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Prevalence of *Schistosoma haematobium* in Bladder Biopsies among Patients Suspected of Bladder Cancer* **Ilegbedion, I.G.¹, Onyije, F.M.¹ and Perede, A.²**

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Author for Correspondence*: Igilegbedion@gmail.com**Abstract**

Schistosomes are parasitic blood flukes, which have a definitive mammalian host and fresh water snails as an intermediate invertebrate host. There are four human *schistosomes* which include *Schistosoma haematobium*, *Schistosoma Mansoni*, *Schistosoma Japonicum*, *Schistosoma Mekongi*. The aim of the study was to determine the prevalence of *Schistosoma haematobium* infections in bladder biopsies. One hundred and ten (110), formalin- fixed, paraffin –embedded bladder tissue samples were obtained from previously archived samples in the histopathology laboratory of Igbenidion University Teaching Hospital, Edo State. The tissue blocks were sectioned and stained using haematoxylin and eosin staining technique. The frequency of patients with bladder lesion suspected to have *Schistosoma haematobium*, showed that age group 30-35 recorded the highest number 35 representing 35.71% of occurrence. The least prevalence occurred in the 20-29 years age group with only 4.08% of the cases. The mean age for the patients was recorded as 47.78 ±--- years. Females recorded the higher number of cases (62%) when compared to their male counterparts (38%). There was mildly infiltrated malignant cell I slide A. **Slides B-F** are characterized by malignant epithelial cells admixed chronic inflammatory cells while slides **D and F** have haemorrhagic perforations. There was no ova of *Schistosoma haematobium* seen using the compound light microscope. The pathologic conditions noticed in this study calls for concern. Therefore, campaign and advocacy on the detrimental effect of *S. haematobium* on the

urinary bladder is recommended.

Keywords: *Bladder; Biopsies; Cancer; Schistosoma haematobium*

Introduction

Schistosoma haematobium is one of the major causes of bladder cancer in our region while bladder cancer is among the major cancers in males and second only to breast cancer in females. Despite this, there is limited information about how often *Schistosoma haematobium* causes bladder cancer, their relationship and which type is more related to it (Shokeir, 2004).

Schistosomes are parasitic blood flukes, which have a definitive mammalian host and fresh water snails as an intermediate invertebrate host. There are four human *schistosomes* which include: *Schistosoma haematobium*, *Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi*. The *S. haematobium* like other *schistosomes* is dioecious and the adult female lives in-copulo in the gynecophoral canal of the male and lives in the venules of the human urinary bladder where they lay eggs. Eggs laid in the urinary bladder produce irritation and tissue fibrosis that may contribute to the development of human carcinogenicity causing bladder cancer (Fried *et al.*, 2011).

Schistosomiasis was first linked to urinary bladder cancer in Egypt (Ferguson, 1911). The study conducted shows that 60% of the Egyptian population was at risk of infection with

Schistosoma haematobium, with rural school children at particular risk because of their proximity to contaminated water. The study also revealed that the overall prevalence of *Schistosoma haematobium* infection in Egypt was 37–48% that decreased due to the anti-bilharzial campaign to 3%. Another study by the Ministry of Health and Population, 2004 revealed that the incidence of urinary bladder cancer in the Middle East and Africa is greater in areas with high rather than low *Schistosoma haematobium* prevalence (MHPD, 2004).

Much evidence supports the association between Schistosomiasis and bladder cancer. This includes the geographical correlation between the two conditions, the distinctive patterns of gender and age at diagnosis, the clinicopathological identity of Schistosoma-associated bladder cancer, and extensive evidence in experimentally infected animals (Burnham, 1989). Burnham also reported that multiple factors have been suggested as causative agents in Schistosoma-associated bladder carcinogenesis. Of these, N-nitroso compounds appear to be of particular importance since they were found at high levels in the urine of patients with Schistosomiasis-associated bladder cancer.

The consensus of available information strongly implicates an association between *S. haematobium* infection and the induction of bladder cancer. This neoplasm accounts for 30.8% of the total cancer incidence in Egypt and is ranked first among all types of cancer recorded among Egyptian males and second only to breast cancer in females which is attributable to endemicity of this parasite in the region (Kahan *et al.*, 1997). It was estimated in a study that of 11,626 cancer cases of all types recorded at the Cairo Cancer Institute from 1970 to 1974, 27.6% were bladder cancer cases associated with schistosomiasis, and that of 2,500 new cancer patients at the Cairo Cancer Institute every year, 27% had cancer of the bladder associated with schistosomiasis as reported by (El-Sebai, 1977). In another study, 28.8% of cancer cases were reported to be bladder cancer associated with schistosomiasis among 6,981 cancer patients recorded in Cairo hospitals during the period

from 1978 to 1979 as reported by (Aboul-Nasr *et al.*, 1986). Again, another study indicates that from 1970 to 1981, the incidence of bladder cancer in men and women ranked first among 25,148 cancer cases accessed by the registry of the National Cancer Institute, Cairo, Egypt. All of these observations support an association between schistosomiasis and bladder cancer in that area.

