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The changing patterns of bladder cancer in Egypt over the past 26 years

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Abstract

Objective—To evaluate temporal changes in histopathological types of bladder cancer and to assess associated changes in demographic, epidemiologic, and lifestyle risk factors.

Methods—We abstracted data from all available medical records from the National Cancer Institute of Cairo University (NCI-Cairo). Six calendar years representing 5-year periods between 1980 and 2005 were evaluated. Information on demographics, schistosomal infection, clinical symptoms of bladder cancer, and tumor pathology was abstracted.

Results—During this 26-year period, important changes in the frequency of histopathological types of bladder cancer occurred. We found a statistically significant association between time period of diagnosis and histopathological type. Patients diagnosed in 2005 had a sixfold higher odds associated with transitional cell carcinoma compared to those patients diagnosed in 1980 (odds ratio (OR) 6.00 (95% CI 4.00–8.97)).

Conclusions—These data strongly suggest that the histopathological profile of bladder cancer in Egypt has changed significantly over the past 26 years. Historically, squamous cell carcinoma was the predominant form of bladder cancer in Egypt; however transitional cell carcinoma has become the most frequent type. These results corroborate findings from a few small-scale hospital-based studies which conclude that the etiology of bladder cancer in Egypt has changed significantly over the past 26 years.

Keywords

Bladder cancer; Schistosomiasis; Histopathology; Epidemiologic trends; Egypt

Introduction

Bladder cancer incidence varies widely throughout the world. Belgium and Italy, for example, have the highest recorded incidence rates in Europe (respectively, 42.5/100,000 and 41/100,000 population) [1], much more than in the United States with an incidence of 24.1/100,000 and an estimated 61,160 newly diagnosed cases in 2007 [2]. Indeed, cancer registries in Slovenia, Croatia, and Switzerland reported even lower European bladder cancer incidence (10.1/100,000, 11.7/100,000, and 12.0/100,000, respectively) [3], with the lowest rates found in Asian and South American countries [1]. Cigarette smoking and certain occupational and industrial exposures are established as the most important risk factors for bladder cancer in the US [4] and Europe [5], but risk factors in other parts of the world may be different. Transitional cell carcinoma (TCC) is the most common histopathological type, occurring in approximately 90% of all bladder cancers in Western countries, with a peak incidence in the seventh decade of life [4, 6, 7], but squamous cell carcinoma (SCC) is the dominant type elsewhere. Fewer studies have evaluated bladder cancer in the Middle East.

In Egypt, bladder cancer has been the most common cancer during the past 50 years [8–13]. In 2002, Egypt's world-standardized bladder cancer incidence was 37/ 100,000, representing approximately 30,000 new cases each year [14]. Interestingly, the most common histopathological type of bladder cancer in Egypt has been SCC, constituting from 59% to 81% of reported bladder cancers between 1960 and 1980 [10, 13, 15]. Contrary to the leading etiology of smoking and occupational exposures in Western countries, chronic bladder infection with *Schistosoma haematobium*, the trematode causing urinary schistosomiasis, has been the most important risk factor for bladder cancer in Egypt [4, 16, 17]. *Schistosoma haematobium*, first identified from Egypt by Theodor Bilharz in 1851 [18], was initially implicated in bladder cancer induction by Fergusson in 1911 [19], and later confirmed in 1994 by the International Agency for Research on Cancer (IARC) [20].

