Prospective Study of Gross and microscopic changes in 146 cases of Cryptorchid Testes at varied locations with particular reference to the incidence of Germ cell Tumours in Biopsy specimens

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ABSTRACT

Background: Cryptorchidism or undescended testes is a commonly observed congenital anomaly of male children seen in patients presenting in general and pediatric surgical practice of our region. In this study, we prospectively studied 146 cases of undescended testes to statistically observe gross and microscopic changes in different such cases.

Objective: To study the gross and microscopic changes in cryptorchid testes at varied locations.

Methods: A hospital-based prospective study of 146 cases of undescended testes was done from November 2014 to December 2019 and the results of gross and microscopic changes in biopsy specimens were statistically analyzed.

Results: A total of 146 cases studied included 45.19% presenting at the age of 4 to 8 years and 25.34% presenting at the age of 8 to 14 years. The study revealed mild testicular atrophy in 6.16% of the cases and moderate to severe atrophy in 36.97%. Epididymal and vassal anomalies were very rare in suprapubic testes but common in high cryptorchid testes. Biopsy specimens showed the incidence of seminomas in 4.79% of intra-abdominal testes but the incidence was lesser in undescended testes at locations lower down.

Conclusion: A strong association was observed between the location of cryptorchid testes and observed gross and microscopic changes including malignant transformation.

Keywords: cryptorchidism, orchidopexy, testes, orchidectomy, testicular biopsy.

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INTRODUCTION

The term Cryptorchidism, derived from the Greek 'Cryptos', meaning 'hidden' is basically reserved for those testes that are truly obscure, usually within the abdominal cavity and 'incomplete descent' or 'maldescent' of the testis is the term reserved for those cases in which testis is arrested at some point in the normal course of its descent and is palpable on clinical examination; but in the present study 'Cryptorchidism' has been used as a general term to describe all types of undescended testes whether palpable or otherwise. Undescended testes are observed unilaterally or bilaterally in one to ten percent of male infants at birth¹ but

the incidence decreases to 0.8 percent at the age of one year due to spontaneous testicular descent.⁽²⁻⁶⁾ The usual sites of arrest are at the internal inguinal ring, within the inguinal canal, or at the external inguinal ring. Recently, it has been suggested that testicular descent occurs in two stages with different anatomic and hormonal mechanisms for each stage.^(7,8) Cryptorchid testes especially those presenting very

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late as in rural settings of north Kashmir have been observed to be associated with gross anatomic abnormalities and microscopic changes especially diminished germ cell counts⁽¹⁷⁻²⁰⁾ and malignant germ cell tumours (seminomas)⁽²¹⁻³⁰⁾. The present study is focussed on the results of gross and microscopic alterations including malignant transformation in the testicular biopsy specimens of 146 cases of undescended testes belonging to various age groups operated at Govt. Medical College Baramulla during a five year period from Nov. 2014 to Dec. 2019.

MATERIAL AND METHODS

This study included 146 male patients in the age group of 0 to 14 years operated in the department of General Surgery at Govt. Medical College Baramulla, Kashmir from Nov. 2014 to Dec. 2019 for undescended testes at varied locations. The patient study was analyzed with respect to 1. Age of the patient at presentation and type of cryptorchidism (right, left, or bilateral). An assessment of the precise location of the undescended testis, presence of any associated inguinal hernia, and an objective confirmation and degree of testicular atrophy, if any, was done by a pre-operative high-resolution ultrasound done in the department of Radiodiagnosis of our institution. 2. An assessment of gross testicular atrophy, vasal, and epididymal abnormalities was done postoperatively by gross testicular examination and measurement of testicular size by calipers and the results were analyzed with respect to the location of undescended testis and age of the patient at presentation. 3. Special focus was put on the histological changes like germ cell counts and malignant transformation in testicular biopsy specimens of the cases presenting for surgery and correlation between the location of cryptorchid testes and incidence of germ cell tumours was thus observed.

OBSERVATIONS AND RESULTS

In the present study, the maximum number of patients (45.19%) presented at the age of 4 to 8 years, though a fairly large group of patients (25.34%) presented later at the age of 8 to 14 years. In addition, most of the patients (70.53%) were older than 4 years and many (25.34%) were older than 8 years; the mean age at presentation was 6.7 years. The age distribution of patients was done in accordance with the incidence of undescended testes in different age groups. There was not a significant difference observed between the incidence of cryptorchid side to the age; the right side was

involved in nearly one half (50.00%) of the cases studied, the left side in 38.37 % while in 11.64% of the cases, the cryptorchidism was bilateral (table 1).

