Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2014; 6(1): 46-53

ISSN- 0975 1556

Research Article

Time Series Trend of Bilharzial Bladder Cancer in Egypt and its relation to Climate Change: A study from 1995-2005

Samia A. Ahmed[1], Amal Saad-Hussein[2], Ayman El Feel[3], *Manal A. Hamed[1]

[1]Therapeutic Chemistry Department, National Research Center, Cairo, Egypt.
[2]Environmental & Occupational Medicine Department, National Research Center, Cairo, Egypt.
[3]Egyptian Mineral Recourses Authority (EMRA), Cairo, Egypt.

Available online: 9th December 2013

ABSTRACT
The present ecological study estimated time series trend of relative frequencies (RF) of bilharzial bladder cancer in different Egyptian governorates in relation to climate change during the period 1995-2005. Results revealed that the mean air temperature has positive trend in all the governorates and the number of days of maximum temperature of 45 °C or more was increased in Upper Egypt, but, did not experience increase in the rest of Egypt. RF was significantly declined in most of Urban, Upper and Lower Egypt, while there was no change in RF trend in Frontier governorates. Male to Female ratio was above 2:1 in most of the Urban and Upper Egyptian governorates, and less than 2:1 in Lower Egypt, except in Ismailia. In conclusion: RF of bilharzial bladder cancer seemed to be declined with time in most of the Egyptian governorates, with the increase in the air temperature. But, this relationship could not be proved and further epidemiological studies are required

Keywords: Climate Change, Bilharzial Bladder Cancer, Geographic Information System (GIS), Gender.

INTRODUCTION

Globally, distribution of Schistosomiasis has been changed significantly in the past 50 years with control successes achieved in Asia, Americas, North Africa and Middle East. But, it is still endemic in at least 75 tropical and subtropical countries, where 600 million people are at risk and over 200 million are infected (Yosry, 2006).

Many years after exposure to Schistosoma haematobium (S. haematobium) infestation spontaneous healing may occur, but cases that have been reported with urogenital lesions led to complications (Richter, 2000). Overall, S. haematobium infection was strongly associated with increase risk for cytologic abnormality in the bladder; more than 2.8 fold relative risk of metaplasia or hyperkeratosis (Hodder, 2000). Clinical and pathology studies demonstrated epidemiological association between urinary schistosomiasis and bladder cancer in Egypt (El-Bolkainy et al., 1982).

Bladder cancer is estimated to be the 9th most common cancer worldwide and the 13th most numerous cause of death from cancer (Parkin, 2008). Currently in Egypt, bladder cancer is the most common solid tumor in men; ranks the first, and representing 16.2% of male cancers (Khaled, 2005). Whereas in females, it ranks second to breast cancer. It is strongly associated with bilharziasis and occurs predominantly in agricultural workers in areas which are famous with S. haematobium (Kahan et al., 1997).

Geographic coincidence of bladder cancer and schistosomiasis is remarkable. This association has been explained through chronic irritation of the urothelium, altered metabolism with elevated urinary level of carcinogenic metabolites and N-nitroso compounds, and/or elevated urinary levels of -glucuronidase (Badawi et al., 1995; Margison and Povey 2002).

Climate change and environmental variables may influence the distribution of schistosomiasis and the type of the species (Brooker, 2002). It was proved that global climatic changes alter the equilibrium of many ecosystems and the distribution of different species, that may affect the distribution and severity of human diseases. Furthermore, the impact of climate change may occur over several time scales, ranging from increasing the amplitude and diurnal or seasonal fluctuations in temperature and precipitation, to more stable increases in mean ambient temperatures over longer periods, particularly in tropical regions where many human diseases are endemic.

In Egypt, there is great evidence of climatic change that occur in the last decades (Egypt-SNC, 2010). The general climate of Egypt is dry, hot, and desertic, with a mild winter season with rain over the coastal areas, and a hot and dry summer season. Data collected by the Egyptian Meteorological Authority and local universities for the period 1961-2000 indicate that there is a general trend towards warming of the air temperature, with increases in the hot days.

Currently, researches predicted that vector-borne diseases such as schistosomiasis will be particularly affected by changes in climate change particularly atmospheric temperature. The aim of the present ecological study is

**Author for correspondence: E-mail: manal_hamed@yahoo.com*

Table 1 Relative frequencies of bilharzial bladder cancer in different Egyptian governorates and the male to female ratio in the studied period (1995-2005)

