A Review of Bladder Cancer in Sub-Saharan Africa: A Different Disease, with a Distinct Presentation, Assessment, and Treatment

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Abstract

Background: Cancer of the bladder is the ninth leading cause of cancer in developed countries. It is the second most common urological malignancy. Transitional cell carcinoma (TCC) is the most common histological subtype in developed countries. In most of Africa, the most common type is squamous cell carcinoma (SCC). Cancer of bladder guidelines produced by the European Urological Association and the American Urological Association, including the tumor, node, and metastasis staging is focused on TCC of the bladder. Objectives: The purpose of the study is to review the pathogenesis, pathology, presentation, and management of cancer of the bladder in Africa and to use this information to propose a practical staging system for SCC. Methods: The study used the meta-analysis guideline provided by PRISMA using bladder cancer in Africa as the key search word. The study collected articles available on PubMed as of July 2017, Africa Online and Africa Index Medicus. PRISMA guidelines were used to screen for full-length hospital-based articles on cancer of the bladder in Africa. These articles were analyzed under four subcategories which were pathogenesis, pathology, clinical presentation, and management. The information extracted was pooled and used to propose a practical staging system for use in African settings. Results: The result of evaluation of 821 articles yielded 23 full-length papers on hospital-based studies of cancer of the bladder in Africa. Cancer of the bladder in most of Africa is still predominantly SCC (53%–69%). There has been a notable increase in TCC in Africa (9%–41%). The pathogenesis is mostly schistosoma-related SCC presents late with painful hematuria and necroturia (20%). SCC responds poorly to chemotherapy or radiotherapy. The main management of SCC is open surgery. This review allowed for a practical organ-based stage of SCC of the bladder that can be used in Africa. Conclusion: Bladder cancer in Africa presents differently from that in developed countries. Guidelines on cancer of the bladder may need to take account of this to improve bladder cancer management in Africa.

Keywords: Africa, bladder carcinoma, squamous cell carcinoma, transitional cell carcinoma

Résumé

Contexte: Le cancer de la vessie est la neuvième cause de cancer dans les pays développés. C’est le deuxième plus fréquent urologique malignité. Le carcinome à cellules transitionnelles (TCC) est le sous-type histologique le plus commun dans les pays développés. Dans la majeure partie de l’Afrique, le plus le type commun est le carcinome épidermoïde (SCC). Lignes directrices sur le cancer de la vessie produites par l’Association européenne d’urologie et American Urological Association, y compris la tumeur, le nœud, et la mise en scène de la métastase est axée sur le TCC de la vessie. Objectifs: Le Le but de l’étude est d’examiner la pathogenèse, la pathologie, la présentation et la gestion du cancer de la vessie en Afrique et d’utiliser cette information pour proposer un système de mise en scène pratique pour SCC. Méthodes: L’étude a utilisé la ligne de méta-analyse fournie par PRISMA en utilisant le cancer de la vessie en Afrique comme le mot clé de recherche. L’étude a recueilli des articles disponibles sur PubMed à partir de juillet 2017, Africa Online et Africa Index Medicus. Les directives PRISMA ont été utilisées pour dépister des articles hospitaliers complets sur le cancer

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de la vessie en Afrique. Ces articles ont été analysés sous quatre sous-catégories qui étaient la pathogénèse, la pathologie, la présentation clinique et la gestion. Les informations extraites ont été regroupées et utilisées pour proposer un système de mise en scène pratique à utiliser dans les contextes africains. Résultats: Le résultat de l'évaluation sur 821 articles, 23 articles complets ont été publiés sur les études hospitalières sur le cancer de la vessie en Afrique. Cancer de la vessie dans la plupart des L'Afrique est toujours principalement SCC (53% - 69%). Il y a eu une augmentation notable du TCC en Afrique (9% - 41%). La pathogénèse est principalement la SCC liée au schistosome se manifeste tardivement par une hématurie douloureuse et une nécroturie (20%). SCC répond faiblement à la chimiothérapie ou la radiothérapie. La gestion principale de SCC est la chirurgie ouverte. Cette revue a permis un stade pratique de la CEC de la vessie qui peut être utilisé. en Afrique. Conclusion: Le cancer de la vessie en Afrique présente différemment de celui des pays développés. Lignes directrices sur le cancer de la vessie Il faudra peut-être en tenir compte pour améliorer la gestion du cancer de la vessie en Afrique.