Changes in exposures linked to bladder cancer have occurred recently in Egypt. Prior to the 1964 completion of the Aswan High Dam, approximately 60%of people in North and South Egypt were infected with *S. haematobium*; a similar proportion was infected with *S. mansoni* (causing intestinal disease) in North Egypt, but rarely seen in southern parts of the country [18]. The dam appears to be responsible for a gradual replacement of *S. haematobium*by *S. mansoni* in North Egypt, and *S. mansoni* has expanded into southern regions [18]. Another change in bladder cancer risk involves rising cigarette smoking in Egypt, which is now 32% among males (but only 7% among females) [21]. Oncologists and pathologists in Egypt have suggested that there is a changing ratio of SCC:TCC types of bladder cancer over the past 10–15 years, however no previously published work has documented this possible trend. Declining SCC rates and rising TCC rates suggest possible changes in the epidemiology of this disease in Egypt. Accordingly, bladder cancer cases recorded from1980 through 2005 at the National Cancer Institute, Cairo (NCI-Cairo) were analyzed to evaluate temporal changes in histopathological types of cancers, and to assess associated changes in demographic, epidemiologic (changes in the risk factor profile related to bladder cancer), and lifestyle risk factors.

Materials and methods

Study years

Data from all cases of bladder cancer recorded at the NCI-Cairo during six calendar years from 1980 though 2005 were chosen (1980, 1983, 1990, 1994, 2001, and 2005). Our initial goal was to choose intervals of exactly 5 years (1980 through 2005) but electronic transfer of records during 1985, 1995, and 2000 was not complete, thus we substituted 1983, 1994, and 2001, respectively. The numbers of all cancers and of bladder cancers for these years were not significantly different from those of the intended years (data not shown); however, there was a large proportion of missing records for the years 1980 and 1983 due the institutional move from paper to electronic medical records in that time frame. Cases were abstracted only if bladder cancer was confirmed by histological evidence by cystoscopic biopsy and/or surgical resection followed by a histopathological examination.

Study population

NCI-Cairo is the largest tertiary cancer hospital in Egypt, drawing patients throughout the country. Patients seen at the NCI-Cairo come from 3 main geographical regions in Egypt: the Cairo Metropolitan Area [CMA] (38% of NCI-Cairo patients), the Nile delta region of North Egypt (40% of NCI-Cairo patients), and South Egypt (22% of NCI-Cairo patients) [22]. The proportion of patients from each region roughly reflects the population living in these regions. Two regional cancer centers established over the past 7 years began to diagnose and treat new patients residing in these regions. Thus, data from the Nile Delta (Gharbiah Population-Based Cancer Registry) and South Egypt (Minia Cancer Center) were included in a secondary analysis. Our two objectives of analyzing data from these 2 centers were: (1) to examine if the observed changes in the bladder cancer profile at the NCI-Cairo could be documented also in the Gharbiah Population-Based Cancer Registry and the Minia Cancer Center and (2) to investigate whether changes at the NCI-Cairo were due to recent increased referral of patients from North and South Egypt to the two new cancer centers. Thus, aggregate data on histopathology and relative frequency of bladder cancer were obtained from the Gharbiah Population-Based Cancer Registry in North Egypt and the Minia Cancer Center in South Egypt.

Data collection and management

Information on demographics (age, sex, and residence) and clinical manifestations of schistosomal infection (history, haematuria, and anti-schistosomal medication) were abstracted from each bladder cancer medical record. Schistosomal status was not always recorded in the medical records, as awareness of this fact did not change the course of treating the bladder tumor. As such, we had a significant amount of missing data for this variable, and acknowledge it as a limitation. We compared patients who had a known schistosomal status to those who did not with regards to demographic factors (age and gender). We found that patients with a known status did not differ significantly from those with an unknown status in regards to gender (gender: χ^2 test, $P = 0.08$) however the difference in mean age did reach significance; the patients of unknown status had a higher mean age (unknown: 56.1 ± 12.1 vs. known: 53.2 ± 11.4, *t*-test: $P = 0.05$).

The diagnosis of schistosomiasis was made by one or more of the following criteria: history of schistosomal infection (indicated by the patient), ever receiving anti-schistosomal medication (indicated by the patient), presence of periportal fibrosis on ultrasonographic examination of the liver, or presence of schistosome ova in the tumor specimen reported by medical or laboratory investigation documents included in the patient medical record.

