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Review

Genitourinary Cancer Care in Low- and Middle-Income Countries: Disparities in Incidence and Access to Care

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Abstract: Despite the considerable global burden of urologic malignancies, Low- and middle-income countries (LMICs) often encounter significant challenges in caring for patients with urologic malignancies. Several interrelated factors impact cancer care in LMICs, which face significant challenges that hinder effective diagnosis, treatment, and management of disease. Socioeconomic and healthcare infrastructure limitations are fundamental issues leading to the disparity observed in cancer care across the globe. This review aims to evaluate the challenges and disparities in access to comprehensive urologic care in LMICs, emphasizing the impact of such global disparities on incidence rates, timely diagnoses, and access to comprehensive care as it relates to prostate, kidney, and bladder cancers.

Keywords: health disparities; low- and middle-income countries; access to care; prostate cancer; kidney cancer; bladder cancer; urologic oncology

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1. Introduction

Urologic cancers, including prostate, bladder, and kidney cancer, pose significant health challenges globally. Timely detection, prompt treatment, and access to appropriate interventions help optimize outcomes and decrease mortality. In low and middle-income countries (LMICs), access to comprehensive urologic cancer care is a critical contributor to patient outcomes. According to the World Bank, low-income countries have a gross national income (GNI) per capita of $1045 or less, lower-middle-income countries range from $1046 to $4095, and upper-middle-income countries fall between $4096 and $12,695. The countries in this review are spread across all continents, with most low-income countries in Africa and Southeast Asia and middle-income countries mainly in South America and the Middle East [1] Several interrelated factors impact cancer care in LMICs, which face significant challenges that hinder effective diagnosis, treatment, and management of disease.

Socioeconomic and healthcare infrastructure limitations are fundamental issues leading to the disparity observed in cancer care between LMICs and high-income countries (HICs). Routine screening practices commonly observed in HICs are often not implemented in LMICs due to limited resources. This leads to lower reported incidence rates but consequently delayed detection and advanced presentations of malignancies. Unfortunately, the availability of resources necessary for delivering evidence-based treatments, such as access to care, equipment, newly approved therapies, and information technology infrastructure, is often lacking in LMICs [2,3].

In this review, we sought to evaluate and highlight the challenges and disparities in access to comprehensive urologic care in LMICs, emphasizing the impact on incidence rates, delayed diagnoses and presentations, and access to care for prostate, kidney, and bladder cancer.

2. Methods

2.1. Search Criteria

A literature search was performed systematically by two authors, KS and JG, reviewing abstracts and publications describing access to urologic care in LMICs utilizing the World Bank definition.

The computerized search was performed utilizing the PubMed, Google Scholar, and Scopus databases, utilizing key terms that included "kidney cancer", "bladder cancer", and "prostate cancer" and "LMIC", "Low-income county", middle-income country", "low and middle-income country". Additional search was performed with key terms including "access to care", "surgery", "radiation", "oncology", and "clinical trial". No language or article-type restrictions were included in the search, but results were limited to those published in 1980 or later and were available in the English language for review. All titles that were populated were uploaded onto an Excel spreadsheet, and the titles were reviewed for potentially relevant studies. The abstracts of all potentially relevant studies were evaluated, after which a subset was chosen for full-text review. We performed cross-reference searches to include articles that may not have been found in previously stated databases when matching our criteria and keywords.

2.2. Study Criteria

See Figure 1 for the diagram outlining the study selection process. These articles were screened by title against predetermined criteria by two independent reviewers, with disagreement resolved by consensus. To be eligible, articles had to meet the following inclusion criteria: (1) included relevant information regarding lower or middle-income countries, (2) studies in the field of urologic oncology. Exclusion criteria included: (1) provided no data regarding access to urologic care in lower and middle-income countries; (2) studies for which only an abstract could be retrieved; and (3) studies unavailable in the English language. After the removal of duplicate articles, a total of 177 were selected for abstract review, and subsequently, 45 articles were selected for full-text review.