Mots-clés: Afrique, carcinome de la vessie, carcinome épidermoïde, carcinome à cellules transitionnelles

INTRODUCTION

There is a 15-fold variation in the incidence of cancer internationally. There is little written on cancer of the bladder in Africa in the literature. The predominant histological subtype of cancer of the bladder in developed countries is transitional cell carcinoma (TCC). In much of Africa, the predominant subtype continues to be squamous cell carcinoma (SCC) of the bladder. Most of the literature has focused on TCC of the bladder. The staging and treatment guidelines focus almost exclusively on TCC. Urologists and surgeons, practicing in Africa, are faced with the challenge of managing bladder cancer of SCC subtypes which presents in a different way from TCC. The aetiology of TCC is associated with working in the dye industry as well as smoking. On the other hand, SCC occurs where countries have a high burden of Schistosomiasis. TCC is common in more industrialized countries while SCC is more common in less industrialized countries. The clinical presentation of TCC is mostly with painless hematuria, while in contrast, that of SCC presents with painful hematuria, bladder mass, and necroturia. Like most urological diseases in developing countries, SCC presents late to the urologist, when the disease is already advanced with muscular invasion. In contrast, most TCC presents relatively earlier with only mucosal involvement. This may relate in part to better access to urology services and better cancer screening programs in developed countries. The management of TCC is mostly by transurethral resection of bladder tumor and bladder instillation therapy. On the other hand, SCC is managed mostly by open surgery. The bladder cancer staging in wide usage is the tumor, node, and metastasis (TNM) staging, this is more suited to TCC rather than SCC. The reason, why this is the case, is that the staging guideline is specifically for TCC (European Urological Association guidelines and AUA guidelines). In addition, the pathogenesis of TCC suggests the disease spreading layer by layer from the mucosa to the serosal layer or inward to outward. In contrast, SCC with the schistosoma eggs implanted in the perivesical plexus; the pathology may be seen to spread in an opposite direction.

METHODS

A meta-analysis was done using the PRISMA guidelines.
## Table 1: Bladder cancer studies in Africa

| Number | Country         | Study type         | n             | Epidemiology | Pathology | Presentation | Management | Source                      |
|--------|-----------------|--------------------|---------------|--------------|-----------|--------------|------------|-----------------------------|
| 1      | South Africa    | Review             | 59 publications | X            | X         | X            | X          | Heyns and van der Merwe CMF CJEU, 2008[6] |
| 2      | South Africa    | Cancer registry    | 2500 patients  | X            |           |              |            | Sutherland, 1968[17]         |
| 3      | South Africa    | Hospital based     | 650           | X            | X         |              |            | Groeneveld et al. BJU, 1996[11] |
| 4      | Zambia          | Hospital based     | 150 patients  | X            | X         | -            | -          | Bowa et al. MJIZ, 2008[10]    |
| 5      | Zambia          | Hospital based     | 53            | X            | X         | X            | -          | Mapulanga et al. MJIZ, 2012[12] |
| 6      | Zimbabwe        | Cancer registry    | 494           | X            |           |              |            | Parkin et al. CEBP, 1994[13]  |
| 7      | Zimbabwe        | Hospital based     | 483           | X            |           | X            |            | Thomas et al. JTHM, 1990[14]  |
| 8      | Nigeria         | Hospital based     | 306           | X            | X         | X            | X          | Mandong et al. NJSR, 2000[15]  |
| 9      | Nigeria         | Hospital based     | 30            | X            | -         | -            | -          | Alashan et al. AJU, 2007[16]  |
| 10     | Nigeria         | Hospital based     | 89            | X            |           |              |            | Ochicha et al. WAJM, 2003[17]  |
| 11     | Tanzania        | Hospital based     | 120           | X            | X         | X            | X          | Ngowi et al. EACJ, 2015[18]   |
| 12     | Kenya           | Hospital based     | 52            | X            |           |              |            | Waihenya and Mungai EJVS, 2004[19] |
| 13     | Malawi          | Hospital based     | 200           | X            |           |              |            | Mtonga et al. MJM, 2013[20]   |
| 14     | Sudan           | Hospital based     | 106           | X            | X         | X            | X          | Husain and Shumo SJMS, 2008[21] |
| 15     | Uganda          | Hospital based     | 83            | X            |           |              |            | Dodge, 1964[22]               |
| 16     | Senegal         | Hospital based     | 428           | X            | X         | X            | X          | Diao et al. PII, 2008[23]     |
| 17     | Morocco         | Hospital based     | 43            | X            |           |              |            | El Ochi et al. BMC, 2017[24]  |
| 18     | Egypt           | Review             | 44 publications | X            | X         | X            | X          | Shokeir BJUI, 2004[25]        |
| 19     | Egypt           | Review             | 70 publications | X            | X         | X            | X          | El-Sebaie et al. ICO, 2005[26] |
| 20     | Egypt           | Hospital based     | 180           | X            | X         | X            | X          | Awawd et al., 2012[27]        |
| 21     | Egypt           | Review             | 101 publications | X            | X         | X            | X          | Alashan et al. JENCI, 2007[28] |
| 22     | Egypt           | Hospital based     | 128           | X            | X         | X            | X          | Khalaf et al. AJU, 2008[29]   |
| 23     | Ethiopia        | Hospital based     | 60 patients   | X            |           |              |            | Biluts and Minas EACJ, 2011[30] |

