours accounted for 0.05% of all the surgical pathology specimens. The paediatric germ cell tumours occurred in 10 male and 29 female patients, giving a male to female gender ratio of 1:2.9.

### Age and Sex Distribution

The ages of the 39 patients ranged from 4 days to 13 years, with a mean age of  $4.1 \pm 4.6$  years. The peak age of occurrence, was in infancy ( $\leq 1$  year of age), accounting for seventeen (43.6%) of the cases (Figure I). The mean of age of the male patients ( $10.9 \pm 15.3$  months) was significantly less than that of the female

patients ( $62.3 \pm 58.1$  months),  $p = 0.009$ . As may be seen from Figure I, all of the children greater than 5 years of age that had germ cell tumours were females.

### Histological Types of Germ Cell Tumours

The most common germ cell tumours encountered in the present study were teratomas, which accounted for 31 (79.5%) of the 39 cases. Twenty-six (83.9%) of these teratomas were mature and five (16.1%) were immature. The slides of sixteen (61.5%) of the 26 teratomas (comprising fourteen mature and two immature teratomas) were available for histological review. These neoplasms displayed varying combinations of ectodermal (skin with sweat glands, pilosebaceous units, glial tissue and uveal tissue), mesodermal (cartilage, bone, fat and smooth muscle) and endodermal (intestinal epithelium, respiratory epithelium, pancreas, liver) differentiation. Figure II shows a representative photomicrograph of a mature teratoma encountered in this study.

Ectodermal differentiation alone was observed in 7 (50%) out of the 14 mature teratomas available for histological review. Five cases (35.7%) showed differentiation into all of the 3 germ layers. A combination of endodermal and ectodermal differentiation and a combination of ectodermal and mesodermal differentiation were seen in 1 (6.1%) case each.

The two immature teratomas that were available for histological review showed mostly primitive neuroepithelial, glial tissue and mesenchymal tissues with the presence of mature uveal epithelium, cartilage, respiratory epithelium and cartilage. Both of immature teratomas were histologically classified as grade 2 neoplasms. Figure III shows a representative photomicrograph of an immature teratoma.

The next most frequent germ cell tumours were yolk sac tumours, which accounted for 7 (17.9%) of the 39 cases. The histological slides of 4 (57.1%) of these 7 cases were available for review. The predominant histological pattern of yolk sac tumour seen was the glandular-alveolar pattern in 3 of the cases. The remaining tumour showed a predominantly papillary pattern. Minor patterns of differentiation were seen in all of the 4 cases. These were solid in three cases and myxomatous in 1 case. Figures IV and V show representative photomicrographs of yolk sac tumours encountered in this study.

The least common germ cell tumour was a solitary mixed germ cell tumour (comprising yolk sac tumour combined with mature teratoma). The yolk sac component of this neoplasm was predominantly

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The total number of paediatric germ cell tumours received in the Department of Pathology, University College Hospital during the 20-year period of the study was 39 cases. During this period, a total number of 74,045 surgical pathology specimens were received in the department. Thus, paediatric germ cell tumours accounted for 0.05% of all the surgical pathology specimens. The paediatric germ cell tumours occurred in 10 male and 29 female patients, giving a male to

**Table I- Sex Distribution of Histological Variants of Germ Cell Tumour**

HISTOLOGICAL DIAGNOSIS	MALE	FEMALE	TOTAL	%
Teratoma	8	23	31	79.5
(Mature)	(7)	(19)	(26)	
(Immature)	(1)	(4)	(5)	
Yolk sac tumour	2	5	7	17.5
Mixed germ cell tumour	0	1	1	2.6
<b>TOTAL</b>	<b>10</b>	<b>29</b>	<b>39</b>	<b>100</b>