Governorate	RF*	Male / Females Ratio
Urban Governorates		
1. Cairo**	28%	2
2. Alexandria	30.3%	2.4
3. Port-Saied	65.3%	4.7
4. Suez	43%	2
Governorates of Upper Egypt		
1. Bani Suef	65.7%	2
2. Fayoum	52%	1.4
3. Minya	53.5%	2
4. Assiut	55.9%	1.7
5. Sohage	51.9%	2.1
6. Qena	46.4%	3.4
7. Aswan	64.8%	1.7
8. Luxor**	88.9%	1.4
Governorates of Lower Egypt		
1. Domiat	61.9%	1.9
2. Sharkia	56.9%	1.5
3. Dakahlia	56.9%	1.2
4. Qalubia**	64.8%	1.6
5. Kafer El-Shikh	56.7%	1
6. Gharbia	52.2%	1.3
7. Menofia**	56.9%	1.8
8. Bheira**	56.6%	1.5
9. Ismailia	35.8%	2.2
Frontier Governorates		
1. Red Sea**	19.7%	2.5
2. South Sinai**	73.1%	5.5

**RF: Relative frequency during the period of the study, ** The data was from 1995 to 2000 only*

estimation of the time series trend of relative frequencies of bilharzial bladder cancer in the different governorates in Egypt according to geographic distribution and gender and it's relation to climate change during the period of the study (1995-2005).

METHODOLOGY

A time-trend ecologic study was conducted to determine the relationship between climate change and the relative frequencies of bilharzial bladder cancer in the different Egyptian governorates during the period 1995 - 2005. The governorates included in the present study were four Urban Governorates (Cairo, Alexandria, Port Said, and Suez), nine governorates located in the Nile Delta (representing Lower Egypt), eight governorates located in the Nile Valley (representing Upper Egypt), and two Frontier Governorates (Red sea and South Sinai).

This work was conducted through collection of the registered data from the selected hospitals; the main hospital in each Governorate, after approval form the different authorities. The collected data included number of diagnosed bladder cancer cases (whatever their etiology). The collected data were supported by the registered diagnosis and confirmed by the histopathological reports. For each case, gender, residential area, and past history of S. haematobium were also collected.

The variability of frequency and severity of extreme weather events in Egypt during the period of the study has been monitored based on the meteorological data of 32 stations distributed all over Egypt.

To provide quantitative information on this issue, statistical evaluation of the yearly relative frequency [RF] of bilharzial bladder cancer to the total number bladder cancer was calculated for each governorate; as total and according to gender, through the following equation (Neter et al., 1992; Riffenburgh, 2006):

Statistical analysis was done through SPSS program version 14. In each governorate, Spearman rank correlation coefficient; a non-parametric version of correlation coefficient, was used to evaluate the time-series trend of the RF of total bilharzial bladder cancer, and according to gender through the period of the study (1995-2005). Spearman correlation is appropriate for ordinal data or for interval data that do not satisfy the normality assumption. It is based on the ranks of the data rather than the actual values (Riffenburgh, 2006). While, Pearson correlation coefficient was used to study the changes in air temperature during the studied period.

RESULTS

In the studied period, the mean maximum air temperature has a positive trend with time (r = 0.3°C, P > 0.05), the mean minimum air temperature has also positive trend (r= 0.3°C, P > 0.05), and the mean air temperature has a positive trend (r = 0.02°C, P > 0.05). The sunshine duration has a negative trend in (r = – 0.01 hour per year, P > 0.05). The number of days of peak temperature equaling to or exceeding 45 °C have increased in Upper Egypt from 52 days to reach 69 days during the period of the study. The rest of Egypt did not experience increase in the number of days with maximum temperature of 45 °C or more.

From registrations, the ages of the bladder cancer cases in all the studied governorates were above 20 years and below the 75 years (21 - 74 years). Table (1) shows that during the period 1995 -2005, RF of bilharizial bladder cancer was above 50% in all the governorates of Upper and Lower Egypt; except in Qena and Ismailia (46.4% and 35.8% respectively). The highest RF of bilharizial bladder cancer was in Luxor (88.9%), and the lowest was in Red Sea (19.7%). Additionally, RF of bilharzial bladder cancer in males was higher than in females in almost all Egyptian governorates (Table 1). Male to Female ratio was over 2:1 in Frontier and Urban governorates and in most of the Upper Egyptian governorates, and less than 2:1 in Lower Egyptian governorates; except in Ismailia.