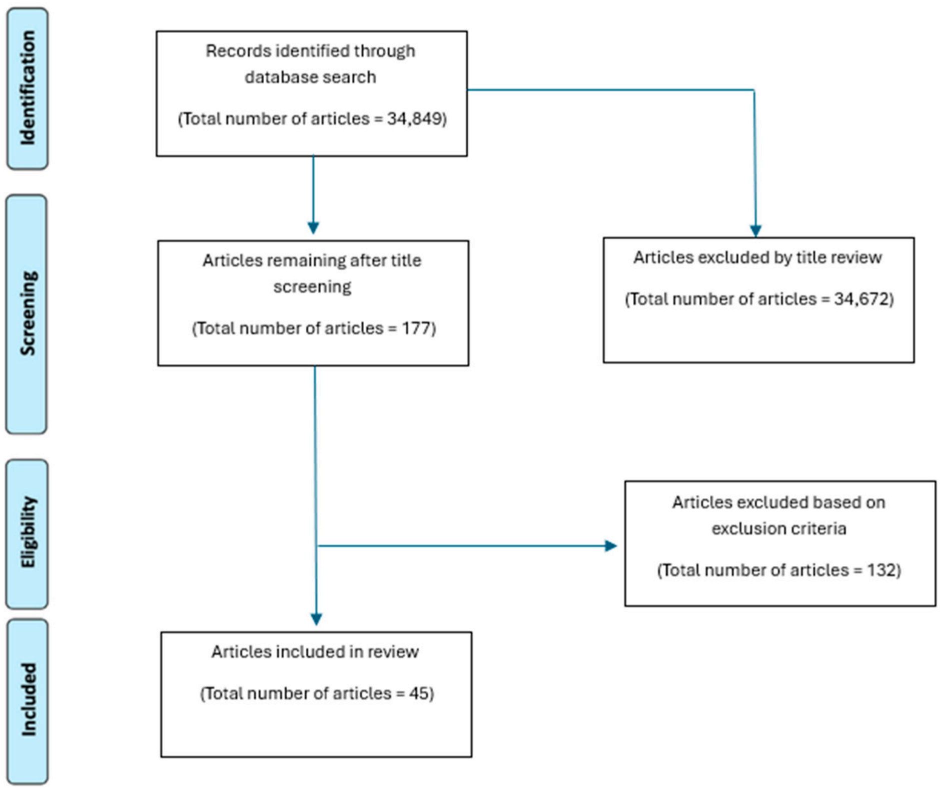

Figure 1. Preferred reporting items for systematic reviews and meta-analyses diagram.

3. Prostate Cancer

Prostate cancer has the 2nd highest incidence of solid organ malignancies worldwide. The risk of prostate cancer increases with age and is most prevalent in countries with higher levels of human development index (HDI) and greater overall development [4]. In these countries, there are longer life expectancies, which consequently increases the likelihood of disease occurrence and diagnosis.

While a lower incidence of prostate cancer is reported in LMICs, patients often present with advanced disease. This suggests that limited disease screening is the cause of decreased incidence rates. A retrospective review assessing prostate cancer presentation in Middle Eastern countries reported a median age of prostate cancer detection of 70 years, with 54% of patients diagnosed with stage IV disease and an average PSA level of 84 ng/mL at the time of diagnosis [5]. The lack of early diagnosis is attributed to the lack of disease awareness and routine PSA screening throughout the Middle East [6] In contrast, Lebanon possesses greater access to tertiary referral centers and as such, reports the highest incidence of prostate cancer among Middle Eastern countries with an age-standardized rate (ASR) of 39.3 per 100,000 [7]. This data demonstrates that access to tertiary-level care can impact screening rates and diagnosis.