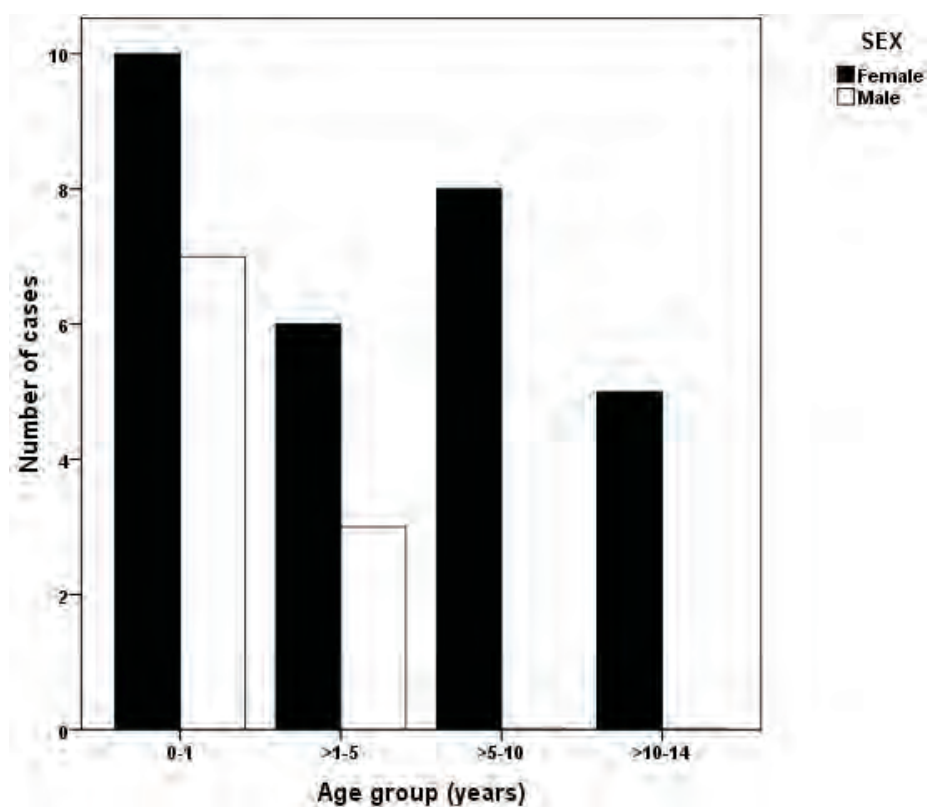
**Table II- Age Group Distribution of Histological Variants of Germ Cell Tumour**

HISTOLOGICAL DIAGNOSIS	AGE (years)				TOTAL (%)
	0-1	>1-5	>5-10	>10-14	
Teratoma	16	4	7	4	31 (79.5)
(Mature)	(11)	(4)	(7)	(4)	
(Immature)	(5)	(0)	(0)	(0)	
Yolk sac tumour	1	4	1	1	7 (17.9)
Mixed germ cell tumour	0	1	0	0	1 (2.6)
<b>TOTAL (%)</b>	<b>17 (43.6)</b>	<b>9 (23.1)</b>	<b>8 (20.5)</b>	<b>5 (12.8)</b>	<b>39 (100)</b>

