

EXPECTED CHANGES IN RISK FACTORS BETWEEN
SQUAMOUS CELL AND TRANSITIONAL CELL CARCINOMA
AMONG URINARY BLADDER CANCER PATIENTS
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Thesis

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ABSTRACT

Bladder cancer ranked first most common cancer site among males and fifth among females in the National Cancer Institute, Egypt. This study was conducted at the NCI, Cairo University. It included two parts: part 1, a cross-sectional part including 223 patients. This part was conducted to figure out the characteristics of bladder cancer patients at the NCI, Cairo University and update the demographic and other risk factors of bladder cancer patients and compare it with the second part of the study conducted at the same institute to detect any change in pattern of bladder cancer. The second is a retrospective part which included 105 cases records from 1995 and 101 from year 2000. It was conducted in the biostatistics and cancer epidemiology unit. This part was conducted to examine pattern and changes in the epidemiology and pathology. The most important change was marked increase of TCC cases in comparison to SCC along the study years from year 1995 to year 2007. The significant risks were age of Patients with TCC were significantly older than those with SCC, females were more frequently affected by SCC compared to males who were affected more by TCC. Past history of bilharziasis was significantly more frequent in urinary bladder cancer patients with SCC. Smoking was far more frequent in patients with TCC, burning micturition and history of urinary tract stones were frequent findings in the two pathological types.

Key words: *Bladder cancer, histopathological changes, risk factors*

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LIST OF ABBREVIATIONS

2-NA	2-naphthylamine
4-ABP	4-aminobiphenyl
ACS	American cancer society
ASR	Age-standardized incidence rates
BC	Bladder cancer
CI	Confidence interval
CIS	Carcinoma in situ
GST	Glutathione s-transferases
NAT 1	N-acetyltransferase 1
NAT 2	N-acetyltransferase 1
NCI	National cancer institute
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PAH	Polycyclic aromatic hydrocarbons
SABC	Schistosomal-associated bladder cancer
SAS	Statistical analysis system
SCC	Squamous cell carcinoma
SCI	Spinal cord injury
SD	Standard deviation
TCC	Transitional cell carcinoma
TNM	Tumor-node-metastasis system

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INTRODUCTION

Bladder cancer (BC) is the most common malignancy affecting the urinary tract. In the United States, approximately 69,000 individuals (51,000 males and 18,000 females) develop BC each year, and 14,100 die from the disease (*Jemal et al., 2008*).

Bladder cancer is the 9th most frequent cancer in the world. 179,000 persons died of bladder cancer worldwide in 2002. The World Health Organization estimated that the burden of bladder cancer in the world in 2002 was 1,002,000 disability-adjusted life years lost in men and 476,000 in women; over 80% of this burden was attributable to mortality (*WHO, 2004*).

In Egypt, bladder cancer is the second or third most common and constitutes between 10% and 14% of all new cancer cases in both sexes (*MOHP, 2002*). In the year 2001, 1869 (8.7%) died of bladder cancer (1486 males and 383 females) (*MOHP & WHO, 2002*).

Bladder cancer exists in several forms with different risk factors, Two main histological types of bladder cancer are identified: the transitional cell carcinomas (TCC), related to cigarette smoking and most prevalent in Western and industrialized countries, and the squamous cell carcinomas (SCC), which are more frequently seen in some Middle Eastern and African countries, where urinary schistosomiasis is an

endemic disease. Other types of bladder cancer include adenocarcinoma and undifferentiated carcinoma (**Sengupta, 2004**).

In industrialized Western countries, transitional cell tumors comprise 90%-95% of bladder tumors. In developing countries in certain locations, up to 75% of cases are squamous cell carcinomas (**Sebaie et al., 2005**).

Bladder cancer in Egyptian patients is characterized by high frequency of squamous cell carcinoma due to schistosomiasis but recently a relative increase in the frequency of transitional cell type in schistosomiasis-associated bladder cancer has been noted. This may indicate the implication of other etiologic factors in Egyptian bladder cancer patients. However, with increased urbanization, industrialization, and cigarette smoking in many African countries, there is an increasing incidence of TCC relative to SCC of the bladder (**Heyns & Vander, 2008**).

Data from all available medical records from the National Cancer Institute of Cairo University (NCI-Cairo) between 1980 and 2005 were evaluated. During this 26-year period, important changes in the frequency of histopathological types of bladder cancer occurred. A statistically significant association between time period of diagnosis and histopathological type was found. Patients diagnosed in 2005 had a six fold 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)]. 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 (*Felix et al., 2008*).

AIM OF THE WORK

Aim of this work:

Improving the preventive strategy of bladder cancer in Egypt

Specific objectives

1. Figure out the characteristics of bladder cancer patients at the NCI, Cairo University and update the demographic and other risk factors of bladder cancer patients
2. Define the epidemiological and pathological changes during years 1995, 2000 and 2007.
3. Define changes in the risk factors underlying different pathological types specially the two major types; squamous cell carcinoma and transitional cell carcinoma in NCI (Cairo-university).