Patients were classified as residing in one of four regions: North Egypt, South Egypt, CMA, or Desert. The cities of Cairo and Giza comprised the CMA, with all cities north of Cairo classified as “North Egypt” and all cities south of Cairo as “South Egypt.” The governorates Marsa Matroh and Sinai were denoted as “Desert” in this study, and excluded from analysis as they represent <0.15% of the sampled population [23].

Additional information included ultrasonographic periportal fibrosis, cystoscopic findings, tumor size, gross pathology, and histopathology. When available, information on the type of surgical procedure, lymph node staging, and metastases was obtained.

Frequently, the pure form of one cell type was recorded; however cases arose where transitional carcinomas showed the presence of squamous or glandular differentiation. If the pathology report recorded a blended form (i.e., transitional cell carcinoma with squamous metaplasia), the type was recoded to match the dominant form. This follows the convention set forth by the WHO classification [24]. To standardize the cell types, all grade levels of a distinct cell type were combined to represent that cell type. Therefore, our final statistical analysis used histopathological types coded as either TCC or SCC (undifferentiated, adenocarcinoma, and sarcoma cell types were excluded from the analysis, as well as patients with missing pathology records).

For the six study years (1980, 1983, 1990, 1994, 2001, and 2005), pathology reports were missing in 3%, 8%, 32%, 9%, 7%, and 8% of all bladder cancer cases, respectively. Generally, pathology reports were created for those who had surgical procedures, tumor biopsies, or urine cytology. Advanced stage patients and patients who did not continue treatment at the NCI-Cairo were most likely to have a missing pathology report. Therefore, the total number of excluded patients included two groups, a) patients who had non-SCC or non-TCC and b) patients who had missing pathology reports. The total number of excluded patients were 680, representing 24.5% of all patients. For the six study years (1980, 1983, 1990, 1994, 2001, and 2005), those patients represented 15%, 20%, 42%, 19%, 14%, and 16% of all bladder cancer cases, respectively. To assess if significant differences between the included and excluded cases existed, we examined the distributions of demographic variables of both groups. We performed an independent samples t-test to evaluate the equality of sample means with regard to age (included cases: 54.3 ± 11.9 years, excluded cases: 53.9 ± 12.6 years, $P = 0.39$). For the categorical demographic variables (gender and residence), Pearson χ^2 test were utilized. Males comprised 79% and 80% of the included and excluded cases, respectively ($P = 0.53$). The residences of the included and excluded cases were also similar. Thirty percent, thirty-three percent, and thirty-seven percent of the included cases resided in the CMA, North Egypt, and South Egypt, respectively. Approximately 30%, 36%, and 34% of the excluded cases resided in the CMA, North Egypt, and, South Egypt respectively ($P = 0.41$). Based on these tests, the included cases did not significantly differ from the excluded cases with respect to age, gender, and residence. In addition, included and excluded cases did not differ by year of diagnosis (data not shown).

Statistical methods and analysis

Information from abstraction forms was captured in an electronic database (Microsoft Excel), and uniformity of coding schema for categorical variables was implemented to improve efficiency of statistical analysis and interpretation of results. All variables were then checked for range and consistency. Cleaning, verification, and correction of the dataset were done with Excel and SPSS version 14.0, (Chicago, IL). Data were analyzed using SAS version 9.0 (SAS Institute, Cary, NC).

Our review of age and sex of patients seen at the NCI-Cairo and the other two centers included in the study did not show a difference between the three cancer centers during the overlapping time period (1999–2005). Given the different study years of the data, we cannot make a statistical comparison between the three centers. With respect to the only year in common between all centers (2001), we performed a χ^2 test to assess whether the proportion of male to female cases was different between the three centers. We found that the proportion of males to females diagnosed with bladder cancer in the year 2001 was not statistically different between the three centers ($P = 0.86$). Since we only have aggregate data for the mean age and standard deviation, we cannot assess this relationship (for the year 2001) statistically. Therefore, without a statistically significant difference between the three centers with respect to sex and a visual assessment of the three mean ages in 2001, adjustment for these variables will not change the reported results.