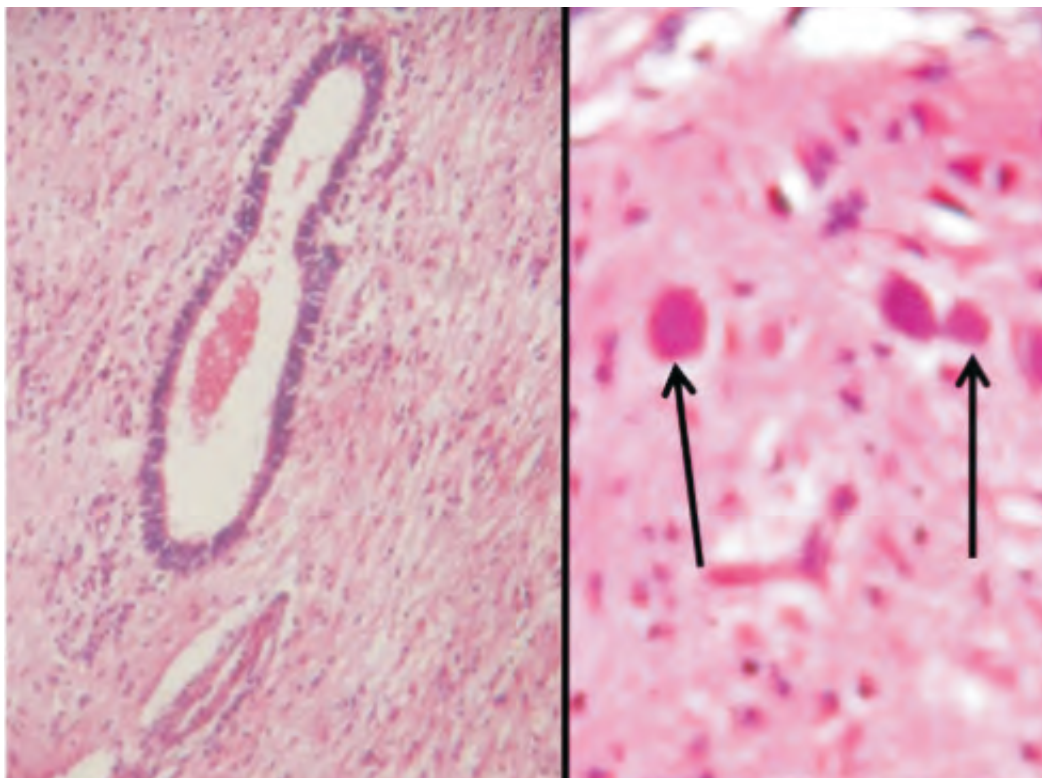
**Table III- Site Distribution of Germ Cell Tumours in Children**

ANATOMICAL SITE	TERATOMA	YOLK SAC TUMOUR	MIXED GERM CELL TUMOUR	TOTAL (%)
Ovary	10	3	-	13 (33.3)
Sacrococcyx	4*	3	1	8 (20.5)
Neck	4*	-	-	4 (10.3)
Intracranial	2*	-	-	2 (5.1)
Lumbar	2	-	-	2 (5.1)
Pelvis	2	-	-	2 (5.1)
Tongue	2*	-	-	2 (5.1)
Anterior fontanelle	1	-	-	1 (2.6)
Kidney	1*	-	-	1 (2.6)
Occiput	1	-	-	1 (2.6)
Testis	-	1	-	1 (2.6)
Thyroid	1	-	-	1 (2.6)
Submandibular	1	-	-	1 (2.6)
<b>TOTAL</b>	<b>31</b>	<b>7</b>	<b>1</b>	<b>39 (100)</b>