Table 1: Relationship of the age of the patient and cryptorchidism type and location

Age (years)	Right-sided n(%)	Left-sided n (%)	Bilateral n (%)
0-2	9(6.16)	5(3.42)	2(1.37)
2-4	12(8.22)	10(6.84)	5(3.42)
4-8	34(23.28)	25(17.12)	7(4.79)
8-14	18(12.33)	16(10.96)	3(2.05)
Total	73(50.00)	56(38.37)	17(11.64)

The analysis of our results regarding cryptorchidism type and location in relation to the age of the patient revealed that the frequency of abdominal undescended testes decreases with increasing age ($p < 0.1$) while that of suprascrotal testes increases with increasing age ($p < 0.001$) (Table 2).

Table 2: Cryptorchidism type and location in relation to age

Age (Years)	Abdominal n (%)	Internal ring n (%)	Intra canalicular n (%)	Suprascrotal n (%)
0-2	2(1.37)	6(4.11)	5(3.42)	3(2.05)
2-4	3(2.05)	8(5.48)	4(2.74)	2(1.37)
4-8	9(6.16)	29(19.86)	26(17.81)	7(4.79)
8-14	6(4.11)	18(12.39)	14(9.58)	5(3.42)
Total	20(13.70)	61(41.78)	49(33.56)	16(10.96)

The study of gross testicular atrophy in relation to the location of testis showed that most suprascrotal undescended testes were normal (fig 1) and mild testicular atrophy was observed in 6.16% of the cases while testes at intracanalicular, an internal ring, and abdominal positions (fig 2) showed moderate to severe atrophy (36.97%). The results were statistically significant ($p < 0.0001$) (Table 3).

Fig 1: Normal histological picture (H&E* 40) in a case of suprascrotal testes.

Fig 2: Intra- abdominal (H&E*400) atrophic testes.

Table 3: Gross estimation of testicular atrophy in relation to testes location

Testis Location	Total no of cases n(%)	Mild atrophy n(%)	Moderate Atrophy n(%)	Severe Atrophy n(%)
Intra abdominal	20(13.70)	2(1.37)	6(4.11)	9(6.16)
Internal ring	61(41.78)	27(18.49)	13(8.90)	9(6.16)
Intracanalicular	49(33.56)	23(15.75)	11(7.53)	6(4.11)
Suprascrotal	16(10.96)	9(6.16)	3(2.05)	0(0.00)
Total	146	61(41.78)	33(22.60)	24(16.44)

Most suprascrotal testes were either normal or had a mild extension and looping of epididymis (1.36%) while the rest of the locations higher up (43.13%) showed moderate or profound epididymal anomalies ($p < 0.0001$). Similarly, vasa anomalies were very rare in suprascrotal testes (1.36%) but common in high cryptorchid testes (29.44%) (Table 4 showing different types of anomalies observed).

Table 4: Epididymal and vasa anomalies

Testis location	Total no cases n (%)	Extended loop-epididymis n (%)	Vasa extension n (%)	Testicular appendages n (%)
Intra abdominal	20(13.70)	6(4.10)	9(6.16)	6(4.11)
Internal ring	61(41.78)	29(19.86)	21(14.38)	15(10.27)
Intracanalicular	49(33.56)	28(19.17)	13(8.90)	24(16.44)
Suprascrotal	16(10.96)	2(1.37)	2(1.37)	2(1.37)
Total	146	65(44.52)	45(30.82)	47(32.19)

The histological findings of testicular biopsies in 53 cases that underwent either excision of the atrophic testis or a testicular biopsy revealed diminished germ cell and spermatogonia counts in 16.42% cases and normal counts in 5.48% of cases (table 5).

Table 5: Histological findings of 53 cases of truly undescended testes

Age (years)	Orchiectomy specimens		Germ cell counts		
	Atrophic n (%)	No parenchyma n (%)	Markedly-decreased n (%)	Slightly-decreased n (%)	Normal n (%)
0-2	2(1.37)	2(1.37)	2(1.37)	2(1.37)	2(1.37)
2-4	2(1.37)	4(2.73)	3(2.05)	2(1.37)	2(1.37)
4-8	2(1.37)	5(3.42)	3(2.05)	3(2.05)	2(1.37)
8-14	2(1.37)	2(1.37)	6(4.11)	3(2.05)	2(1.37)
Total	8(5.48)	13 (8.90)	14 (9.59)	10(6.85)	8(5.48)

Histological findings also correlated with testis location. Markedly diminished germ cell counts were found in 12.17% of cases of higher cryptorchidism and 1.37% of suprascrotal testes. In contrast, normal germ cell counts were found in 6.16% of suprascrotal testes but only in 0.68% of cases of abdominal and Intracanalicular testes. The rest of the cases studied (6.85%) revealed moderate germ cell counts at both locations (Table 6).