There also exists a disparity within LMICs based on proximity to urban centers. Within India, urban cities report a higher incidence of prostate cancer as compared to rural cities, suggesting that the prostate cancer screening rate is higher in urban areas [8]. Africa also displays significant variability in incidence and mortality rates of prostate cancer. A retrospective analysis revealed that prostate cancer incidence in Northern Africa was about 13.2 cases per 100,000 individuals in 2018. In contrast, Central and Southern Africa showed a notably higher incidence at 35.9 and 64.1 cases per 100,000 individuals, respectively, in 2018 [9].

Limited access to routine screening can negatively affect patient outcomes. A retrospective analysis conducted in China revealed that the mortality-to-incidence ratio for prostate cancer was 0.57, which is significantly higher than in North America (0.13) [10]. The authors inferred that most prostate cancers were diagnosed on digital rectal exams or diagnostic imaging, with fewer cases diagnosed based on PSA. This discrepancy suggests that most cases in China were diagnosed in advanced stages, leading to lower survival rates. Similar data has been demonstrated in other LMICs. A comparison of prostate cancer incidence between India and the United States revealed the former to be 5.0–9.1 per 100,000/year, compared to 110.4 per 100,000/year for White Americans and 180.9 per 100,000/year for African Americans [11]. In these populations, 85% of prostate cancers in India were detected at stages III and IV, compared to only 15% in the United States [11]. Notably in the Middle East, a retrospective review assessing treatment modalities for prostate cancer found that 20% of patients with localized disease opted against active surveillance or treatment [5]. This is in stark contrast to available data from the Surveillance, Epidemiology, and End Results Program for prostate cancer management [12]. It is unclear whether socioeconomic, cultural, or access to health care are reasons to explain the high proportion of patients electing to forego guideline-directed management of prostate cancer.

4. Kidney Cancer

Kidney cancer is the 14th most common malignancy globally, with roughly 400,000 new cases diagnosed annually [13]. Kidney cancer is found to have a higher incidence in North America and Europe and higher incidence is found in regions with high median incomes. ASR for incidence in Europe, and North America is approximately 8.3–12.2/100,000 annually, while ASR for incidence was significantly lower across LMICs in Asia, Africa, and South America, ranging from 1.0 to 5.2/100,000 annually. Variations in kidney cancer detection also exist within LMICs. A retrospective review of patients with renal malignancies in Jordan and Iraq revealed a median age of diagnosis at 56 years of age. Most cancers were diagnosed due to hematuria, with significantly lower rates of incidentally diagnosed tumors [14]. In this population, only 16% of malignancies were found incidentally in comparison to neighboring Saudi Arabia, where approximately 57% of kidney cancers are diagnosed incidentally [15]. Much of this variability in incidence between HIC and LMIC is hypothesized to be due to the widely available access to imaging in HICs. This leads to higher rates of incidental diagnosis of small renal masses during imaging conducted for other purposes.

ASR for mortality from kidney cancer remains the highest in North America and Europe, with relatively lower rates of mortality in LMICs [13]. While there is no obvious cause for higher ASR mortality rates in HICs as compared to LMICs, the overall mortality rates in HICs have been decreasing, likely due to access to immunotherapy used in advanced kidney cancer. Due to the disparity in detecting renal masses between HIC and LMIC in relation to limited access to cross-sectional imaging, it is challenging to interpret kidney cancer mortality to incidence rates between nations, as the incidence in HIC has increased with time due to incidental findings on imaging. Other factors that may impact this disparity in kidney cancer incidence and outcomes include the prevalence of risk factors within populations. Similar to bladder cancer, tobacco smoking is an established and modifiable risk factor for kidney cancer, with a pooled RR in smokers for incidence and mortality of 1.31 and 1.23, respectively [16]. Obesity and hypertension are additional risk factors that are associated with kidney cancer [17]. Such risk factors vary within geographic location and likely contribute to variations in kidney cancer incidence and mortality rates.

