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Original article

A RETROSPECTIVE OBSERVATIONAL CHART ANALYSIS OF PATIENTS UNDERGOING RADICAL ORCHIDECTOMY AT A REGIONAL LEVEL HOSPITAL.

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ABSTRACT.

Background
The global incidence of testicular cancer is on the rise, although it remains a rare cancer accounting for 0.5% of all malignancies. Among South African men there appears to be a higher-than-expected incidence in Indian men.
Objectives
To determine the demographics of patients undergoing radical orchidectomy at St Aidan's Regional Hospital

Methods.
A retrospective observational chart review of all radical orchiectomy patients seen at St Aidan's hospital over 5 years from January 2015 to December 2019. The 2016 national census data was used to calculate the cancer incidence rates for this study period.

Results.
A total of 40 radical orchidectomies were performed during the 5 years, there were 26 malignant cases and 13 benign cases. The all-population incidence rate was 1.52%. When broken down by racial groups, of the 40 cases, 52.5% were Indian men with an incidence rate for testicular cancer of 5.62%, followed by 35% African men with an incidence rate of 0.3%, 7.5% Caucasian men with an incidence rate of 2.81% and lastly 5% were colored men with an incidence rate of 5.62%.

Conclusions.
Testicular cancer in KwaZulu-Natal is more common in Indian men and the incidence rate among Indian men is much higher than that observed in India or as reported in other parts of the world. This provides a unique opportunity for further characterization of testicular risk factors and genetics involved in cancer development. African men with a testicular mass are likely to have a benign cause rather than testicular cancer.

Recommendation.
We recommend broader studies, epidemiological, and germline mutations, and somatic mutations in testicular cancer affecting Indian males.

Keywords: Chart Analysis, Radical Orchidectomy, Testicular Cancer, Cancer Development
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DEFINING THE CLINICAL PROBLEM.

There is a paucity of local reported data surrounding the incidence and prevalence of testicular cancer in terms of its distribution amongst the general South African population and racial distribution of the disease. Anecdotally there appears to be a local disparity in the racial distribution of the disease as compared to reported international data. A retrospective audit of the patients undergoing radical orchidectomies at St. Aidan's Regional Hospital would aid in better describing the demographics of the disease as well as the outcomes for patients afflicted with the disease.

The objectives were to:

To determine the epidemiology of the disease.
To determine the histopathology of the orchidectomy specimens.
To determine the length of waiting time from initial presentation to operation.
To determine the results of radiological staging investigations.
To determine the number of patients requiring Oncology referral.

METHODS.

The required authorization was received for the review of medical records to extract the required data using the data collection tool.
The theatre logbooks were used to identify all cases of Radical Orchidectomy performed over the 5-year study period from January 2015 to December 2019.
A search on the National Health Laboratory Services (NHLS) results database was also carried out to identify the specimens submitted by St Aidan's hospital and analyzed during the study period.
The relevant patient files for the identified cases were requested from patient records and data was captured per the data collection tool.
A further file review at Inkosi Albert Luthuli Hospital was carried out for patients referred there.

Setting.

St Aidan's Urology Hospital is a regional hospital located in Durban, which is the capital city of KwaZulu Natal province. It also serves as a teaching hospital for the University of KwaZulu Natal Nelson R. Mandela School of Medicine, and a tertiary referral hospital for complicated cases within the southern part of KwaZulu Natal province.

Study Design

The study design will be retrospective observational and descriptive.

Participant Selection and Sampling Strategy.

Patients who are referred to St Aidan's Regional Hospital from its drainage area within KwaZulu Natal who have undergone a Radical Orchidectomy or were diagnosed with Testicular cancer during the study period were eligible for inclusion into the study. Thus, a purposive sampling method was employed.
The patient population of St Aidan's largely represents the population makeup of KwaZulu Natal, mostly black patients, followed by Indian, white, and least of all colored patients.
All orchidectomies done were collected using more than one source record to ensure a complete record, thus minimizing bias.

Ethical consideration.

Ethical clearance for the study was obtained from the Biomedical Research Ethics Committee, approval number, BREC/00002293/2021. The lead investigator was required to undergo an ethics course for which certification was issued before applying for ethics clearance.

Inclusion Criteria.

All patients who underwent radical orchidectomy at St Aidan's Hospital from 1 January 2015 to 31 December 2019
All patients who were diagnosed with Testicular cancer on histology specimens at St Aidan's Hospital during the study period.

Exclusion criteria.

Patients whose specimen samples were lost or were unsuitable for pathological analysis.
Patients already known with Testicular cancer before 1 Jan 2015

Measurements.

A data collection tool was used to gather demographic data and collate using an Excel data sheet.

Data Collection and Statistical Analysis. Statistical methods.

We summarized categorical variables using count (percent) and measured variables using mean (standard deviation) or median (interquartile range) depending on the distribution. Stata 17 (College Station, Texas 77845 USA) was used for the descriptive statistics. We used the male population size of eThekwini district (the hospital catchment area), to compute the cancer incidence rates. We report the incidence rates with the corresponding Fisher's exact 95% confidence intervals. WinPepi Version 11.65 was used to compute the cancer incidence rates.