## Table 2: The factors associated with bladder cancer pathogenesis in Africa

|       | SCC   | TCC   | Publication                  |
|-------|-------|-------|------------------------------|
| Schistosomiasis | 29%-85% | 10%   | Alashan et al.,[13]  Waihenya and Mungai, 2004[22] Groeneveld et al.,[23] Thomas et al.,[13] Heyns and van der Merwe, 2008[6] Diao et al.,[28] Khalaf et al.,[10] |
| Spinal injury    | 2.5%-10% |       | Heyns and van der Merwe, 2008[6]  Shokeir 7[7] |
| Smoking          | 70% smoking in Egypt | 30%-60% | Waihenya and Mungai, 2004[22] Ngowi et al.,[25] Thomas et al.,[21] |
| Industrial chemicals | 27%   |       | Heyns and van der Merwe, 2008[6]  Awawd et al.,[22] |

## Table 3: The pathology findings in cancer of the bladder in Africa

|       | SCC   | TCC   | Publication                  |
|-------|-------|-------|------------------------------|
| Site  | Solitary, bladder fundus predominantly | Multifocal | Alashan et al.,[13]  Waihenya and Mungai, 2004[22] Groeneveld et al.,[23] Thomas et al.,[13] |
| Shape | Nodular or ulcerating 83% | Bladder base predominantly | Fern-like sessile |
| Size  | >3 cm | <3 cm | El-Sebaie et al.,[13]  Heyns and van der Merwe, 2008[6]  Shokeir[7] |
| Grade | Grade 1 40-70% | Grade 2 and 3 69%-86% | Waihenya and Mungai, 2004[22] Ngowi et al.,[25] Thomas et al.,[21] |
| Stage | T3 and T4 Muscle invasive 90% | T1 and T2 Nonmuscle invasive 70%-76% | Heyns and van der Merwe, 2008[6]  Shokeir[7] |
| Lymph node spread | 2%-10% Late due to fibrosis | Early lymph node spread 17% | Khalaf et al.,[10]  Heyns and van der Merwe, 2008[6]  Shokeir[7] |