In sub-Saharan Africa alone, it is estimated that 70 million individuals experience haematuria, 32 million with difficulty in urinating (dysuria), 18 million with bladder wall pathology, and 10 million with major hydronephrosis from infection caused by *Schistosoma haematobium*. Mortality rate due to non-functioning kidney (from *S. haematobium*) and haematemesis has been put at 150,000 per year as cited by (Richard *et al.*, 2008).

It has been reported recently that Schistosoma-induced chronic inflammation and irritation in the urinary bladder are associated with increased cancer initiation at the site of inflammation. Inflammatory cells such as macrophages and neutrophils are important sources of endogenous oxygen radicals, which are also implicated in the formation of carcinogenic nitrosamines. Moreover, inflammatory cells induce genotoxic effects, such as mutations, sister chromatid exchanges, and DNA strand breaks. These toxic effects may result from the formation and release of hydroxyl radicals from the inflammatory cells. Inflammatory cells also participate in the activation of procarcinogens, such as aromatic amines and polycyclic aromatic hydrocarbons, to their ultimate carcinogenic metabolites (i.e., the final reactive form of the carcinogen). Since the aromatic amines are an important group of bladder carcinogens, an increased number of inflammatory cells in the urinary bladder of Schistosomal patients may enhance the carcinogenic potential of these agents by increasing their rate of activation (Malik *et al.*, 1975).

Materials and Methods

Sampling

A retrospective cross-sectional study was carried out using simple random sampling

technique to obtain the sample. One hundred and ten (110), formalin- fixed, paraffin –embedded bladder tissue samples were obtained from previously archived samples in the histopathology laboratory of Igbenidion University Teaching Hospital Edo State. The tissue blocks were sectioned and stained using haematoxylin and eosin staining technique.

Data analysis

All data were analyzed using descriptive analysis using graph pad prism® software version 5.01. A p-value of < 0.05 were considered statistically significant.

Results

Table 1 show the frequency of patients with bladder lesion suspected to have *Schistosoma haematobium*, where age group 30-35 recorded the highest number 35 representing 35.71% of occurrence. This was followed by age group 40-49 which recorded 21 representing 21.42%. The third in line was the age group 70 and above

(16.28%) and was closely followed by age group 50-59 (13.26%) and age group 60-69 (11.22%). The least occurred in age group 20-29 with only 4.08% of the cases. The mean age for the patients was recorded as 47.78 ± ----- years.

Figure 2 shows the frequency of patients with bladder lesion suspected to have *Schistosoma haematobium* by gender, where females recorded the highest number of cases (62) when compared to their male counterparts (38).

Figure 3 shows the photomicrograph of urinary bladder, **slide A** shows Mucosa of the urinary bladder with transitional epithelial cell and under lining connective tissue mildly infiltrated malignant cell. **Slide B-F** are characterized by malignant epithelial cells admixed chronic inflammatory cells with slides **D and F** have haemorrhagic and perforations. There was no ova of *Schistosoma haematobium* seen using the compound light microscope.

Table 1: Frequency of Patients with Bladder Lesion suspected to have *Schistosoma haematobium* and by Age

| | Number of Patients (%) | Mean age/ Group | Lower 95% CI | Upper 95% CI | Mean age |
|---------------|------------------------|-----------------|--------------|--------------|----------|
| 20-29 | 4 (4.08) | 28 | 24 | 29 | 47.78 |
| 30-39 | 35(35.71) | 36 | 35 | 36 | |
| 40-49 | 21(21.42) | 44 | 42 | 45 | |
| 50-59 | 13(13.26) | 53 | 53 | 56 | |
| 60-69 | 11(11.22) | 64 | 62 | 65 | |
| 70> | 14(14.28) | 78 | 75 | 81 | |