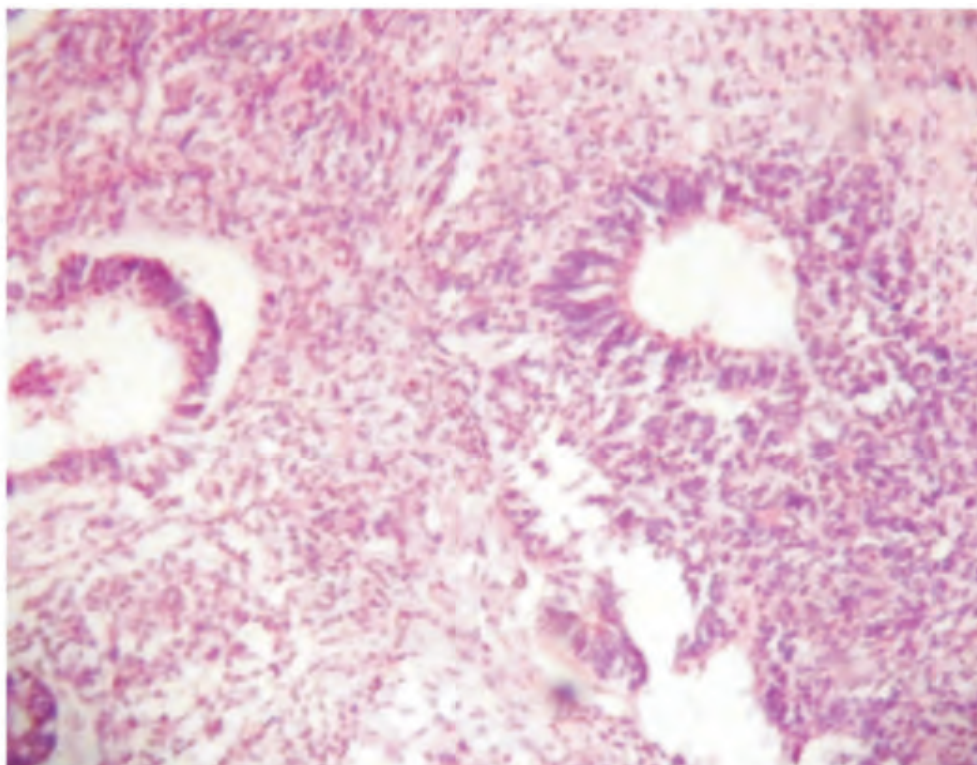
\*One teratoma in each of these sites was immature