SCC=Squamous cell carcinoma, TCC=Transitional cell carcinoma

## Results

There were 821 articles identified in the data search using the term “Bladder Cancer in Africa.” Using the PRISMA guidelines, 23 articles were included in the study. The PRISMA guide in Flow Chart 1 shows the process and Table 1 shows the articles identified through this search.
Table 4: The epidemiology of cancer of the bladder key subtypes in Africa countries

| Country               | SCC                  | TCC                  | Publication                          |
|-----------------------|----------------------|----------------------|--------------------------------------|
| Zambia                | 71%-60%              | 13%  (1987)          | Bowa et al.\cite{10} Mapulanga et al.\cite{12} |
|                      |                      | 30%  (2011)          |                                      |
| Senegal               | 58%                  | 38%                  | Diao et al.\cite{29}                  |
| Nigeria               | 39%-66%              | 26%-60%              | Ochicha et al.\cite{20} Madong c et al.\cite{19} Alhasan et al.\cite{13} |
| Zimbabwe              | 52%-71%              | 21%-31%              | Heyns and van der Merwe\cite{20}      |
| Tanzania              | 18%-72%              | 20%-75%              | Heyns and van der Merwe\cite{20}      |
| Egypt                 | 53%  (1990)          | 23%  (1990)          | Heyns and van der Merwe\cite{20}      |
|                      | 23%  (2000)          | 67%  (2000)          |                                      |
| Kenya                 | 13%                  | 53%-67%              | Heyns and van der Merwe\cite{20}      |
| South Africa (Africans) | 53% (blacks)     | 30% (blacks)         | Heyns and van der Merwe\cite{20}      |
| South Africa (White)  | 2%                   | 95%                  | Heyns and van der Merwe\cite{20}      |
| South Africa (Asian)  | 18%                  | 75%                  | Heyns and van der Merwe\cite{20}      |
| South Africa (Western cape) low schisto | 6% | 79% | Heyns and van der Merwe\cite{20} |
| Ethiopia              | 5%                   | 80%                  | Biluts and Minas\cite{27}             |

SCC=Squamous cell carcinoma, TCC=Transitional cell carcinoma

Table 5: Clinical presentation of cancer of the bladder patients in Africa

|                      | SCC                  | TCC                  | Publication                          |
|----------------------|----------------------|----------------------|--------------------------------------|
| Age                  | 45-65                | 65-75                | Bowa et al.\cite{10} Alashan et al.\cite{26} Waihenya and Mungai\cite{22} Groeneveld et al.\cite{11} Thomas et al.\cite{13} Mapulanga et al.\cite{12} |
| Sex                  | 5-1                  | 2-1                  | Kalaf et al.\cite{10} Heyns and van der Merwe\cite{6} Shokeir\cite{7} |
| Symptoms             | Painful Hematuria     | Painless Hematuria   | Waihenya and Mungai\cite{22} Groeneveld et al.\cite{11} Thomas et al.\cite{13} Diao et al.\cite{29} |
| Necroturia           | 80%-95%, bladder mass 46% | 90%                  |                                      |
| Clinical stage       | T2-T4 (MIBC)         | T1 (NMIBC)           | Heyns and van der Merwe\cite{20} Ngowi et al.\cite{23} Rambau et al.\cite{28} Shokeir\cite{7} |
|                      | 60%-98%              | 49%                  |                                      |

SCC=Squamous Cell Carcinoma, TCC=Transitional Cell Carcinoma, MIBC=Muscle-invasive bladder cancer, NMIBC=Nonmuscle-invasive bladder cancer

Pathogenesis
The review identified four key factors associated with bladder cancer in Africa. The key factors are listed in Table 2.

Pathology
The review itemized the key aspects of the pathology of the bladder in Africa which highlighted the site, the shape, the size, the grade, the stage, and lymph node spread. This is shown in Table 3. In addition, Table 4 highlights the subtype and proportion by African country.

Presentation
Table 5 shows the clinical presentation of the patients based on age, sex, symptoms, and clinical stage.

Management
Table 6 shows the management of each major subtype with the three key parameters of surgery, chemotherapy, and radiotherapy.