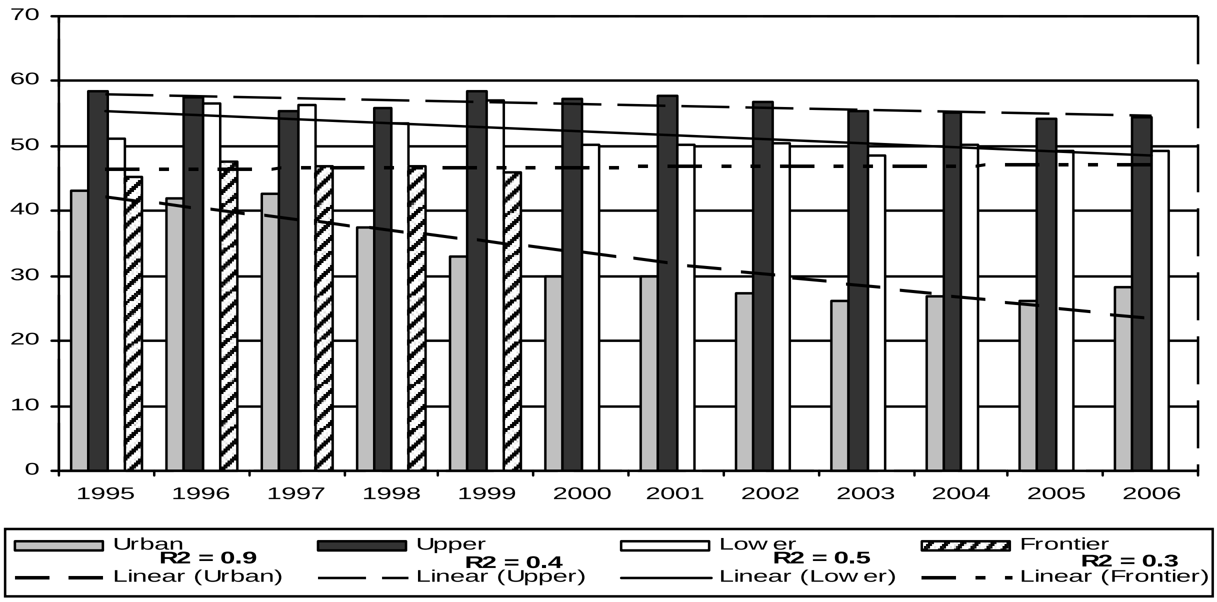
There was significant decline in the RF of bilharzial bladder cancer in Urban, Upper Egyptian and Lower Egyptian governorates (r = -0.9, P< 0.001, r = -0.6, P< 0.005, and r = -0.7, P< 0.001 respectively). But, there was no significant change in the RF trend in Frontier governorates (r = 0.1, P> 0.05), (Figure 1).

Table 2 Time series trend of the relative frequencies (RF) of bilharzial bladder cancer in the different Egyptian governorates as regard each gender in the studied period (1995-2005)

Governorate	RF to years		Male RF to years		Female RF to years	
	r	P-value	r	P-value	r	P-value
Urban Governorates						
1.Cairo**	-0.9	P= 0.05	-0.2	NS	-0.3	NS
2. Alexandria	-0.8	P< 0.005	-0.5	NS	-0.7	P= 0.01
3. Port-Saied	-0.5	NS	-0.1	NS	-0.1	NS
4. Suez	-0.7	P= 0.01	-0.8	P< 0.005	-0.1	NS
Governorates of Upper Egypt						
1. Bani Suef	-0.3	NS	-0.4	NS	-0.1	NS
2. Fayoum	-0.1	NS	0.3	NS	-0.1	NS
3. Minya	-0.8	P< 0.005	-0.7	P= 0.01	-0.8	P< 0.005
4. Assyut	-0.02	NS	0.3	NS	-0.6	NS
5. Sohage	0.7	P< 0.01	-.004	NS	0.7	P< 0.01
6. Qena	-0.1	NS	0.1	NS	0.6	NS
7. Aswan	0.5	NS	-0.1	NS	0.5	NS
8. Luxor**	-0.8	P= 0.05	0.5	NS	-0.6	NS
Governorates of Lower Egypt						
1. Domiat	-0.7	P= 0.01	-0.8	P< 0.005	-0.4	NS
2. Sharkia	-0.4	NS	-0.6	NS	-0.1	NS
3. Dakahlia**	-0.2	NS	-0.4	NS	0.3	NS
4. Qalubia	0.5	NS	0.1	NS	0.6	NS
5. Kafer El-Shikh	0.5	NS	0.7	P< 0.05	-0.01	NS
6. Gharbia	-0.2	NS	-0.8	P< 0.005	0.5	NS
7. Menofia**	0.3	NS	-0.1	NS	0.6	NS
8. Bheira**	-0.6	NS	-0.6	NS	-0.2	NS
9. Ismailia	-0.1	NS	-0.7	P< 0.05	-0.4	NS
Frontier Governorates						
1. Red Sea**	0.6	NS	0.6	NS	0.2	NS
2. South Sinai**	0.4	NS	0.5	NS	0.1	NS

r = Spearman's rank correlation coefficient
*** The data was during the period 1995 – 2000.*

Figure 1 Time series trend of RF of bilharzial bladder cancer in the different geographic areas in Egypt



Figures (2a,b,c) illustrate the differences in the RF of bilharizial bladder cancer in each governorate between the years 1995, 2000, and 2005 through geographic information system (GIS). The changes in the colors of the different governorates reflect the changes in the RF of bilharizial bladder cancer in the different governorates in the three maps; except in Cairo, Luxor, Qalubia, Menofia, Beheira, Red Sea and South Sinai. The data of the period 1995 to 2000 in these governorates was accurate and properly collected, but, some data was dropped during collection for the period 2001-2005 in some governorates. The RF of bilharzial bladder cancer in Cairo, Alexandria, Suez, Minya, Luxor, and Domiat were significantly decreased during the period of the study (1995-2005 years). While, in Sohage, RF was significantly increased. The other governorates had no significant change in the pattern of RF of bilharzial bladder cancer (Table 2). Moreover, according to gender, there was significant decline in the RF in females in Alexandria, and in males in Suez, Domiat, Gharbia, and Ismailia. In Minya, RF was significantly decreased in both males and females. While, there was significant increase in the RF of bilharzial bladder cancer in the females in Sohage, and in males in Kafer El-Shakh.