Univariate analyses of continuous variables involved tests for normality and skewness, and frequency distributions were calculated for categorical variables. Univariate associations between histopathological type (dependent variable) and *S. haematobium* infection, gender, residence, age, and year of diagnosis were assessed using χ^2 test. Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) associated with each predictor variable, after adjusting for all covariates in the model. Interactions between variables were formally tested by comparing the log likelihood ratio tests. Given that the interactions were significant, we have based the ORs on the full model.

Results

We abstracted data on 2,778 patients seen at the NCI-Cairo over the six predetermined years from 1980 through 2005. The year 1990 is an outlier with respect to the number of bladder cancer cases seen at the NCI-Cairo. The increasing number of cancer patients may have stimulated a need for new cancer centers that began to working in full capacity by 1992–1993.

Certain demographic characteristics of bladder cancer patients varied during the study period, while others were stable (Table 1). The mean age at diagnosis changed significantly during the study years (*F*-test, $P < 0.001$) (Table 1). The M:F sex ratio, however, did not vary (χ^2 test, $P = 0.57$), with approximately 4 times more males than females experiencing bladder cancer during the period. However, the residence of patients changed among the study years, with South Egypt representing the larger pool during the 1980s (43% and 45% for 1980 and 1983, respectively), and then declining during the 1990s through 2005 (χ^2 test, $P < 0.001$) (Table 1). Prevalence of *S. haematobium* infection among bladder cancer patients differed among study years; however no clear trend was seen (Table 1). Geographic variation in patients with schistosomal infection was observed. In 1980 and 1983, bladder cancer patients at the NCI who had *S. haematobium* infection were equally likely to come from all geographical regions in Egypt. In 1990, bladder cancer patients who had *S. haematobium* infection were more likely to reside in North Egypt (χ^2 test, $P = 0.02$), while the last 3 years of the study demonstrated that bladder cancer patients with evidence of *S. haematobium* infection were significantly more likely to reside in South Egypt (data not shown). The ratio of SCC and TCC histopathological types changed, with SCC decreasing

and TCC increasing during the period. This trend was still obvious when gender was considered (Table 2). Male bladder cancer patients experienced a 39% decline in SCC prevalence coupled with a 44% increase in TCC. Similar changes were observed among females, although the magnitude was less pronounced. The first half of the study period at the NCI-Cairo was dominated by SCC (proportion of tumors that were SCC: 78%, 83%, and 55% for 1980, 1983, and 1990, respectively). Subsequently, TCC replaced SCC as the more prevalent histopathological type. In 1994, 2001, and 2005 SCC comprised 39%, 42%, and 27% of all diagnosed bladder tumors, respectively (Table 3).

Additional aggregate histopathological type data, collected from the Gharbiah Population-Based Cancer Registry in North Egypt and the Minia Cancer Center in South Egypt, were also analyzed (Table 3). The decreasing proportion of SCC cases was also observed at the Gharbiah and Minia centers. The relative frequencies of bladder cancers were similar at each of these cancer centers (Table 3). Age, gender, residing in the South, recent year of diagnosis, and *S. haematobium* infection were all significantly associated with the TCC histopathological type of bladder cancer in the univariate analyses (Table 4). These variables were included in a multivariable logistic regression model, showing that year of diagnosis was significantly associated with histopathological type. Compared to those diagnosed in 1980, patients diagnosed 26 years later had 6 times greater odds of being diagnosed with TCC (OR 6.00, 4.00–8.97). Older age at diagnosis also was significantly associated with a TCC histopathological diagnosis. Males were significantly more likely than females to have a TCC type (OR 1.57, 1.23–1.99). Associated schistosomal infection risk varied with residence, with negative patients living in the South being 55% less likely to have a TCC diagnosis (OR 0.45, 0.31–0.66) compared to bladder cancer patients living in the CMA with no schistosomal infection.

