Published in final edited form as:

J Nephrol Res. 2015 June ; 1(1): 22–24. doi:10.17554/j.issn.2410-0579.2015.01.4.

Bladder cancer and urinary Schistosomiasis in Angola

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Abstract

Schistosomiasis haematobia is among the most prevalent parasitosis in Angola. The pathology is characterized by serious and irreversible lesions in the urogenital tract induced by chronic infection with the parasite that can eventually lead to squamous cell carcinoma of the bladder. Considering the frequency and severe morbidity observed, even in younger ages, the purpose of this study was to assess the prevalence and morbidity of S. haematobium infection in Angola. A baseline survey was conducted between November 2007 and February 2008. A randomly sample of 300 inhabitants aged 15 to 75 years old participated in this study. Prevalence of S. haematobium infection was 71.7 % (215/300). Infection was higher in females (56.3 %) but no significant difference was found in prevalence and intensity between gender and age groups. The predominant selfreported symptoms were dysuria (91.2 %), hypogastralgia (88.7 %) and haematuria (87.1%) and these symptoms were strongly associated with S. haematobium infection ($p<0.05$). Ultrasound and cystoscopy examinations performed in a sub-sample of 29 individuals revealed pathological conditions at the urinary tract in all examined. Considering the high prevalence of S. haematobium infections in Angola and schistosomiasis-associated bladder cancer, our results indicate that this population should be targeted for follow up and implementation of measures for treatment and control of schistosomiasis.

Schistosomiasis is an endemic disease in 76 countries of America, Africa and Asia. According to World Health Organization (WHO) [1], this disease affects 200 to 300 million people and 650 millions are estimated to be at risk of infection. In some countries transmission of this disease was interrupted namely Portugal, Cyprus, Tunisia, Israel and Japan [2], but the risk of re-introduction persists as recently observed in Corsica, France [3].

In the case of S. haematobium 120 millions show urinary symptoms, of which 70 millions have haematuria, 18 millions morphological alterations of the vesical wall [4] and 10-40 millions have obstructive uropathy [5]. Lesions in urinary tract caused by S. haematobium in sub-Saharan Africa are characterized by signs and symptoms like haematuria, dysuria and hipogastralgy, and in advanced stages can evolve to cancer [6,7]. Ultrasound analysis

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permits the detection of alterations of urinary tract, kidneys (hydronephrosis), as well as lesions and presence of “sandy patches” in the vesical wall [1,7,8].

Angola is situated in the western part of Western Africa. It occupies a territory of 1 246 700 Km^2. Its political frontiers are north Republic of Congo, south Namibia, east Republic of Zambia and Democratic Republic of Congo (ex-Zaire) and west the Atlantic Ocean. The territory is divided in 18 provinces: Bengo, Benguela, Bié, Cabinda, Kunene, Huambo, Huíla, Kwanza Norte, Kwanza South, Kwando Kubango, Luanda, Lunda North, Lunda South, Malange, Moxico, Namibe, Uíge and Zaire. In 2007 the population was estimated in 12 263 600 inhabitants. Angola has 5 major rivers: Kwanza, Kunene, Kubango, Cuvo and Bengo. Like other water born diseases, deficient sewerage and water treatment, as well as population education, are the main causes of schistosomiasis which is characterized as a neglected disease.

Given the increase in the migratory flux of the rural population to urban areas, and the degradation of socio-economic conditions in the last years, the consequences of this infection are underestimated.

Our study addressed *S. haematobium* infection in a population of 300 individuals aged 15-75 years in Angola. This is the first report involving such a wide region in this country where we have obtained an appalling prevalence of 71.7% (215/300). This region should be considered hiperendemic in as much as its prevalence of schistosomiasis is above the 50 % threshold determined by WHO [9].

The infection pattern in the study population is normal in males showing a decrease in prevalence and intensity of infection with age. This is explained by the reduction of exposure to contaminated water [10]. On the contrary females, besides being more infected, presented a pattern of infection highest in the intermediate age group (25-34). This reflects an association between reproductive age and higher exposure to contaminated water due to domestic activities.

This study proved that in the rural environment, agriculture is the main source of subsistence and also the main activity responsible for exposure to *S. haematobium* infection in both gender, followed by domestic activity affecting only females.

Haematuria, dysuria and hypogastralgia are signs and symptoms of the acute phase of schistosomiasis and easily percepted by infected individuals. Therefore they are of great value to alert health authorities in endemic areas of *S. haematobium* [11]. In our report dysuria (91.2%), hypogastralgia (88.7%) and haematuria (74%) were the most frequent complaints by the participants and they were significantly associated with infection.

Twenty nine (9.7%) individuals with ages ranging between 25 and 34 years were selected for ultrasonographic analysis because of the severity of their complaints. All of them exhibited thickening of the vesical wall. This is due to the aggressiveness of eggs deposited in the venules of the bladder, leading to decresed volume of the bladder and later to vesico-ureteral reflux and hydronephrosis [11,12]. Here hydronephrosis was identified in 7 (24.1%) cases.

Cystoscopy confirmed the lesions from ultrasonography as well as allowed to evaluate the extension of lesions. This exam indentified granulomas in 13 cases (44. 8%), calcifications of the bladder wall in 3 cases (10.3%) and 1 vesical tumor (3.4%). This tumor was classified as squamous cell carcinoma (SCC). The low frequency of tumors found in our series is in agreement with other authors who reported that the incidence of SCC is 3-4/100 000 cases [7].

Histopathological exam of biopsies confirmed the lesions in which were predominantly granulomas with calcified eggs (72.4%). Presence of these lesions in younger ages (15-24 years) were 17.2%. This is in agreement with other reports [12].

The alterations detected by ultrasonography and cystoscopy allowed the detection and grading of the lesions in the urogenital tract of 29 patients. Given the significantly elevated prevalence of vesical schistosomiasis in Angola, these exams should be mandatory in all cases with severe symptoms.

Future studies should be developed for non-invasive, indirect tests to detect precursor lesions of bladder cancer. Our group has been developing such methodology with the use of biomarkers specific of *S. haematobium* [13,14]. We have previously described estrogen metabolites to be associated with schistosomiasis infected persons [15,16,17,18]. These metabolites can be expected to provide deeper insights into the carcinogenesis of urinary schistosomiasis-induced bladder cancer, and as biomarkers for diagnosis and/or prognosis of this neglected tropical disease-associated cancer.

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