DISCUSSION

The present study was conducted in region with a uniquely high incidence of bladder cancer and endemic urinary schistosomiasis. National Cancer Institute Cairo University (NCI) recorded that bladder cancer constitutes 30.3% of all cancers (El-Mawla et al., 2001). In Egypt, many studies proved the relationship between history of urinary schistosomiasis and bladder cancer (Mustaechi and Shimkin, 1958; Badwani et al., 1998).

Overall, the present study revealed that during the studied period (1995-2005) bilharziasis was the predominant causative agent for bladder cancer in Upper and Lower Egypt compared with the Urban areas. Urinary schistosomiasis could consider to be the main risk factor in around 50% of bladder cancer cases in Upper and Lower Egyptian governorates. So, over 50% of bladder cancer is a potential preventable disease. Groeneveld et al. (1996) suggested that effective management of bladder carcinoma would depend on the eradication of schistosomiasis, and the early detection of cancer at a curable stage. In agreement with us, Zarzour et al. (2008) found that a positive past history of bilharzial infestations was obtained from 87.7% of the cancer bladder cases included in their study (OR = 5.8, 95% CI: 3.3–10.4, $P < 0.001$).

The current study revealed that RF of bilharzial bladder cancer in Great Cairo, Alexandria, Suez, Minya, Luxor, and Domiat were significantly decreasing during the period of the study (1995-2005 years). While, in Sohage RF was significantly increasing. The other governorates had no significant change in the pattern of RF of bilharzial bladder cancer.

Recently, there is some believe in the responsibility of climate change in the difference in the ecology and the geographic distribution of schistosomiasis. Brooker (2002) proved that climate change and environmental variables may influence the distribution of schistosomiasis, as the intermediate host (snails: Bulinus, Biomphalaria, and Oncomelania) can tolerate a wide temperature range. At low temperatures, snails are effectively dormant and fecundity is virtually zero, but survival is good. At high temperatures, schistosomal egg production can be increased. However, snails are mobile and can move to avoid extreme temperatures within their habitats and water can act as an efficient insulator.

Thus, climate change may allow schistosomiasis transmission to extend its range to higher altitudes. Conversely, increasing atmospheric temperatures can decrease transmission unless the snails move to cooler refuges. Moreover, water shortages result from climate change could create greater need for irrigation, particularly in arid regions. If irrigation systems expand to meet this need, host snail populations may increase, leading to greater risk of human infection with the parasite.

In recent decades, changes in climate parameters have been observed in Egypt. The data collected by the Egyptian Meteorological Authority and local Universities indicate that there is a general trend towards warming of the air temperature, with increases in the number of hazy days, the misty days, turbidity of the atmosphere, and frequency of sand storms (Egypt-SNC, 2010). In addition, the extremely hot days of maximum temperature equaling to or exceeding 45 °C have increased in Upper Egypt from 50 days in the first decade to 52 days in the second decade, reaching 69 days in the third decade, and in the Western Desert amounted to 37 days in the third decade, compared to 22 days in each of the prior decades. The rest of Egypt did not experience increase in the number of days with a peak temperature of 45 °C or more.

In agreement with the Second National Communication for Climate Change in Egypt (Egypt-SNC, 2010), the present results has detected positive trend in the mean maximum and minimum air temperature all over Egypt. The number of days of peak temperature ≥ 45 °C were increased in Upper Egypt from 52 days to 69 days during the period of the study, but, were not changed in the rest of Egypt.

This general trend towards warming of the air temperature over Egypt can be considered as a risk factor for reduction in the distribution of S. haematobium through the Egyptian governorates. But due to the sequels to climate change, coastal zone; specially Nile Delta, are expected to suffer from the direct impacts of global climate warming through sea level rise and inundation of low elevation areas (Egypt-SNC, 2010). It is estimated that sea level rise of 50 cm combined with local Nile Delta subsidence present serious impacts on low land Delta regions. Coastal zones are also expected to suffer from indirect impacts such as salt water intrusion and contamination of ground water resources, exacerbating soil salinity and affecting food security. In addition, the increase in frequency and severity of storm surges will definitely impact coastal structures. Furthermore, coastal areas below sea level constitute high risk areas.