Table 6: Management of cancer of the bladder in Africa

|                      | SCC                  | TCC                  | Publication                          |
|----------------------|----------------------|----------------------|--------------------------------------|
| Open surgery (cystectomy, partial cystectomy or diversion) | 75%-50% | Uncommon | Waihenya and Mungai\cite{22} Groeneveld et al.\cite{11} Thomas et al.\cite{13} Diao et al.\cite{29} Alashan et al.\cite{13} |
|                      | 5 years survival     |                      |                                      |
| Radiotherapy         | Radioreistant         | Radioreponsive       | Heyns and van der Merwe\cite{6} Ngowi et al.\cite{23} Rambau et al.\cite{28} Shokeir\cite{7} |
| Chemotherapy         | Chemoresistant        | 30%-60%              | Waihenya and Mungai\cite{22} Groeneveld et al.\cite{11} Thomas et al.\cite{13} Diao et al.\cite{29} Alashan et al.\cite{13} |
| TURBT (endoscopic)   | 90% with 5 years survival |                     | Shokeir\cite{7} Heyns and van der Merwe\cite{6} |
| Inoperable           | 27% fixed tumor       |                      | Heyns and van der Merwe\cite{6} Diao et al.\cite{29} |

SCC=Squamous cell carcinoma, TCC=Transitional cell carcinoma, TURBT=Transurethral resection of bladder tumor

Discussion
The results show that SCC in Africa is still largely associated with schistosomiasis infection in up to 85% of cases. However, there is a changing pattern of SCC which is being influenced by smoking, industrialization, and schistosomiasis control.\cite{21-24} It has been noted, particularly in Egypt, that there has been an increasing habit of smoking, which is associated with
an increased risk of cancer of the bladder. With increased
schistosoma control, industrialization, and westernized
lifestyles, the relative proportions of SCC and TCC are
changing in favor of TCC.[25-27] There are notable changes
in the proportion of SCC and TCC across individual African
countries. In particular in Tanzania, where regions which are
close to inland freshwater lakes continue to have high relative
proportions of SCC relative to areas further away.[28,29] In South
Africa, they are marked differences across racial groups such as
native populations, Asian, colored, and expatriate populations.
In general, there appears to be a high proportion of SCC among
native black population groups, where SCC is as high as 53%.
In contrast among the Asian, colored, and white populations,
SCC represents only 18%, 6%, and 2%. This may be related
to genetic, social, and behavior factors.[28-30]
The pathology shows that SCC tends to be focally locate as an
ulcerative and nodular mass in the bladder fundus. The mass being
usually >3 cm in size at first presentation.[31-33] The SCC is also
muscle invasive in 80% of cases at the time at first presentation.[34]

In contrast, TCC tends to be multifocal small and papillary like
with little or no muscle invasion at first presentation.[35] SCC
also has a lower grade usually Grade 1 when patients are first
seen in the hospital.[35] TCC on the other hand tends to be of
Grade 2 or 3 at first presentation. TCC also spreads early to the
lymph nodes, whereas SCC spreads late possibly due to fibrosis
of the lymphatic channels caused by the schistosoma eggs.[35,36]

In SCC, only in 2% to 10% is lymph node spread observed.[35,36]
In clinical presentation, patient with SCC tends to be younger
and male. In contrast, TCC has a higher proportion of females
and presents in an older age group.[35,36] The most frequent
clinical presentation of TCC is of painless hematuria, in a person
older than 40 years of age. With SCC, the patient presents
with painful hematuria associated with irritative symptoms,
necroturia, or a bladder mass.[37,38] In relation to treatment,
the two subtypes of cancer of the bladder tend to be treated
very differently. Closed surgery by transurethral resection
is most frequent mode in TCC, and this is supplemented by

1. Stage 1 - Cancer less 3cm in longest width not invading
   the serosa (no fixity)
2. Stage 2 - Cancer greater than 3cm in longest diameter with
   ureteric invasion (Hydronephrosis) (no fixity).
3. Stage 3 - Cancer less 3cm involving the trigone area not
   invading the serosa (no fixity).
4. Stage 4 - Cancer which has invaded the serosa.
   a. With partial fixity
   b. With complete fixity
5. Stage 5 systemic disease

Box Chart 1: Cancer which has invaded the serosa. (a) With partial
fixity. (b) With complete fixity

Figure 1: Cancer <3 cm in longest width not invading the serosa (no fixity)

Figure 2: Cancer >3 cm in longest diameter with ureteric
invasion (hydronephrosis) (no fixity)

Figure 3: Cancer <3 cm involving the trigone area not invading the
serosa (no fixity)
chemotherapy and radiotherapy depending on the tumor grade. On the other hand, SCC is generally radio- and chemoresistant. It is managed mainly by open surgery with partial or total cystectomy. TCC has a better 5-year survival of about 90% in 5 years compared to SCC which has a 5-year survival of close to 70%. Up to 27% of SCC may be fixed and inoperable, especially if located below intraureteric bundle of Mercier.