BLADDER CANCER

EPIDEMIOLOGY.....

Magnitude of the Problem:

Bladder cancer represents a global health problem. It ranks ninth in worldwide cancer incidence. It is one of the most common cancers worldwide, with the highest incidence in industrialized countries (*Cancer Facts and figures, 2007*).

The incidence of bladder cancer in the United States increased from 1973 to 1990 while during 1992-1998; it declined slightly but significantly in both males and females. Between the early 1970s and the late 1980s, mortality for bladder cancer decreased significantly in both whites and blacks, the 1990s, mortality rates continued to decline among blacks, but remained fairly constant among whites (*Cancer Facts and figures, 2002*).

In Egypt, between 1975 and 1986, bladder cancer constituted 30% of new cancer cases (*Ibrahim, 1986*). From 1987, A gradual decrease in the number of new bladder cancer cases presenting to NCI; it constituted 24% of all cancer cases for both men and women in 1987 to reach 10% in 2002 (*El-Attar et al., 2003*).

Geographical variation

Bladder cancer worldwide:

Worldwide an estimated 356,600 new cases of bladder cancer occur each year and, in terms of overall cancer frequency, it is ranked as ninth (**IARC, 2002**).

Age-standardized incidence rates (ASR) higher than 40 per 100,000 for males were reported from Europe (Belgium, 42.5; Italy, 41.0). In most European countries, the United States, and Canada, rates are between 20 and 30. Bladder cancer incidence is lowest in Asia and South America, approximately 70% lower than in Western industrialized countries (**Stein, 2001**).

The lowest median bladder cancer ASR for males was in Asia (5.9), and the highest in Europe (23.9). Rates for females were much lower, but followed the same geographical pattern as for males (**Stein, 2001**).

Marked variation in bladder cancer incidence occurs not only between but also within countries. Italy, which had one of the highest rates for males worldwide (41.1 in Genua province), also had a rate of 27.9 in Ragusa province. Nonetheless, because of its high recurrence rate, the actual prevalence of active bladder cancer is estimated to be about 10 times the number of new cases (**Stein, 2001**).

Bladder cancer in USA and UK

Bladder cancer is the 4th commonest cancer in men and the 12th in women in the USA. It is estimated that about 67,160 Americans were diagnosed with bladder cancer in 2007 and 13,750 died of the disease (***Cancer Facts and Figures, 2007***).

Bladder cancer is a common cancer in the UK, with 10,278 new cases in 2005. It is the most frequently occurring tumor of the urinary system and accounts for 1 in every 28 new cases of cancer each year in the UK (***N. Ireland Cancer Registry, 2008***).

Bladder cancer in African countries

Accurate epidemiological data about the incidence and mortality of bladder cancer are unavailable for most African countries. Transitional cell carcinoma (TCC) of the bladder is probably less common in rural African regions than in industrialized countries, due to lower levels of exposure to carcinogenic chemicals. In areas with endemic schistosomiasis (bilharzia) caused by parasitic schistosomes (blood flukes), most bladder cancer cases are comprised of squamous cell carcinoma (SCC). However, with increased urbanization, industrialization, and cigarette smoking in many African countries, there is an increasing incidence of TCC relative to SCC of the bladder (***Heyns & Vander, 2008***).

Bladder cancer in MECC countries and Egypt

Bladder cancer was one of the more common cancers in Middle East Cancer Consortium MECC countries (Cyprus, Egypt, Israel, and Jordan) – especially Egypt, where it ranked first in males, representing 16.2% of male cancers. Among Egyptian females, its frequency was 4.0%, by far exceeded by breast cancer (37.6% of female malignancies). For both sexes together, the frequency of bladder cancer was 10.1%, nearly the same as non- Hodgkin lymphoma (10.5%) and next in frequency to breast cancer (18.9%) Other MECC registries reported relative frequencies of bladder cancer in males of 12.3% for Cypriots, 10.0% for Israeli Jews, 9.9% for Jordanians, and 8.1% for Israeli Arabs. The proportions in females were much lower, and bladder cancer was not among the 10 most frequent types of cancer in females in these registries. For both sexes together, relative frequencies in other MECC countries were all lower than for Egypt, ranging from 7.5% down to 5.0%. The relative frequency in the United States was lower than in MECC countries for males, and similar to MECC countries for females (***Ibrahim & Khaled, 2006***).

Overall Incidence

Results, based for the first time on population data, show that Egypt had a serious problem of bladder cancer. The highest ASR for both sexes together was that of Egyptians (16.6), followed by Israeli Jews (15.1), Cypriots (11.2), and Israeli Arabs (8.6). Jordanians had the lowest ASR (7.6), with less than half the rates of Egyptians and Israeli Jews. Egyptians and Israeli Jews had the highest ASR for males (27.5),