Thus, the direct and indirect impacts of global climate change on the Egyptian coastal zone are expected to lead

Figure (2a) Geographic Information System (GIS) of the RF of bilharzial bladder cancer Map at 1995

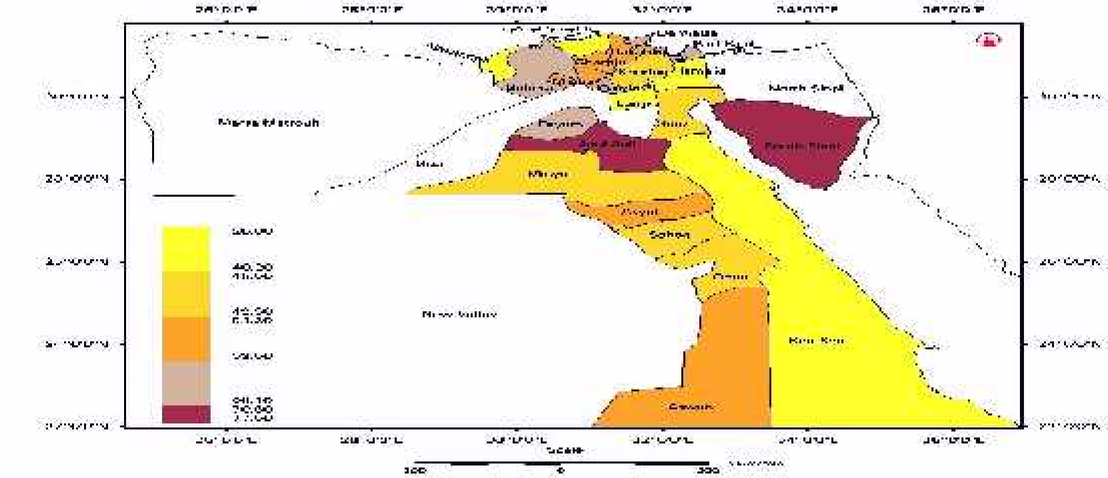


Figure (2b) Geographic Information System (GIS) of the RF of bilharzial bladder cancer Map at 1999

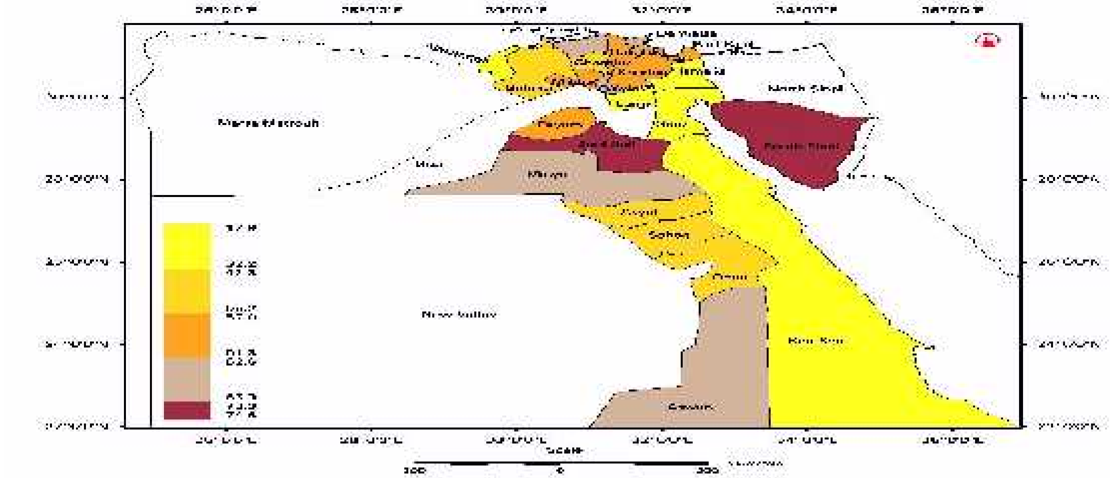
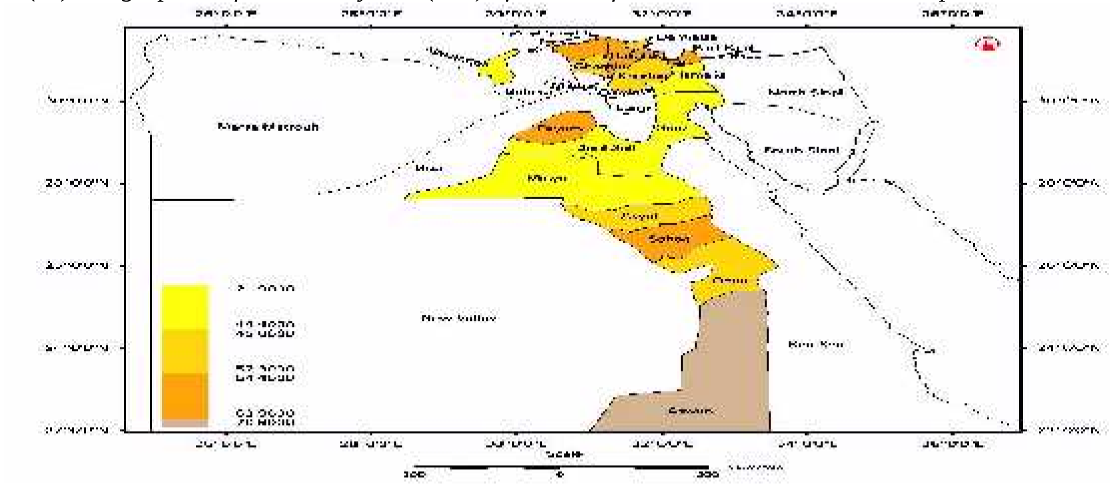