Staging

The differences in the pathogenesis, pathology, clinical presentation, and management between the two common subtypes of cancer of the bladder in Africa suggest that the approach to the two may need to be varied. In particular, while the TNM classification is well suited to the staging of TCC, it may not be as well suited to SCC. The TNM is a histological-based staging, which focuses on the luminal spread of the cancer across the bladder wall. This is better and easily applied to TCC. However, with SCC, an organ-based staging is more suitable of SCC. The Africa papers appear to suggest that SCC is locally invasive and spread along the bladder from the fundus to the bladder neck area. Therefore, the staging instead of being transmural should be vertical from the fundus to the bladder neck. Box Chart 1 shows an organ-based staging, which follows the method of cancer spread. Figure 1 is a small cancer <3 cm confined to the bladder fundus. Figure 2 is cancer >3 cm without involvement of the ureters or the serosa. Figure 3 is cancer which has invaded either one or both ureters. Figure 4a is cancer which has invaded the serosa or the Trigone area of the Bladder. This cancer is only partially fixed. Figure 4b is cancer that has invaded the pelvic organs and is fixed. Figure 5 is distant metastasis.

Most cases of bladder cancer in Sub-Saharan African countries are predominantly SCC subtype. In developed countries, on the other hand, SCC is uncommon while TCC represents over 90% of bladder cancer type. The main causes of bladder cancer in developed countries are smoking and industrial chemicals. In many developing countries, however, there has been a notable increase in the proportion of TCC with the increase in industrialization. In spite of this change, SCC continues to be the predominant subtype in much of Sub-Saharan Africa. It occurs especially in predominantly high burdened schistosomiasis areas. It is proportionately a disease of men and presents at a mean age of 50 years. On the other hand, TCC presents a decade later with an almost equal male-to-female ratio. The SCC presents late with painful hematuria or other bladder symptoms. This is in contrast to TCC which presents earlier with painless hematuria and with minimal symptoms. In over 70% of cases, the bladder muscle wall is invaded at the time of presentation, while in TCC, over 90% of cases present with nonmuscle invasive disease. In practice, most urologists in Africa will use an organ-specific staging to plan for bladder cancer management due to this early muscular invasion.

Conclusion

SCC has little or no pelvic node involvement at presentation. In contrast, TCC spreads early to pelvic nodes, once it has invaded the muscle wall. SCC is mostly radioresistant and does not respond to chemotherapy. TCC, on the other hand, shows a good response to radiotherapy, bacillus Calmette-Guérin or mitomycin instillation, and chemotherapy. This study proposes a simple practical organ-based staging based on current knowledge of SCC pathology in Africa.