**Figure I: Age and Sex distribution of cases.**

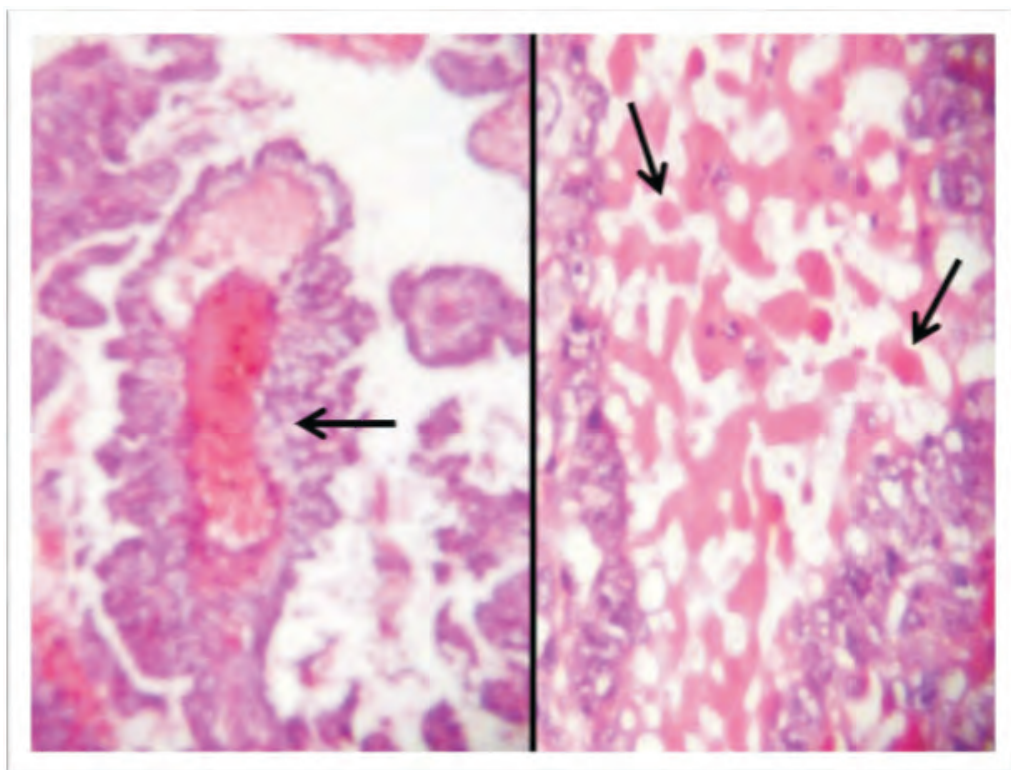




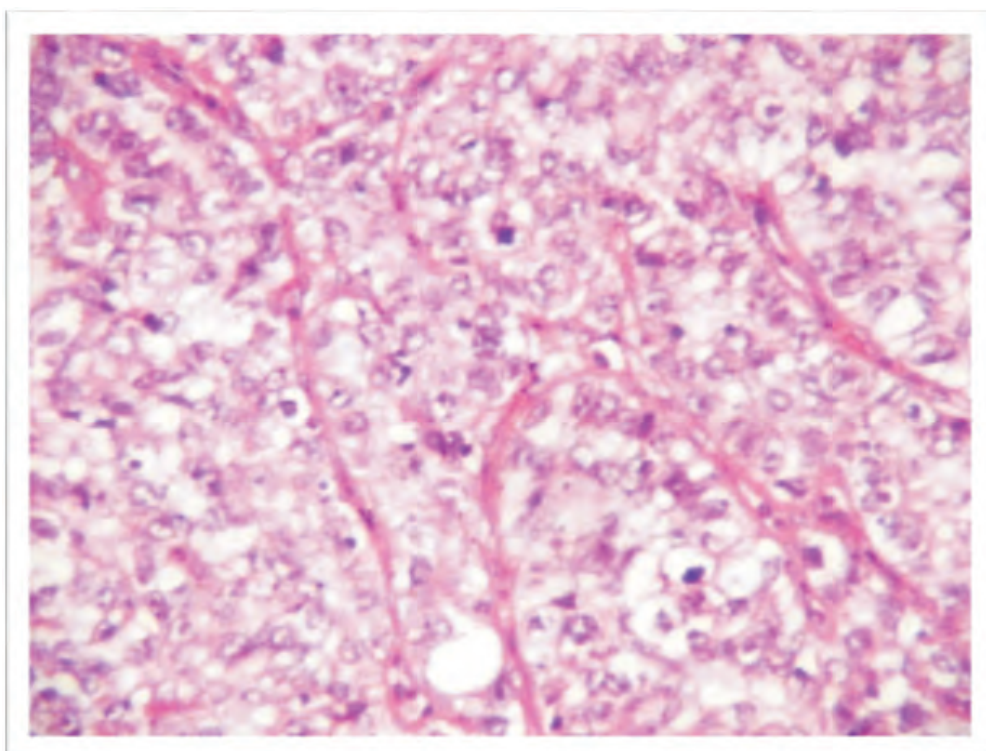
**Figure II-** Photomicrographs showing glial tissue in a mature cystic ovarian teratoma from a 7-year-old girl. The picture on the left shows a central ependymal lined canal (Haematoxylin and eosin, X40), while the picture on the right shows neurons (Haematoxylin and eosin, X100).



**Figure III-** Photomicrograph showing primitive neuroepithelium and mesenchymal tissue in an immature sacrococcygeal teratoma from a 12-day-old girl (Haematoxylin and eosin, X40).