Figure (2c) Geographic Information System (GIS) of the RF of bilharzial bladder cancer Map at 2005



N.B. the data of some governorates were from 1995 to 2000 only refer to the previous tables

to the immigration of 6 to 7 million people from the Nile Delta (Egypt-SNC, 2010). So, climate change and it's sequels are suitable factors for increasing the migration of the population especially farmers from the Nile Valley and Delta to other governorates such as Urban and New governorates. This migration scenario may lead to change in the eco-geographic distribution of endemic diseases; such as schistosomiasis, and may explain the emerging and increasing in the RF of bilharzial bladder cancer in the Urban and Frontier governorates. It also may have a significant role in the reduction of the RF in the Nile Valley and Delta.

In agreement with our suggestions, World Health Organization (1998) denoted that environmental changes linked to water resources development, and increased population movements have led to the spread of schistosomiasis to previously low or non-endemic areas.

But, our suggestions need further socio-demographic researches.
Additionally, previous household surveys, noticed reduction in the prevalence of S. haematobium infestations among the Egyptian governorates (El-Sayed et al., 1995; Fawzy et al., 1996; Abdel-Wahab et al., 2000; Gabr et al., 2000). These previous studies attributed this reduction to the change in irrigation practices (El-Sayed et al., 1995), to the long-standing schistosomiasis control program (Abdel-Wahab et al., 2000) and to the repeated chemotherapy (Gabr et al., 2000). El-Hawey et al. (2000) mentioned that S. mansoni has almost completely replaced S. haematobium in most of Nile delta. It was noticed that there has been a striking change in the geographic distribution of the 2 species of Schistosoma since the construction of the Aswan High Dam 25–30 years ago (Abdel-Wahab et al., 1979; Michelson et al., 1993). They believed that this change was caused by less silt and variability in velocity and volume of water flow since construction of the dam, that resulted in an increase in S. mansoni and concomitant decrease in S. haematobium prevalence spreading from the Nile delta into Upper Egypt. This reversal in human infection rates apparently followed a similar change in abundance of snail vectors for the two parasites.
All the above factors might affect the incidence of bilharzial bladder cancer, and might explain the change in the eco-geographic distribution of schistosomiasis and bilharzial bladder cancer cases in Egypt. But, we could not exclude the direct and indirect effects of climate change. So, further epidemiological study is required.
Male-to-female bladder cancer ratios during the period of the present study, were higher among Frontier governorates, and most of Urban and Upper Egypt governorates than among Lower Egyptian Governorates, except in Ismaila. The ratio in Frontier governorates ranged from 2.5:1 to 5.5:1, in Urban governorates between 2.0:1 to 4.7:1, and in the Upper Egypt governorates between 1.4:1 to 3.4:1. While in the Lower Egypt it ranged from 1:1 to 1.9:1.
The high male to female ratio in the Frontier and Urban governorates compared to the Lower governorate may be attributed to the migration of male farmers away from the Nile Valley and Delta. While, the higher ratio in Upper Egypt may explained by the fact that women in Upper Egypt aren't equally involved in farming activities with men. Hence, they are less exposed to the risk factors of the disease that are linked to this occupation. Schistosomiasis was considered to be an occupational related disease spread frequently among farmers (Bedwani et al., 1998; el-Mawla et al., 2001).
In Upper Egypt, male to female ratio seemed to be within the same international ratio of 3:1 as mentioned by el-Mawla et al. (2001), in contrast to the result, detected by Zarzour et al. (2008), who found that male to female ratio in Upper Egypt was 5.5: 1.
Moreover, most of the previous epidemiological studies proved that males are more risky (El Katsha and Watts, 1995; Fawzy et al., 1996; Hammad et al., 1997). It has been estimated that the prevalence of schistosomal infestations among males was 2-folds that among females in Nile Delta (Gabr et al., 2000). Differences in exposure patterns to canal water among age and gender subgroups explained small portion of the variation in infestation rates (Hammad et al., 1997).
In industrialized countries, bladder cancer is strongly linked to occupational and environmental exposures to carcinogenic chemicals and, in Europe, one half of male and one third of female cases may be attributed to smoking (Zeegers et al., 2000). This may explain the current findings of the low RF of bilharzial bladder cancer in the Urban governorates in Egypt. Also, the present study, as well as Badawi et al. (1995), attributed the high incidence of bladder cancer in males than females in Egypt to the combined effect of smoking that was more frequent among males.
Moreover, in the present study the RF of bilharzial bladder cancer was significantly increasing among females during the period of the study in Sohage and non-significantly increasing in Qena and Aswan, and in four governorates in Lower Egypt (Menofia, Qalubia, Gharbia and Dakahlia).
Koraitim et al. (1995) suggested that change in male-to-female ratio is probably due to more exposure of women to schistosomal infestations than has occurred previously. The same explanation can be used in the present study, as it is suspected that there is increasing in the migration of male farmers from the Nile Valley and Delta to the Urban and Frontier governorates seeking for new jobs and safety for their families. So, the females in some of these governorates suspected to take place of their husbands in agriculture and thus they may expose to high schistosomal infestations than has occurred previously.
But this can not be the only explanation, as the situation is different in some other governorates, as the RF of bilharzial bladder cancer was decreasing in both males and females. So, there is still a question about the increased incidence of bladder cancer among females in some Egyptian governorates; that needs further ecological and socio-economic studies of bladder cancer among females in these risky governorates.
Conclusion:
Urinary schistosomiasis had attributed to around 50% of bladder cancer in most of the Upper and Lower Egyptian governorates. RF of bilharzial bladder cancer was significantly declined with time during the period 1995-2005 in almost all the included Egyptian governorates, with some variations. Climate change could explain some of these variations specially the variation according to gender.
Recommendations:
Since almost over 50% of bladder cancer cases in Egypt are due to schistosomiasis, the importance of early detection is obvious. Emphasis should be placed on the need for medical education programs aiming at early diagnosis of the disease by general practitioners and primary care medical personnel. Further socio-demographic studies are needed to clarify the receptivity of climate change.