Discussion

This study demonstrated significant changes in the histopathological types of bladder cancer in Egypt over the past 26 years; the relative frequency of TCC in this multi-year sample increased from 22% in 1980 to 73% of bladder diagnoses in 2005, while SCC decreased from 78% of diagnosed bladder tumors in 1980 to 27% of diagnosed bladder tumors. Moreover, a significant decrease in the relative frequency of bladder cancer at the NCI-Cairo was noted, although bladder cancer remains the most common cancer among males in Egypt [1, 25]. In the early years of the study (1980, 1983, and 1990) bladder cancer accounted for approximately 25–27% of all cancers seen at the NCI-Cairo while in the latter years of 2001 and 2005, this percentage declined significantly to account for approximately 10% of all cancers seen at the NCI-Cairo.

Despite the significant decline in the relative frequency of bladder cancer in Egypt, a persistent gender disparity with predominance of the disease among males was observed in the data from all cancer centers participating in the study. Our data revealed a 4:1 male to female ratio of bladder cancer cases in all years of the study, which concurs with other major studies from Egypt [11, 26–28]. This gender gap might be a reflection of differences in the magnitude of environmental or lifestyle exposures related to bladder cancer etiology, such as schistosomal infection, smoking, and exposure to occupational and agriculture-related

chemicals [18, 29, 30]. Another possible explanation of this gender gap might be due to a possible role of a putative tumor-suppressor gene on the Y chromosome that has been deleted. Loss of the Y chromosome was observed in 7 of the 17 (41%) Schistosomiasis-associated bladder cancer cases studied by Khaled et al. (2000) using the fluorescence in situ hybridization (FISH) technique [31]. A similar gender-based trend (male predominance) in bladder cancer risk was observed in the US and European countries, where smoking rates and occupational exposures are more prevalent among males [5, 32–34]. However, in countries where males and females are equally exposed to risk factors of bladder cancer, the gender difference is not observed. For example, in Mozambique, where males and females work equally in the fields, no gender disparity in the occurrence of bladder cancer is evident [35].

The risk factor profile of Egyptian bladder cancer has changed over the last 26 years. As TCC became the more dominant histopathological type, the age at diagnosis increased possibly due to the long induction period associated with cigarette smoking and exposure to chemical carcinogens [36–38]. Studies from Western countries demonstrate the mean age at first bladder cancer diagnosis to occur between the sixth and seventh decades of life [6, 7, 39]. In our study population, we found that the mean age at first diagnosis was significantly higher for TCC patients compared to SCC patients (58.3 vs. 50.3 years, $P < 0.001$).

Conversely, SCC associated with schistosomal infection has an aggressive progression rate and is associated with the chronic inflammatory process that occurs during infection [40, 41]. At first diagnosis, patients presenting with SCC associated with schistosomal infection have locally advanced tumors and a mean age, that is, generally 10–20 years younger than that of patients with non-schistosomal bladder cancer, indicating the rapid development of this type, irrespective of the aging of the general population [42]. El-Bolkainy et al. (1981) reported a significantly lower age at diagnosis in egg-positive bladder cancer patients compared to egg-negative cases in a pathology series consisting of radical cystectomy specimens [10]. The late presentation, that is, usually associated with bladder cancer is due to the fact that patients infested with schistosomal ova have the same clinical symptoms that are associated with bladder cancer development, e.g., haematuria. Moreover, this late presentation occurs locally in the pelvis due to associated pelvic fibrosis that occurs with schistosomal infection.

Schistosomal infection significantly declined in bladder cancer patients at the NCI-Cairo over the study period; however no clear trend was present in the data. This relative decline in schistosomal infection is the manifestation of several reasons; primarily, the Schistosomiasis Research Project, sponsored by the Egyptian Ministry of Health and the United States Agency for International Development was designed with the specific purpose to understand the transmission characteristics of the infection in an effort to reduce mortality and morbidity from the disease [18]. Additionally, health educational efforts and several successful media campaigns have been successful in reducing the occurrence of schistosomal infection through targeted efforts at rural populations who bear a significant proportion of the risk [43].