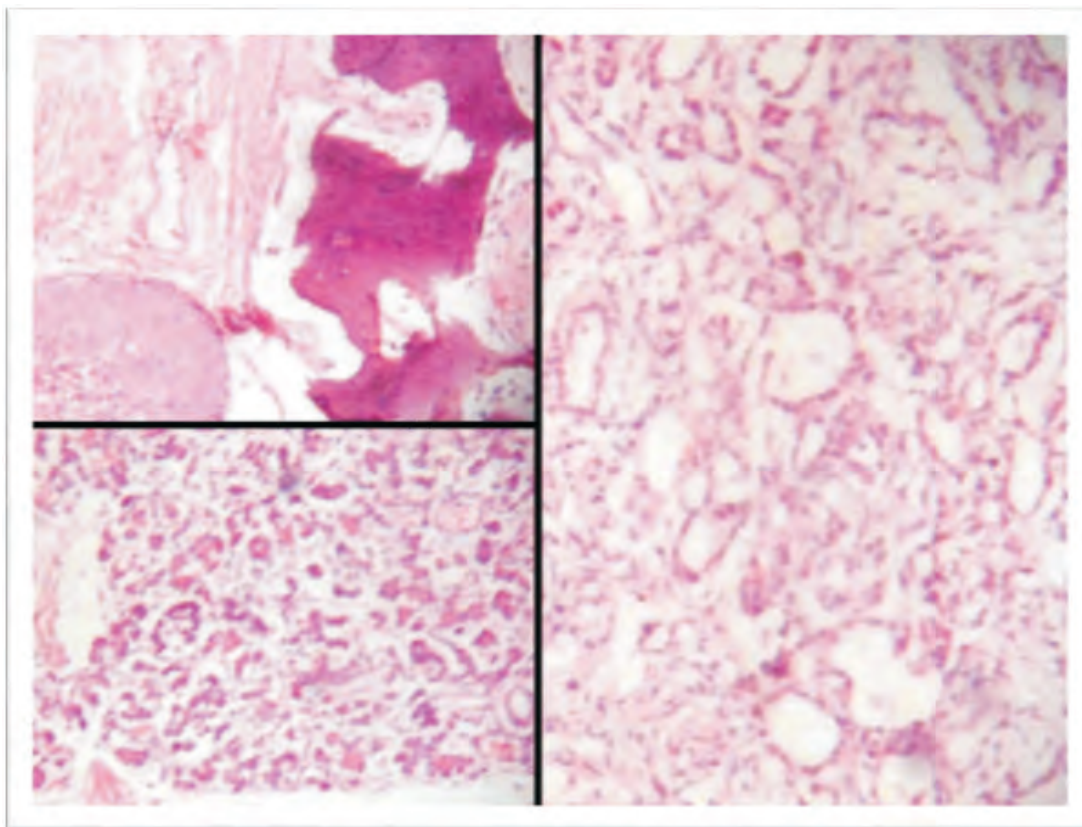


**Figure IV-** Photomicrographs showing ovarian yolk sac tumour from a 13-year-old girl. The picture on the left shows a Schiller-Duval body, indicated by the arrow (Haematoxylin and eosin, X40). The picture on the right (from the same patient) shows multiple hyaline globules, indicated by the arrows (Haematoxylin and eosin, X100).



**Figure V-** Photomicrograph showing solid pattern of yolk sac tumour from the ovary of a 7-year-old girl (Haematoxylin and eosin, X40).





**Figure VI- Photomicrographs showing sacrococcygeal mixed germ cell tumour from a 2½-year-old girl. The picture on the upper left shows bony tissue and squamous epithelium (Haematoxylin and eosin, X40). The picture on the lower left shows pancreatic tissue (Haematoxylin and eosin, X100). The picture on the right shows polyvesicular-vitelline pattern of yolk sac tumour in the same patient (Haematoxylin and eosin, X40).**

## DISCUSSION

In the present study, only 0.05% of all surgical biopsy cases were paediatric germ cell tumours. This is in support of the observation of Cushing et al <sup>7</sup> that germ cell tumours are infrequent in childhood.

Paediatric germ cell tumours were more common overall in females than males in this study, with a female to male ratio of 2.9:1. The female predominance observed in this study is in agreement with the 2.2:1 female to male ratio reported by Marsden et al <sup>8</sup> in the Manchester University Children's Tumour Registry. Teratomas demonstrated female gender predominance, with a female to male ratio of 2.9:1, which is consistent with the finding of female to male ratios ranging from 2:1 to 5:1 reported from previous African series <sup>9-11</sup>.