ACKNOWLEDGMENTS:

We thank the technical staff in the selected hospitals for their ready assistance in this work.

REFERENCES

1. Abdel-Wahab MF, Esmat G, Ramzy I, Narooz S, Medhat E, Ibrahim M, El-Boraey Y, Strickland GT. The epidemiology of Schistosomiasis in Egypt: Fayoum Governorate. American Journal Tropical Medicine and Hygiene, 2000, 62 (2 Suppl): 55-64.
2. Abdel-Wahab MF, Strickland GT, El-Sahly A, El-Kady N, Zakaria S, Ahmed L. Changing pattern of schistosomiasis in Egypt, 1935–1979. Lancet, 1979; 2: 242–244.
3. Badawi AF, Mostafa MH, Probert A, O'Connor PJ. Role of schistosomiasis in human bladder cancer: evidence of association aetiological factors and basic mechanisms of carcinogenesis. European Journal of Cancer Preview, 1995, 4:45-59.
4. Bedwani R, Renganathan E, El Kwhsky F, Braga C, Abu Seif HH, Abul Azm T, Zaki A, Franceschi S, Boffetta P, La Vecchia C.Schistosomiasis and the risk of blader cancer in Alexandria, Egypt. British Journal of Cancer, 1998; 77 (7):1186-9.
5. Brooker S. Schistosomes, snails and satellites, Acta Tropica., 2002; 82:207–214
6. Egypt-CAPMAS (Egypt-Central Agency of Public Mobilization and Statistics) (2010). Population Census 2006. Online website: http://www.capmas.gov.eg/
7. Egypt-SNC (Egypt-Second National Communication, Egypt) (2010). Second National Communication Report of Egypt: submitted to the United Nations Framework Convention on Climate Change". Egyptian Environmental Affairs Agency (EEAA).
8. El Bolkainy MN. Cancer of urinary tract, in El Bolkainy MN (ed): Topographic pathology of cancer. Cairo, Egypt, National Cancer Institute, 1998; 59-63.
9. El Katsha S, Watts S The public health implications of the increasing predominance of Schistosoma mansoni in Egypt: a pilot study in the Nile Delta". Journal of Tropical Medicine and Hygiene, 1995; 98 (2): 136-40.
10. El-Bolkainy MN, Chu EW, Ghoneim MA, Ibrahim AS Cytologic detection of bladder cancer in rural Egyptian population infected with schistosomiasis. Acta Cytology, 1982; 26(3): 303-10.
11. El-Hawey AM, Amr MM, Abdel-Rahman AH, El-Ibiary SA, Agina AM, Abdel-Hafez MA, Waheeb AA, Hussein MH, Strickland GT. The epidemiology of Schistosomiasis in Egypt: Gharbia Governorate. American Journal Tropical Medicine and Hygiene, 2000, 62 (2 Suppl): 42-8.
12. El-Mawla NG, el-Bolkainy MN, Khaled HM. Bladder cancer in Africa: update. Semin Oncol 2001;28:174 – 8.
13. El-Sayed HF, Rizkalla NH, Mehanna S, Abaza SM, Winch PJ. Prevalence and epidemiology of Schistosoma mansoni and S.haematobium infection in two areas of Egypt recently reclaimed from the desert. American Journal of Tropical Medicine and Hygiene, 1995, 52(2): 194-98.
14. Fawzy AF, Abdalla HF, Oteifa NM, Abdel Maksoud MK. Prevalence of schistosomiasis and dynamics of its distribution in some villages in Qalyoubia Governorate. Journal of Egyptian Society of Parasitology, 1996, 26(1): 131-42.
15. Gabr NS, Hammad TA, Orieby A, Shawky E, Khattab MA, Strickland GT The epidemiology of Schistosomiasis in Egypt: Minya Governorate. American Journal Tropical Medicine and Hygiene, 2000, 62 (2 Suppl): 65-72.
16. Groeneveld AE, Marszalek WW, Heyns CF. Bladder cancer in various population groups in the greater Durban area of Kwazulu. Natal, South Africa. British Journal of Urology, 1996; 78(2): 205-8.