Assessing kidney cancer burden in China from 1990 to 2019 showed increasing trends in incidence and mortality rates, albeit with a lower burden compared to global averages. Modifiable risk factors like smoking and high BMI contributed significantly to disability-adjusted life-years. Wang et al. proposed that the rising incidence may stem from China's aging population, while mortality rates showed slower growth likely due to incidental findings and improved treatments [18]. In sub-Saharan Africa, kidney cancer is diagnosed at a mean of 47 years of age after an average duration of symptom onset to presentation of 17.6 months. Delayed diagnosis led to advanced disease presentations, with patients presenting with locally advanced to metastatic tumors averaging 15.1 cm in size [19].

5. Bladder Cancer

Bladder cancer ranks 9th among all solid organ malignancies in incidence. Globally, a higher incidence and mortality occur in nations with a higher HDI as well as a higher Gross Domestic Product (GDP) per capita [20,21]. Current data demonstrates a worldwide ASR for incidence of 9.0 and 2.2 cases per 100,000 in men and women, respectively. Nations with high and very high HDIs have a male ASR for an incidence of 10.8–16.7 cases per 100,000, whereas nations with low and medium HDIs have a male ASR for an incidence of 3.1 and 4.7 per 100,000. While much of Asia has relatively low incidence and mortality rates, the Middle East, including North Africa, has disproportionately high incidence and mortality rates of the disease. Similar to Asia, the incidence and mortality rates are relatively low in Central America, South America, and Africa [20].

It is well known that one modifiable risk factor for bladder cancer is tobacco smoking, with about half of all cases of bladder cancer being associated with tobacco use [22]. A 2015 meta-analysis identified a pooled relative risk of bladder cancer incidence and mortality in smokers being 2.58 and 1.47, respectively [16]. It is no surprise that the higher prevalence of bladder cancer may be seen in higher HDI countries due to their historically increased prevalence of tobacco use [20]. A unique disease entity with an established association with squamous cell carcinoma of the bladder is *S. haematobium* urinary tract infection, which is endemic in Africa. The annual incidence of bladder cancer in individuals infected with *S. haematobium* is about 3–4/100,000 [23]. A retrospective study found that in Egypt from 2001 to 2010, there was a significant decrease in squamous cell bladder cancer incidence (73 to 25%) within the country that followed a trend of decreased incidence of schistosomal infection. Intriguingly, the incidence of urothelial carcinoma of the bladder during the same period demonstrated a significant increase in incidence (20 to 66%) [24].

In Middle Eastern LMICs, bladder cancer presents a significant health concern, with an age-standardized incidence rate (ASIR) of 9.9/100,000, surpassing the global ASIR [25]. Among 22 Arab countries, LMICs like Egypt, Tunisia, and Libya exhibited the highest age-standardized mortality rates (ASMR) at 7.8, 5.2, and 5.0 per 100,000, respectively [26]. In contrast, India showed a notably lower ASIR at 3.57/100,000, with a male-to-female ratio of 4:1 compared to 8.9:1 in the Middle East [26,27]. China demonstrated ASIRs below the global average at 5.16/100,000 in 2019, with an ASMR of 2.23/100,000 [28]. Across Africa, ASIRs varied regionally, with Northern, Western, and Southern Africa showing rates of 8.2, 2.6, and 4.2 per 100,000, respectively. Corresponding ASMRs were 5.5, 2.0, and 2.7 per 100,000 [29]. Unlike other LMICs, bladder cancer in Africa predominantly presents as squamous cell carcinoma, with schistosomiasis playing a significant role in its prevalence [29].

In the USA, localized disease is seen in 93% of patients at initial presentation, with 4% presenting with metastatic disease [30,31]. Similar data from LMICs is sparse, with a 2022 Iranian study showing an 8% country-wide incidence of metastasis at presentation [32]. While such data cannot be applied broadly to all LMICs, this higher incidence of metastatic presentation is likely due to underlying issues with access to care encountered across LMICs.