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Conflicts of interest

There are no conflicts of interest.
REFERENCES

1. Ploeg M, Aben KK, Kiemenej LA. The present and future burden of urinary bladder cancer in the world. World J Urol 2009;27:289-93.
2. American Cancer Society. Global Cancer Facts & Figures 3rd ed. Atlanta: American Cancer Society; 2015.
3. Chavan S, Bray F, Lorlet-Tieulent J, Goodman M, Jemal A. International variations in bladder cancer incidence and mortality. Eur Urol 2014;66:59-73.
4. Serretta V, Pomara G, Piazza F, Gange E. Pure squamous cell carcinoma of the bladder in western countries. Report on 19 consecutive cases. Eur Urol 2000;37:85-9.
5. Ahmadi M, Ranjbaran H, Amiri MM, Nozari J, Mirzajani MR, Azadkhah M, et al. Epidemiologic and socioeconomic status of bladder cancer in Mazandaran province, Northern Iran. Asian Pac J Cancer Prev 2012;13:5053-6.
6. Heyns CF, van der Merwe A. Bladder cancer in Africa. Can J Urol 2008;15:3899-908.
7. Shokeir AA. Squamous cell carcinoma of the bladder: Pathology, diagnosis and treatment. BJU Int 2004;93:216-20.
8. El Ochi MR, Oukabli M, Bouaifi E, Chadhi H, Boudhias A, Allaloui M, et al. Expression of human epidermal growth factor receptor 2 in bladder urothelial carcinoma. BMC Clin Pathol 2017;17:3.
9. Hassan TM, Al-Zahrani IH. Bladder cancer: Analysis of the 2004 WHO classification in conjunction with pathological and geographic variables. Afr J Urol 2012;18:118-23.
10. Khalaf I, El-Mallah E, Elsotouhi I, Abu-Zeid H, Elmeligy A. Pathologic pattern of invasive bladder carcinoma: Impact of schistosomiasis. Int J Clin Oncol 2005;10:20-5.
11. Khalaf I, El-Mallah E, Elsotouhi I, Abu-Zeid H, Elmeligy A. Pathologic pattern of invasive bladder carcinoma: Impact of schistosomiasis. Int J Clin Oncol 2005;10:20-5.
12. Raghavan D, Shipley WU, Garnick MB, Russell PJ, Richie JP. Biology and management of bladder cancer. N Engl J Med 1990;322:1129-38.
13. Hassan TM, El-Mallah E, Elsotouhi I, Abu-Zeid H, Elmeligy A. Pathologic pattern of invasive bladder carcinoma: Impact of schistosomiasis. Int J Clin Oncol 2005;10:20-5.
14. Groeneveld AE, Marszalek WW, Heyns CF. Bladder cancer in various population groups in the greater Durban area of Kwazulu-Natal, South Africa. Br J Urol 1996;78:205-8.
15. Mapulanga V, Labib M, Bowa K. Pattern of bladder cancer at university teaching hospital, Lusaka, Zambia in the era of HIV epidemic. Med J Zambia 2012;39:22-6.
16. Thomas JE, Bassett MT, Sigala LB, Taylor P. Relationship between bladder cancer incidence, schistosoma haematobium infection, and geographical region in Zimbabwe. Trans R Soc Trop Med Hyg 1990;84:551-3.
17. Mohammed AZ, Edino ST, Ochicha O, Gwarzo AK, Samaila AA. Cancer in Nigeria: A 10-year analysis of the Kano cancer registry. Niger J Med 2008;17:280-4.
18. Ghoneim MA, el-Mekresh MM, el-Baz MA, el-Attar IA, Ashamallah A. Radical cystectomy for carcinoma of the bladder: Critical evaluation of the results in 1,026 cases. J Urol 1997;158:393-9.
19. El-Bolkainy MN, Mohammed NA, Hussein MH. The impact of schistosomiasis on the pathology of bladder carcinoma. Cancer 1981;48:2643-8.
20. Zaghloul MS, Bladder cancer and schistosomiasis. J Egypt Natl Canc Inst 2012;24:151-9.
21. Martin JW, Carballido EM, Ahmed A, Farhan B, Dutta R, Smith C, et al. Squamous cell carcinoma of the urinary bladder: Systematic review of clinical characteristics and therapeutic approaches. Arab J Urol 2016;14:183-91.
22. Prudnick C, Morley C, Shapiro R, Zaslau S. Squamous cell carcinoma of the bladder mimicking interstitial cystitis and voiding dysfunction. Case Rep Urol 2013;2013:924918.
23. Izard JP, Siemens DR, Mackillop WJ, Wei X, Leveridge MJ, Berman DM, et al. Outcomes of squamous histology in bladder cancer: A population-based study. Urol Oncol 2015;33:425.e7-13.
24. Aswad H, El-Baki HA, El-Bolkainy N, Burgers M, El-Badawy S, Mansour M, et al. Pre-operative irradiation of T3-carcinoma in bilharzial bladder: A comparison between hyperfractionation and conventional fractionation. Int J Radiat Oncol Biol Phys 1979;5:787-94.
25. El-Sebai M, Zaghloul MS, Howard G, Mokhtar A. Squamous cell carcinoma of the bilharzial and non-bilharzial urinary bladder: A review of etiological features, natural history, and management. Int J Clin Oncol 2005;10:20-5.