Table 6: Histological findings of testicular biopsies in relation to testes location

Testis location	Markedly decreased Germ cell Counts n (%)	Slightly decreased Germ cell counts	Normal Germ cell Counts n (%)
High (abdominal/canalicular)	12(12.17)	4(2.74)	1(0.68)
Low (suprascrotal)	2(1.37)	6(4.11)	9(6.16)
Total	14(9.59)	10(6.85)	10(6.85)

The incidence of germ cell tumours on microscopic examination of 53 samples of orchidectomy/testicular biopsy specimens showed an incidence of 4.79% of seminomas in histological specimens of intra-abdominal testis while the samples were taken from high scrotal, inguinal canal and internal ring testis revealed an incidence of 0.00 %, 2.05% and 2.74% respectively (Table 3 and 4) (Table 7).

Table 7. Incidence of Germ cell tumours (seminomas) on histological examination of biopsy specimens in relation to testes location

Testes location	Incidence of Germ cell tumours	
	Seminoma n (%)	Others n (%)
Intra abdominal	7(4.79)	0(0.00)
Internal ring	4(2.74)	0(0.00)
Intracanalicular	3(2.05)	0(0.00)
Suprascrotal	0(0.00)	0(0.00)
Total	14(9.59)	0(0.00)

Fig 3: Seminoma (H&E* 400) in a case of high inguinal testes

Fig 4: Seminoma (H&E* 400) in a case of intra-abdominal testes

DISCUSSION

The first major finding from our study was that most of the patients (70.57%) were older than four years and many (25.38%) were older than eight years. Ignorance, social and ethical prejudices of patients in our social setup play an important role in delayed presentation and referral to a surgeon. The age distribution for the various sites of cryptorchid testes shows that with increasing age, the incidence of intra-abdominal testes decreases while the frequency of suprascrotal testes increases. This is due to the misconception of some parents and physicians that low cryptorchid testes may spontaneously descend later in childhood. Thus, patients with impalpable, intra-abdominal testes present earlier, while those with palpable suprascrotal testes wait longer hoping a spontaneous cure and are referred late before they seek medical assistance.

The gross morphological changes in the present study reveal moderate to severe atrophy of testes in

intracanalicular and intra abdominal testes than those in suprascrotal position. The gross alterations of testicular volume and shape were accompanied by analogous microscopic findings (diminished germ cell counts, hypoplasia or atrophy) thereby revealing that the pathological changes parallel with gross morphological findings. There were markedly diminished germ cell counts in high cryptorchid testes than in those in suprascrotal position. In addition, older children more often showed significantly diminished germ cell counts than younger children and infants. These observations are correlating with previous studies showing that the location of cryptorchid testes and patient age at the time of orchidopexy are the major determinants of subsequent fertility in these individuals.⁹

Most of the undescended testes in suprascrotal position were normal or had a mild extension and looping of epididymis (1.37%) while most of the intracanalicular, internal ring and abdominal testis showed moderate or profound epididymal anomalies (table 4 for different types of anomalies observed) (35.13% ; $P < 0.0001$). Similar observations have been made in other studies as well wherein it has been found that gross alterations of epididymis and vas frequently accompany cryptorchid testes^(22,23).

The incidence of testicular germ cell tumours (seminomas) observed in our study in suprascrotal, intracanalicular and internal ring positions was very low (0.00%, 2.05% and 2.74% respectively; $P < .001$) while in case of intra abdominal testis it showed a significantly higher incidence of 4.79% ($P < .0001$). The higher incidence of testicular germ cell tumors in cryptorchid testes notably seminomas are due to the transformation of primordial germ cells (PGCs) into pluripotent germ cells which develop into precursor cancer cells. At an abnormal location, especially an intra abdominal one, the primordial germ cells also known as gonocytes continue to proliferate or undergo improper differentiation, resulting in a higher incidence of testicular germ cell tumors at these locations.⁽²¹⁻³⁰⁾

CONCLUSION

Considering all these facts, it is thus concluded that cryptorchid testes are associated with gross morphological derangements as well as histological changes especially diminished germ cell counts and malignant transformation at locations higher up and even though the necessity of early

surgical correction is well established, still patients, especially in the northern region of Kashmir valley, tend to present very late with consequent increased risks of infertility and malignant transformation.

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