We found an interesting interaction between residence and schistosomal infection, such that, bladder cancer patients living in the South with no schistosomal infection had a 55% reduced risk of TCC compared to bladder cancer patients living in the CMA with no schistosomal infection. This reduction of risk may be attributable to differences in smoking behaviors between the two regions. Since we do not have data on smoking levels by region in Egypt, we were not able to assess this hypothesis.

The recent establishment of two new cancer centers in Egypt has been postulated to account for the changing histopathological patterns seen at the NCI-Cairo. Cumulative data collected from these centers reflect the current patterns of histopathology seen at the NCI-Cairo; both the Gharbiah Cancer Registry (North delta region) and the Minia Cancer Center (South Egypt) reported a 2:1 predominance of TCC over SCC. Additionally, the relative frequencies of bladder cancer reported at all three centers were similar. The consistency of findings from these cancer centers repudiates the possibility that the trends seen at the NCI-Cairo are an indication of changing referral patterns.

The results of this study are in agreement with a few other small-scale hospital-based studies describing the profile of bladder cancer in Egypt over the past few decades. In the 1980s and early 1990s, studies from Egypt documented SCC as the predominant histopathological type of bladder cancer, with high rates of egg deposition found in tumor specimens [9–11]. Recent studies in Egypt indicated the emergence of TCC. In a hospital-based case-control study from Alexandria Egypt, TCC comprised 67% of histologically confirmed bladder cancers while SCC accounted for 18% in 1997 [44]. Additionally, data from the Middle East Cancer Consortium showed that TCC accounted for approximately 63% of bladder cancers while SCC accounted for 26% of patient diagnoses during the period of 1999–2001 in Gharbiah, Egypt [1].

This study has several strengths. The large dataset allowed us to document the changing histopathological trends that occurred in Egypt over the past 26 years. As far as we know, this is the first study from Egypt that spans a 26-year time period.

Second, the successful coordination with several cancer centers in Egypt allowed us to propose meaningful hypotheses about the patterns of bladder cancer for the whole country of Egypt. Third, quality control of the data was generally high as data collection, coding, and data entry were performed by one study personnel member, which limits variability that would have otherwise occurred with several study members.

A few limitations are present in this study. Case accrual in 1980 and 1983 involved less than 50% of the total bladder cancer patients seen at the NCI-Cairo (data not shown). We compared the tumor profile of the 1980–1983 dataset with previously published data from the NCI-Cairo. Data from the present study revealed that bladder tumors diagnosed in 1980 and 1983 were more frequently in late stages; 85.3% of our 1980 sample and 87.4% of our 1983 sample was diagnosed as late stage (T3a, T3b, T4a, and T4b). This is in agreement with data from several NCI-Cairo pathological series from the late 1970s and 1980s; El-Sebai [45] reported between 86% and 91% of patients present with advanced stage disease (T3 and T4). Similarly, El-Bolkainy reported 85.4% of bladder tumor diagnoses to be stage

T3 or later [46]. Between 1985 and 1990, Mohktar found 86.2% of patients diagnosed with bladder tumors to be diagnosed in the T3 or T4 stage [11]. Moreover, histopathological data were similar to the previously mentioned studies from the NCI-Cairo. El-Sebai, El-Bolkainy, and Mohktar reported SCC to comprise between 65% and 81% of diagnosed tumors. SCC accounted for 78–83% of diagnosed bladder tumors in our 1980 and 1983 sample. Since SCC has a distinct etiologic profile, the associated risk factors (schistosomal infection) are likely to be well represented among our sample. Although we were unable to collect data on the majority of patients treated at the NCI-Cairo in the years 1980 and 1983, evidence suggests that our sample is unbiased due to the similarity in stage profile and histopathological outcomes to previously published data from the NCI-Cairo.