RESULTS:

A total of 55 cases were initially identified from the theatre register captured as Radical orchiectomy. However, of these cases, 15 were noted to have been erroneously recorded as such the majority being patients who had undergone unsuccessful inguinal orchidolysis for undescended testis. Some were orchidectomies for testicular torsion.
40 cases were considered for the study and the respective data parameters were recorded on the data capture tool. Of immediate significance was that despite St Aidan's draining the larger part of the Southern region of KwaZulu-Natal all cases of confirmed Testicular cancer had residential addresses within the eThekwini district.
The following table shows the racial distribution of confirmed radical orchidectomy cases.

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Tabulation of race

Race	Frequency	Percentage	Cumulative
Indian	21	52.2	52.5
African	14	35.0	87.5
Caucasian	3	7.5	95.5
Coloured	2	5.0	100.0
Total	40	100.0	

Testicular cancer is a rare cancer with a worldwide incidence of less than 1 per 100,000. Testicular cancer rates. The recorded incidence rates for the Indian subcontinent and sub-Saharan Africa are similar, less than 1 per 100,000.

Of these 40 cases, 1 histology result could not be retrieved hence 39 cases were eventually analyzed.

Tabulation of Histology

Histology	Frequency	Percentage	Cumulative
Malignant	26	66.67	66.67
Benign	13	33.33	100.0
Total	39	100.0	

From the 39 histology results, 13 cases were noted to be benign histology and 26 cases were confirmed malignant testicular cancers of varying histology.

Breakdown of cancer cases per racial grouping.

KZN population was 11,065 240 as per 2016 census figures.

eThekwini district 3 702 231, of which 47.9% were males (n=1 777 071)

An interesting finding was that all the malignant cases were from eThekwini district although St Aidan's Hospital drains much of southern KZN.
Total cancer cases = 27

eThekwini male population Racial breakdown used: using n =1 777 071

Racial distribution

Blacks	1 315 033	Cases = 4
Indian	319 873	Cases = 18
White	106 624	Cases = 3
Coloured	35 5541	Casers = 2

Thus, the following incidence / prevalence rates were calculated.

Overall rate = 1.51935 per 100000, confidence intervals (per 100000): Fisher's 95% C.I. = 1.00103 to 2.21066

Racial groups	**Population size**	**Number of cases**	**Calculated rate**	**95% CI**
Indian	319 873	18	5.62	3.33 to 8.890
African	1 315 033	4	0.30	0.08 to 0.077
White	106 624	3	2.81	0.58 to 8.22
Colored	35 514	2	5.62	0.68 to 20.3155
All populations	1 777 071	27	1.52	1.00 to 2.21
Excluding African			4.97	3.15 to 7.46

Of note is that of the 14 radical orchidectomies done in African black males, only 4 cases [1 embryonal, 1 Squamous cell carcinoma, 1 Sertoli cell, and 1 mixed germ cell tumor] were confirmed as Testicular cancer. All the other cases were testicular masses secondary to infectious causes, nonspecific orchitis, TB, and schistosomiasis. Thus, at St Aidan's Regional Hospital, there was less than 1 case a year of a positive testicular cancer in Black males from 2015 to 2019.

The following table illustrates the disease stage at presentation.

Tabulation of Disease Stage

Disease stage	**Frequency**	**Percentage**	**Cumulative**
x	5	15.15	15.15
1	19	57.58	72.73
2	4	12.12	84.85
2B	1	3.03	87.88
3	4	12.12	100.00
Total	33	100.00	

x- Unclassified due to lack of supporting information.

The frequencies of risk factors such as smoking, Hypertension, diabetes, or retroviral infection were so infrequent that they did not produce any significant analysis outcomes.

Tabulation of age category.

Age	**Frequency**	**Percentage**	**Cumulative**
< 40 years	20	74.07	74.07
≥ 40 years	7	25.93	100.00
Total	27	100.00	

Waiting times for treatment.

The average waiting time between diagnosis at the base to the day of radical orchidectomy was 14 days, with an interquartile range of 10.5 days to 33.5 days.

DISCUSSION.

St Aidan Regional Hospital drains much of the southern half of KwaZulu-Natal province. From this drainage area, Radical orchidectomies during the period of the study from 2015 to 2019 would have all been performed at St Aidan's Hospital as one of the only 2 main Urology Units during that period in KZN, the other being Grey's Hospital in Pietermaritzburg which drains the Northern half of the province. Limited urology services, mainly clinics, were available at other hospitals within the Durban metropolitan area however all major surgeries were performed at St Aidan's Hospital. Our findings thus represent the majority of the KZN population who generally use State hospitals and this is across all racial groups.

Generally, Testicular cancer incidence rates are highest among young men between the ages of 15 to 40 years and represent 1% of all adult neoplasms. (1) Presentation is usually a result of a painless hard lump discovered through self-examination in older men or found incidentally, such as after imaging for trauma in children. The global trend of a general increase in testicular cancer incidence is likely to be observed as suggested by various studies including Park et all 2018 and the International Agency for Research on Cancer which projects an increase of 72.7% in new testicular cancer cases by 2040. (2) Our findings reflect this observation as described in the literature.