In the present study, paediatric germ cell tumours displayed a peak age of occurrence in the first year of life. This is in accordance with the report of germ cell tumours by Bernstein et al <sup>2</sup> that there is high age specific incidence rate in the first year of life, followed

by a decline up until the age of eight years.

It was clearly shown that all of the paediatric germ cell tumours among subjects greater than five years of age in the present study were females. This can be explained by the fact that the majority of these neoplasms occurred in the ovaries and most of these cases were teratomas. In agreement with this finding a previous study from Ibadan showed that all of the childhood teratomas in patients aged 4 years and above were females<sup>9</sup>. Similarly seventeen (89.5%) of the 19 children aged greater than 5 years in the South African teratoma study were females, which is also in agreement with our findings<sup>12</sup>.

The most common germ cell tumours encountered in the present study were teratomas, which accounted for 79.5% of the cases. In a series of 137 childhood germ cell tumours, Marsden et al <sup>8</sup> observed that teratomas were the most common germ cell tumours, comprising 63.5% of their cases, which is in agreement with the findings in the present study.

The majority (83.9%) of teratomas in the present study were mature (benign), teratomas while 16.1% were immature (malignant). In the series of Marsden et al<sup>8</sup> from Manchester, England, 88.4% of cases were benign, 8.1% were malignant and 3.5% were of uncertain malignant potential, which closely corresponds to our findings. By contrast, in a study of 45 childhood teratomas from South Africa, Bezuidenhout et al<sup>12</sup> noted that although mature teratomas were most common (60%), immature teratomas accounted for 35% of cases.

In the present study, immature teratomas were restricted to the first year of life and all of them were extragonadal. In agreement with this finding, ten (90.9%) of the eleven extragonadal immature childhood teratomas in one South African series occurred in children less than one year of age<sup>12</sup>.

The ovary, sacrococcyx and neck were the three most common locations of teratomas in this study. This is in agreement with previous studies of childhood teratomas from Ibadan, South Africa and England, which showed a predominance of ovarian teratomas<sup>9,8,12</sup>. By contrast, some other African studies have revealed a predominance of sacrococcygeal over ovarian teratomas in children<sup>11,13</sup>.

All of the gonadal teratomas in the present series were mature and all of them occurred in the ovary. In contrast with our findings, in the series of ovarian childhood tumours by Junaid<sup>14</sup> 86.4% of teratomas in children less than 15 years of age were mature and 13.6% were immature. There was no case of testicular teratoma in the present study. This confirms the rarity of testicular germ cell neoplasms in blacks<sup>15</sup>. In a series of 35 childhood and adolescent tumours from Ibadan, Junaid<sup>16</sup> observed only one teratoma in the 0-5 years of age group and none in older children less than 15 years of age.

Yolk sac tumours were the second most common paediatric germ cell tumours encountered in the study, accounting for 17.9% of cases. This is in agreement with the findings of Marsden et al<sup>8</sup> that yolk sac tumours were the second most frequent childhood germ cell tumours, overall, accounting for 25.5% of cases. In the present study, yolk sac tumours were the most frequent of all the malignant germ cell tumours encountered, which is also in agreement with the observation of Marsden et al<sup>8</sup>.

The gonads were the most frequent location in the present study accounting for 57.1% of cases (three ovarian and one in the testis), followed by the sacrococcyx (3 cases) accounting for 42.9% of cases.

This is in agreement with the observation by Marsden et al<sup>8</sup> that 54.3% of cases occurred in the gonads. However, in our study, the ratio of ovarian to testicular yolk sac tumours was 3:1, whereas in Marsden et al's<sup>8</sup> study the ratio of ovarian to testicular yolk sac tumours was 1:2.3. This difference can be explained by the relative rarity of testicular tumours in the Ibadan population.