6. Access to Surgical Care

While there is sparse data quantifying access to urologists in LMICs, there is data on overall access to surgical care. In a study by Holmer et al. examining the global surgical, anesthetic, and obstetrical workforce, the investigators demonstrated that of the 1.1 million surgical specialists globally, only 19% are found within LMICs. Of particular contrast is the difference in the density of surgeons per region, with a ratio of 0.7 and 5.5 per 100,000 in low-income countries and LMICs, respectively, as compared to 56.9 surgeons per 100,000 in HICs [33]. In order to identify and target the needs of global surgery, the Lancet Commission on Global Surgery was initiated in 2014. While their takeaways are regarding surgery globally, their findings are pertinent to global urological oncology needs. The Commission estimates that about 5 billion individuals globally "do not have access to safe, affordable surgical and anesthesia care when needed" and "33 million individuals face catastrophic health expenditure due to payment for surgery and anesthesia each year" [34]. With this in mind, it is imperative to expand access to surgical care, and in particular urologic care within LMICs.

In HICs, localized prostate cancer management typically entails a choice of radiation and androgen deprivation therapy versus radical prostatectomy. The same remains true in LMICs; however, access to either treatment modality incurs a substantial prohibitive step for many patients. Radical prostatectomy has historically been the preferred treatment for localized prostate cancer in most sub-Saharan African countries. However, even though it is cost-effective, many eligible patients are still unable to access care due to a shortage of expertise in this area [19]. In HICs, treatment of metastatic prostate cancer involves systemic therapy, but this is not financially feasible for most LMICs. While sparsely used in the USA, surgical castration, with bilateral orchiectomy, remains a cost-effective and low-risk procedure for symptomatic control in LMICs and still has prominent utility in sub-Saharan Africa [35].

A significant proportion of surgical treatment for urologic cancers is dependent on endoscopy. Endourologic care for bladder cancer, amongst other urologic pathologies, was investigated between LMICs and HICs. Watson et al. used sub-Saharan Africa as a surrogate for LMICs globally and investigated barriers to transurethral operations. The authors identified factors impacting access to transurethral surgery, which included a lack of equipment, the need to reuse disposables, and the need for patients to purchase certain key equipment, such as irrigant fluid [36].

While there is no consensus statement by national urologic associations on the development and progression of robotic surgery, this modality of surgery has become a mainstay in the USA and other HICs. The rationale for using robotic platforms includes data supporting shorter hospitalization, lower blood loss, and fewer complications. Advocates for robotic surgery in LMICs point to further advantages such as reducing surgical site infections due to smaller incisions, allowing for faster discharges and minimizing overcrowding of already strained hospitals. The current limitation in expanding robotic surgery in LMICs is the significant upfront financial burden the equipment incurs. It is further challenged by the need to train local surgeons in this modality [37]. Currently, Middle Eastern countries have access to about 1% of global installations of the da Vinci® Surgical Systems (Intuitive Surgical Inc., Sunnyvale, CA, USA). This includes 19 systems in Saudi Arabia, six in Qatar, two each in Kuwait and Lebanon, three in the United Arab Emirates, and one in Egypt [38]. Similarly, LMICs in Asia have a scarcity of da Vinci® Surgical Systems, with a total of 26 systems in China, 20 in India, 7 in Singapore, 3 in Malaysia, 2 in the Philippines, 1 in Indonesia as of 2013 [39]. Variations among Low- and Middle-Income Countries (LMIC) are evident in Turkey, where the presence of over 32 robotic Da Vinci systems reflects advancements in healthcare technology; this increased prevalence may be attributed to improved educational systems that enhance medical training and health policies prioritizing investment in advanced medical infrastructure [40]. There is a potential to offset such limited access to minimally invasive technologies with the development of more affordable robotic platforms.