Testicular cancer has a cure rate of over 90% due to the efficacy of platinum-based chemotherapy. The risk-adjusted treatment and follow-up strategies have minimized the side effects of radiation therapy, chemotherapy, and surgical resection of lymph nodes while maintaining high rates of cure. During our study, the biggest challenge was following up on the patients' oncology appointments and treatment, as we only managed to trace 9 out of 40 patients. Patients were not all being seen at Inkosi Albert Luthuli Hospital for oncology follow-up.

Testicular cancer is not common in the Indian subcontinent with a crude rate of 0.6 per 100 000 according to the 2020 National Cancer Registry Programme, India. A total number of 4352 cases of testicular cancer cases were recorded in India in 2020. (3) In South Africa, according to the 2019 National Cancer Registry 2019, the testicular cancer lifetime risk is 1 in 1578 for all men. The lifetime risk for Black males was 1 in 4 505 compared to Asian males which was 1 in 674, significantly higher. (4)

As with our results, this is an unexpected and unexplained finding, given that India's incidence rates and Africa's incidence rates are very similar.

KwaZulu-Natal experienced the arrival of an estimated 154 184 Indian migrants between 1860 and 1911 to work as labourers in the sugarcane plantations. (5)"ship list,". These migrants came mainly from Madras and Bengal Presidencies and Provinces of Agra and Oudh. (6) Thus, currently most of the local Indian population is made up of the 3rd and 4th generation descendants of these migrant workers. The rates of testicular cancer shown in eThekwini district amongst Indian males are much higher than recorded rates in India and other parts of the world among Indian males. These differences are likely due to specific local factors, genetics, and other associated risk factors such as family history, cryptorchidism, occurrence of gem cell neoplasia in situ, and environmental chemical exposure.

An important factor to consider in this case would be exposure to the many different inorganic and organic chemicals used as pesticides and fungicides within the sugarcane industry. Some of these compounds included arsenic products, sulphuric acid, by-products of coal gas production, nitrophenols, DDT, 2,4-D, and many others. These compounds whose toxicity profile ranged from acute toxicity to humans, mutagenicity, carcinogenic, teratogenicity, neurotoxicity, and so forth, were used in great abundance as it led to greater food production and a reduced need for a bigger labour force (7).
In a cohort study conducted in Norway, to identify parental risk factors for testicular cancer among farmer's sons vs that of the general rural population, they found the study population had a much higher incidence of testicular cancer than did the total rural population, particularly at ages of 15 to 19 years. Also identified were specific fertilizer regimens being more associated with nonseminoma cancers. (7)
The oestrogen excess theory proposes that testicular germ cell tumor is initiated in utero during embryogenesis. The developing gonad is affected if there is an excess amount of oestrogens during early pregnancy causing it to harbor premalignant cells that may eventually turn into testicular intraepithelial neoplasia (TIN). The endocrine stimuli of puberty, plus other factors, are then believed to trigger the final replication and development of cancer cells. (8)
Male children exposed to diethylstilbesterol had an increased risk of testicular abnormalities including undescended testicles or epididymal cysts.
Women may be exposed to a variety of exogenous oestrogens resulting in a state of oestrogen dominance that can manifest with heavy menstrual bleeding, insomnia, anxiety, migraines, fibrocystic breast disease, etc. Xenoestrogens are found in foods such as soy which has a high concentration of isoflavones, sesame seeds, flax seeds, cruciferous vegetables such as cauliflower or cabbage, garlic, peanuts, etc. Beauty products such as nail polish and removers, lip gloss, shampoos, sunscreen, and skin lotion with parabens have been implicated as containing xenoestrogens and importantly birth control pills.

Interestingly the rates of undescended testis correction surgery among Indian males at St Aidan's Hospital is very minimal compared to black males which is much higher. As of March 30th, 2023, the number of Indian males on the waiting list was 3 compared to 92 black males. Which just further highlights the uniqueness of this population.

CONCLUSIONS.

Currently, a solid testicular mass is managed with experience with the assumption of testicular cancer irrespective of the patient's race. This study offers some reason to consider an alternative local approach. Given the very high cure rates of stage 1 and stage 2 disease, it might be reasonable to delay radical orchiectomy amongst black males to obtain more diagnostic confirmation. The standard ultrasound exam may not have the desirable specificity for testicular cancer diagnosis in African-black males.

Furthermore, the Indian population in the eThekwini district has an uncharacteristically higher rate of testicular cancers and may provide a unique opportunity to study causative factors associated with testicular cancer pathophysiology beyond the unanimously accepted risk factor of cryptorchidism.

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CONFLICT OF INTEREST.

There is no conflict of interest to declare.

ABBREVIATIONS

NHLS, national health laboratory services

KZN, KwaZulu Natal province

BREC, biological research ethics committee

C.I., confidence interval

DDT, dichloro-diphenyl-trichloroethane

2,4-D, 2,4-dichlorophenoxyacetic acid

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