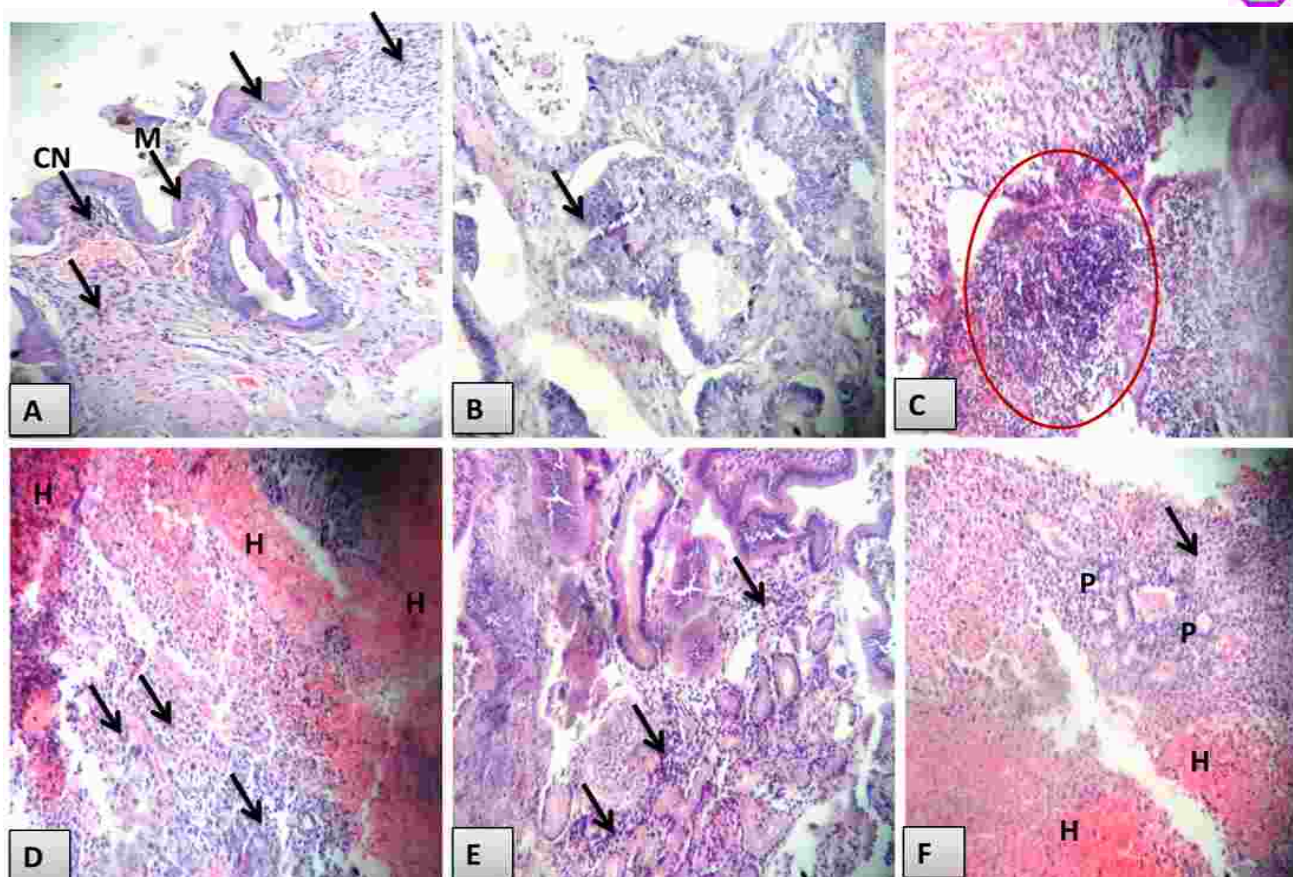


Figure 3: Photomicrograph of urinary bladder, slide A shows Mucosa of the urinary bladder with transitional epithelial cell and under lining connective tissue mildly infiltrated malignant cell. Slide B-F are characterized by malignant epithelial cells admixed chronic inflammatory cells with slides D and F have haemorrhagic and perforations.

Adult schistosomes do not usually cause an inflammatory reaction in the venous system. In fact, their presence is associated with increased protection of the host against reinfection by cercariae. In general, dead eggs and dead flukes cause a more severe inflammatory reaction than living ones (Gryseels *et al.*, 2012). Deposition of *Schistosoma* eggs in the bladder causes eosinophilic inflammation, necrosis and ulceration, followed by fibrosis with chronic inflammatory infiltrates. Pathological changes in the urinary tract due to schistosomiasis are far more common in chronic infections than in acute ones, these chronic lesions induce granuloma formation (Shebel *et al.*, 2012).

The result of this present study reveals that **slide A** shows Mucosa of the urinary bladder with transitional epithelial cell and underlining connective tissue mildly infiltrated malignant cell. While **slides B-F** are characterized by malignant epithelial cells admixed chronic

inflammatory cells. However, slides **D and F** show haemorrhagic and perforations. There was no ova of *Schistosoma haematobium* seen. This study agrees with the study of Ahmed *et al.* (2017) which reported chronic schistosomiasis haematobium due to presence of chronic irritation, squamous metaplasia of the bladder.

This study recorded the frequency of patients suspected to have bladder cancer, where age group 30-35 recorded the highest number (35.71%). This did not agree with the work of Dawaki *et al.* (2016) who recorded 34.5% of cases in age group 11-20. Our study recorded more males (38%) than female (62%) but this is at variance with the study of Dawaki *et al.* (2016) who reported higher males (61.7%) than females (38.3%).

Conclusion

Schistosoma haematobium is still one of the major risks of developing squamous cell

metaplasia and urinary bladder cancer in the world today. The mildly infiltrated malignant cell, chronic inflammatory cells, haemorrhagic and perforations noticed in our study calls for concern. Therefore, campaign and advocacy of the detrimental effect of *S. haematobium* on the urinary bladder is recommended.

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