7. Access to Radiation Therapy Care

The same limitations for prostate cancer patients seeking radiation therapy can be inferred for bladder cancer patients seeking bladder sparing or palliative radiation or kidney cancer patients in search of palliative radiation. Access to radiation centers in LMIC is low, with 29% of low-income countries and 65% of low-middle-income countries offering radiation services [41]. Access and growth of facilities is limited by financial constraints, lack of reliable electricity, challenges with transport of patients from rural centers to centralized hubs, and adequately trained staff, be it physicians, physicists, or nurses [42]. A retrospective review of prostate cancer management in Central Africa revealed that although resources for radiation therapy are available, most patients bear the costs for screening, diagnosis, and treatment. Radiation therapy faces constraints due to equipment shortages and clinical proficiency [35]. Moreover, the necessity for recurrent treatments entails travel and time off work, which is beyond reach for some patients.

8. Access to Medical Oncology Care

Barriers to accessing medical oncology care in LMICs exist. The cost of novel systemic treatments is prohibitive, with many low- and middle-income countries unable to afford or offer these therapies. A survey of clinical practice patterns and consensus amongst urologists and medical oncologists in Southeast Asian countries revealed that a major limiting factor to patients obtaining necessary diagnostics and treatment was the financial burden due to a lack of publicly funded healthcare [43]. In a systematic review of the number of oncologists globally, the majority of African nations identified were seen to have patient-to-oncologist ratios (>1000) that far exceeded the USA and much of Europe (<150). In 40% of Asian nations, ratios exceed 500 patients per oncologist, and in 5 out of 7 Latin American countries, ratios exceed 150 patients per oncologist. Additionally, no oncologists existed in 7 African and one Asian nation, further exemplifying limited access [44].

9. Access to Clinical Trials

While there is widespread and robust infrastructure for clinical trials in HIC, there is much to be desired within LMICs. A retrospective cohort study of phase 3 oncologic trials was conducted by Wells et al. The authors identified only 8% of clinical trials being led by LMICs, of which most studies were smaller and their results published in lower impact factor journals [45]. Another major resource for cancer care is access to cancer registries. In sub-Saharan Africa in particular, there is a paucity of cancer registries, present in only

25 of 46 countries. Even in those with registries, the data tends to be skewed towards city centers, and a limiting step in the efficient function of registries is access to funding and support [43]. The concern of the above findings is the potential for lack of generalizability of studies published from HIC populations and their applicability to LMICs.

10. Limitations

A key limitation in our review article is that income alone cannot explain the challenges and quality of urologic cancer care, as factors like health policies, literacy rates, and geography also create significant variations among LMICs, even those classified as middle-income [40]. In several lower- and middle-income countries (LMICs), life expectancy rates are observed to be similar to or even slightly exceed those of certain high-income countries, including the United States; however, it is important to note that data obtained from the literature on various LMICs may not be directly comparable due to differences in methodologies, healthcare infrastructure, and demographic factors [40].

11. Conclusions

Differences in access to comprehensive urologic cancer care between LMICs and HICs underscore the pressing need for concerted global efforts to address these disparities. Despite the considerable global burden of urologic malignancies, LMICs often encounter significant challenges in promptly detecting and accessing suitable interventions, resulting in delayed diagnoses and advanced disease. Screening practices, commonly observed in HICs, are not routinely implemented in LMICs due to socioeconomic constraints. This disparity highlights the critical importance of targeted interventions to enhance access to care in LMICs while considering the financial implications.

In addressing the pitfalls in the management of urologic cancers in LMICs, it is evident that improvement in access to surgical, medical, and radiation therapies is paramount. With only a fraction of global surgical specialists located in LMICs, disparities in healthcare infrastructure exacerbate the struggle to provide adequate treatment. Barriers to endourologic and robotic surgery are limited by access to technology, financial constraints, and training. Access to radiation therapy faces similar hurdles, with limited facilities and resources. The shortage of oncologists further compounds these challenges, highlighting the need for increased investment in healthcare infrastructure to facilitate equitable access to care. Through comprehensive strategies focused on screening and developing infrastructure, we can strive to reduce the burden of urologic malignancies and improve outcomes for patients in LMICs.

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