Second, incomplete data on schistosomal infection for a large proportion of the patients was evident. For each of the study years (excluding 1980) between 20% and 53% of patients had missing data on schistosomal infection. Moreover, the diagnosis of schistosomiasis was not based strictly on diagnostic tools, e.g., presence of schistosomal ova or pathologic lesions in bladder tissue; past schistosomal infection as indicated by the patient medical record was sufficient for a positive schistosomiasis diagnosis in this study. Information on past history is liable to some bias as patients from rural Egypt may give a false negative history because of fear of receiving anti-bilharzial injections [42]. Therefore, estimates on schistosomal infection from our study are an underestimate and would conservatively bias ORs toward the null value.

Third, the lack of data on individual smoking behaviors and occupational data was a limitation in the study. Since physicians were not uniform in recording smoking habits, data at the national level was used as a proxy measure to indicate the prevalence of smoking. Due to the lack of data on smoking levels, we have not been able to include this variable as a predictor in our logistic regression analysis model. The absence of smoking data and occupational data is not unusual, even in Western countries, because systematic collection of data is not essential for the treatment of patients [47].

So, bladder cancer in Egypt has significantly changed within the last 26 years. The decreasing relative frequency of bladder cancer and the decline in SCC are indicative of changes in exposures related to bladder cancer induction; the recent opening of cancer centers in North and South Egypt cannot explain these differences. Reductions in schistosomal infection and increases in cigarette smoking and chemical exposures related to occupational hazards have resulted in a temporary unique situation that needs urgent future studies. In countries where cigarette smoking is a prevalent behavior, cancer of the lung, esophagus, and mouth are correspondingly high, which is not the case in Egypt. Studies to parse out the underlying mechanism that favors bladder cancer formation instead of lung cancer need to be performed in Egypt to understand this paradox. Additionally, future studies to distinguish the molecular differences between schistosomal bladder cancer and nonschistosomal bladder cancer are needed. Characterization of the genetic alterations in schistosomal bladder tumors will elucidate the mechanism related to this type of bladder cancer induction.

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Table 1

Characteristics of bladder cancer patients treated at the NCI-Cairo during years of the period 1980 through 2005

	1980	**1983**	**1990**	**1994**	**2001**	**2005**	***P*-value**
Age (years)	N[c] = 274	N = 310	N = 861	N = 465	N = 359	N = 509	
Mean (SD)	46.5 (10.0)	48.0 (9.6)	52.9 (11.2)	55.4 (11.7)	58 (10.4)	60 (11.0)	<0.0001
Median (range)	46 (19–69)	50 (20–70)	54 (15–87)	55 (25–97)	59 (32–85)	60 (25–86)	<0.0001
Gender	N = 271 (%)	N = 310 (%)	N = 861 (%)	N = 465 (%)	N = 359 (%)	N = 501 (%)	
Male	208 (77)	247 (80)	670 (78)	370 (80)	291 (81)	406 (80)	0.572
Female	63 (23)	63 (20)	191 (22)	95 (20)	68 (19)	95 (19)	
Residence	N = 267 (%)	N = 298 (%)	N = 858 (%)	N = 464 (%)	N = 346 (%)	N = 504 (%)	
North	90 (34)	105 (35)	348 (41)	160 (34)	85 (25)	137 (27)	<0.0001
South	116 (43)	134 (45)	283 (33)	158 (34)	117 (34)	191 (38)	
CMA	61 (23)	59 (20)	227 (26)	146 (31)	144 (42)	176 (35)	
[a]Schistosomal infection	N = 273 (%)	N = 248 (%)	N = 403 (%)	N = 292 (%)	N = 217 (%)	N = 369 (%)	
No	137 (50.0)	61 (19.7)	52 (6.0)	27 (5.8)	10 (2.8)	132 (26.0)	<0.0001[b]
Yes	136 (49.6)	187 (60.3)	351 (40.8)	265 (57.0)	207 (57.7)	237 (46.6)	
Unknown	1 (0.40)	62 (20.0)	458 (53.2)	173 (37.2)	142 (39.5)	140 (27.5)	