## CONCLUSION

This study shows that paediatric germ cell tumours affect all age groups between 0 to 14 years. They are predominantly seen in females and the most common type is teratoma, which is most often seen in the first year of life. Extragonadal germ cell tumours are more common than the gonadal germ cell tumours in this study as compared to studies in Caucasian children, in which gonadal tumours are more than the extragonadal tumours<sup>8</sup>. In view of the paucity of studies on germ cell tumours from Nigeria and other parts of Africa, it is recommended that further studies of this unique group of neoplasms should be carried out in other centres from Nigeria in order to confirm or refute the findings of this study.

## REFERENCES

1. Rosai J, Cushing B, Perlman EJ. Male reproductive system. In Rosai and Ackerman's Surgical Pathology. 9<sup>th</sup> Edition. St. Louis, MO, USA: Elsevier Mosby; 2004. Pp 412-482.
2. Bernstein L, Smith MA, Lui L, Deapen D, Friedman DL. Germ cell, trophoblastic and other gonadal neoplasms. In Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995. Bethesda, MD, USA: National Cancer Institute; 1999. Pp125-137.
3. Marsden HB. The classification of childhood tumours. In Parkin DM, Stiller CA, Draper GJ, Bieber CA, Terracini B, Young JL (Eds.). International incidence of childhood cancer. Lyon: IARC Scientific Publications; 1988. Pp 9-16.
4. Streck CJ, Davidoff AM. Extragonadal germ cell tumors. In Pediatric Surgery and Urology: Long Term. Outcomes, 2<sup>nd</sup> Edition. Cambridge: Cambridge University Press; 2006. Pp 815-825.
5. Parkin DM. Materials and methods. In Parkin DM, Stiller CA, Draper GJ, Bieber CA, Terracini B, Young JL (Eds.). International incidence of childhood cancer. No. 87. Lyon: IARC Scientific Publications; 1988. Pp 17-22.
6. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. World Health Organization Classification of Tumours.



- Pathology and genetics of tumours of the urinary system and male genital organs. Lyon: IARC Press; 2004. Pp 217-278.
7. Cushing B, Perlman EJ, Marina NM, Castleberry RP. Germ cell tumours. In Pizzo P, Poplack D (Eds). Principles and Practice of Paediatric Oncology, 4th edition, Philadelphia: Hippincot Williams & Wilkins; 2001. Pp.1091-1113.
  8. Marsden HB, Birch JM, Swindell R. Germ cell tumours of childhood: a review of 137 cases. J Clin Pathol. 1981; 34:879-883.
  9. Akang EE, Odunfa AO, Aghadiuno PU, Childhood teratomas in Ibadan, Nigeria. Hum Pathol. 1992; 23(4):449-453
  10. Elesha SO, Aina A.O, Odunjo E.O. Sacrococcygeal teratomas in Lagos, Nigeria: relationship of age, sex, clinical type and histopathology to prognosis in 30 cases. East Afr Med J. 1989; 66(10):685-692.
  11. Mambo NC. Teratomas in children: Review of cases in the 0-12 year age group seen at Harare Hospital over ten year period, 1960-1969. Cent Afr J Med. 1974; 231-235
  12. Bezuidenhout J, Schneider JW, Hugo F, Wessels G. Teratomas in infancy and childhood at Tygerberg Hospital, South Africa, 1973-1992. Arch Path Lab Med. 1997; 121:499-502.
  13. Nmadu PT. Childhood teratoma in Zaria, Nigeria. East Afr Med J. 1995; 72(9):551-553.
  14. Groeber WR. Ovarian tumours during infancy and childhood. Am J Obstet Gynecol. 1963: 1027-1035
  15. Exelby PR. Testis cancer in children. Semin Oncol. 1979;6(1):116-120
  16. Junaid TA. Testicular cancer in children and adolescents in Ibadan, Nigeria. Urology. 1981;18:510-513.