17. Hammad TA, Gabr NS, Hussein MH, Orieby A, Shawky E, Strickland GT. Determinants of infection with schistosomiasis haematobium using logistic regression. American Journal of Tropical Medicine and Hygiene, 1997; 57(4): 464-8.
18. Hodder SL, Mahmoud AA, Sorenson K, Weinert DM, Stein RL, Ouma JH, Koech D,
19. King CH. Predisposition of urinary tract epithelial metaplasia in Schistosoma haematobium infection American Journal of Tropical Medicine and Hygiene, 2000; 63(3-4): 133-8.
20. Kahan E, Ibrahim AS, El Najjar K, Ron E, Al-Agha H, Polliack A, El-Bolkainy MN. Cancer patterns in the Middle East-special report from the Middle East Cancer Society. Acta Oncol 1997; 36:631 – 6.
21. Khaled HM. Systemic management of bladder cancer in Egypt: revisited; as well as: Expert Opin Investig Drugs. J Egypt Natl Canc Inst 2005, 17(3):127-31.
22. Koraitim MM, Metwalli NE, Atta MA, el-Sadr AA. Changing age incidence and pathological types of schistosoma-associated bladder carcinoma. Journal of Urology, 1995; 154 (5): 1714-6.
23. Margison GP, Povey AC. Chemical Carcinogenesis. In: Souhami RL, Tannock I, Hohenberger P, Horiot J-C, editors. Oxford textbook of oncology.2nd ed. Oxford; 2002. p. 129 – 49.
24. Michelson MK, Aziz FA, Gamil FM, Wahid AA, Richards FO, Juranek DD, Habib MA, Spencer HC. Recent trends in the prevalence and distribution of schistosomiasis in the Nile delta region. Am J Trop Med Hyg1993; 49: 76–87.
25. Mustaechi P and Shimkin MB. Cancer of the bladder and infestation with Schistosoma haematobium. Journal of National Cancer Institute, 1958, 20: 825-42.
26. Neter J, Wasserman W, Whitmore. Applied Statistics. USA, A Division of Simon and Schuster Inc., 1992.
27. Parkin DM. (2008). The global burden of urinary bladder cancer. Scand J Urol Nephrol Suppl. 2008 Sep; (218):12-20.
28. Richter J Evolution of schistosomiasis-induced pathology after therapy and interruption of exposure to schistosomes: a review of ultasonographic studies. Acta Tropica, 2000; 77(1): 111-31.

29. Riffenburgh RH. Statistics in medicine. 2nd edit. Elsevier Academic Press, Boston. 2006.
30. Saad-Hussein A and Samia AA. Vulnerability and Adaptation of climate change: Schistosomiasis in Egypt. 3rd International Conference "Environmental Science and Technology, Egypt 2008", National Research Center, April 1-3, 2008, Egypt.
31. SNC "Second National Communication for climate change: Egypt. (2010). Report of second national communication of Egypt submitted to United Nations Framework Convention on Climate Change". Egyptian Environmental Affairs Agency (EEAA).
32. World Health Organization (1998) Schistosomiasis control: Geographic distribution. WHO Division of Control of Tropical Diseases.
33. Yosry A. Schistosomiasis and neoplasia. Contrib Microbiol. 2006; 13:81-100.
34. Zarzour AH, Selim M, Abd-Elsayed AA, Hameed DA and AbdelAziz MA (2008). Muscle invasive bladder cancer in Upper Egypt: the shift in risk factors and tumor characteristics. BMC Cancer; 8:250-5.
35. Zeegers MP, Tan FE, Dorant E, van Den Brandt PA. The impact of characteristics of cigarette smoking on urinary tract cancer risk: a metaanalysis of epidemiologic studies. Cancer 2000; 89: 630 – 9.