[a]Defined as the following: history of schistosomal infection, ever receiving anti-schistosomal medication, presence of periportal fibrosis on ultrasonographic examination of the liver, or presence of schistosome ova in the tumor specimen

[b]This *P*-value is based only on the non-missing cases

[c]Sample size variations are due to missing data

Table 2

Prevalence of SCC and TCC[a] stratified by gender and year at the National Cancer Institute—Cairo

Histopathological type	Squamous (N = 1,059)		Transitional (N = 1,037)		
Gender	Male	Female	Male	Female	*P*-value
Year	No. (%)	No. (%)	No. (%)	No. (%)	
1980 (N = 234)	138 (59)	45 (19)	40 (17)	11 (5)	0.65
1983 (N = 247)	159 (64)	47 (19)	37 (15)	4 (2)	0.06
1990 (N = 502)	204 (41)	73 (15)	181 (36)	44 (9)	0.07
1994 (N = 378)	113 (30)	33 (9)	188 (50)	44 (12)	0.39
2001 (N = 309)	92 (30)	39 (11)	154 (51)	24 (8)	0.005
2005 (N = 426)	84 (20)	32 (8)	261 (61)	49 (12)	0.006

[a]Excluded cases were Adenocarcinoma (118), Sarcoma (4), Undifferentiated (100), and Missing (418)

Table 3

Proportion of all cancers that were of the bladder during the years of this study (NCI-Cairo) and from two other Egyptian cancer centers during 1999–2004, and the prevalence of squamous cell carcinoma for each year

Year	Proportion of all cancers that were of the bladder (%)	Prevalence of SCC
	NCI-CAIRO	N (%)
1980 (N = 234)	25	185 (78)
1983 (N = 247)	27	206 (83)
1990 (N = 502)	27	280 (55)
1994 (N = 378)	17	146 (39)
2001 (N = 305)	10	127 (42)
2005 (N = 432)	10	118 (27)
	Gharbiah cancer registry (north)	N (%)
1999 (N = 229)	8	72 (31)
2000 (N = 263)	10	73 (28)
2001 (N = 231)	8	60 (26)
2002 (N = 252)	8	54 (21)
	Minia cancer center (south)	N (%)
2000 (N = 219)	11	90 (47)
2001 (N = 282)	11	121 (53)
2002 (N = 265)	10	87 (43)
2003 (N = 316)	13	121 (48)
2004 (N = 273)	11	70 (34)

Table 4

Logistic Regression model to predict transitional cell carcinoma versus squamous cell carcinoma in bladder cancer patients treated at the NCI-Cairo between 1980 and 2005

N = 2,094	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Age (5 years interval)	1.40 (1.33–1.46)	1.24 (1.18–1.30)
Sex		
Female	1.00[b]	1.00[b]
Male	1.61 (1.31–1.99)	1.57 (1.23–1.99)
Positive schistosomal status[a,c]		
CMA	1.00[b]	1.00[b]
South	–	0.96 (0.82–1.12)
North	–	1.10 (0.44–2.72)
Negative schistosomal status[a,c]		
CMA	1.00[b]	1.00[b]
South	–	0.45 (0.31–0.66)
North	–	0.80 (0.55–1.16)
Year		
1980	1.00[b]	1.00[b]
1983	0.17 (0.12–0.24)	0.75 (0.47–1.2)
1990	0.77 (0.63–0.94)	2.39 (1.64–3.48)
1994	1.80 (1.43–2.26)	4.46 (3.0–6.63)
2001	1.52 (1.19–1.94)	3.52 (2.33–5.32)
2005	3.45 (2.73–4.35)	6.00 (4.00–8.97)

[a] Patients with an unknown infection status are excluded from the analysis

[b] Reference group

[c] The interaction between region and schistosomal infection was significant