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A Five-year Survey of Cancer Prevalence in Sudan

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Abstract. *Background: While cancer epidemiology is well-investigated in developed countries, the cancer burden in Africa is less well documented. We provide cancer statistics of 33,201 patients from all Sudan diagnosed at the Radiation and Isotope Centre in Khartoum (RICK). This hospital covers approximately 80% of patients with cancer in Sudan and is, therefore, considered representative for the situation in this country. Materials and Methods: Data from 2009-2013 were collected at RICK. Cancer diagnoses were made by standard pathological and radiological methods. Epidemiological data were categorized by age, gender, resident state, marital status etc. and subjected to statistical analyses by SPSS 21v. Results: The cancer prevalence rate per year was 5,000-7,000 among adults and 300-400 among children, with increasing tendency for adults. Male:female ratios were 1:1.18 for adults and 1.46:1 for children. The five most frequent tumour types were breast cancer, leukaemia, prostatic carcinoma, lymphoma and colorectal carcinoma in adults and leukaemia, lymphoma, eye tumours, sarcoma and brain tumours in children. Remarkably, the median age of cancer diagnosis was 10-20 years higher in men than in women, mainly due to earlier onset of gender-related tumours in females (cancer of breast, cervix, or ovary) than in men (prostatic carcinoma). Chronic myeloid leukaemia was the most frequent haematopoietic malignancy in adults and acute lymphoblastic leukaemia in children. Comparing cancer cases with population numbers of Sudanese states, Northern Sudan, River Nile and Khartoum revealed up to 8-fold higher cancer incidence rates than Al Gedarif, Southern Dafur and Blue Nile. The other states had intermediate incidence rates. Interestingly, oesophageal carcinoma occurred proportionally more frequently in Kassala (rank 3) than in the entire Sudan (rank 7) or other states. Conclusion: This is the largest survey on cancer burden in Sudan. It may serve as basis for governmental programmes for assessing risk factors, improving cancer prevention (e.g. by educational and vaccination programmes) and cancer therapy in the future.*

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Cancer is one of the leading causes of death worldwide. It is estimated that the global cancer burden will even grow in years to come and will reach 21.4 million new cases and 13.2 million deaths by 2030 (1). According to a projection of the World Health Organization, cancer is considered as the second cause of death in developing countries (10.4%), whereas it is the first cause of death in developed countries (26.6%) (2). In Africa, about 681,000 new cases and 512,400 deaths were reported in 2008 (1). Thus, cancer poses a tremendous burden for the health system, as well as the entire economy, throughout Africa because of both treatment costs and drop-out of working power of patients.

Sudan is the third-largest country in Africa, located in the Northeast of the continent, with the Nile river as its most noticeable geographical feature. It is surrounded by seven countries, namely Egypt, Libya, Central African Republic, Chad, South Sudan, Ethiopia and Eritrea. Sudan is well-described as an Afro-Arabian country because of its rich amalgamation of ethnic, social and cultural diversity. As of 2013, the Sudanese population is estimated at about 36 million.

Sudan's cancer burden is not well-documented because the attention of the health system mainly focuses on communicable diseases such as malaria, tuberculosis and human immunodeficiency virus (HIV)/AIDS, which is comparable to all developing countries in Africa. A survey of Sudanese hospitals conducted in 2000 revealed that cancer

was the third leading cause of death after malaria and viral pneumonia, accounting for 5% of all deaths (3). Most published data on cancer in Sudan are small hospital-based case studies (4, 5). The main sources of cancer data are: the Radiation and Isotope Center in Khartoum (RICK), located in the national capital Khartoum, Khartoum State and the National Cancer Institute of the University of Gezira in Wadmadani, Capital of the Gazira State, both centres are located in the densely populated center of Sudan (6). A National Cancer Registry was established in 2009 to collate cancer data into a single centrally accessible system (7). However, large and reliable datasets on cancer incidence and mortality in Sudan are still lacking.

In the present cross-sectional study, we describe cancer prevalence in Sudan with the RICK as the source of information for the years 2009-2013. To the best of our knowledge, this represents the largest study yet, in which more than 33,000 cancer cases were involved. We provide statistics on this large number of patients in order to obtain reliable estimations on cancer prevalence in this country. Moreover, we identified a geographical hotspot for oesophageal carcinoma in Kassala, one of the Sudanese states. The long-term goal of our efforts is to recommend an action plan for the future improvement of cancer prevention and treatment in Sudan.

Materials and Methods

Population demographics of Sudan. According to Sudan's Central Bureau of Statistics, the Sudanese population was estimated to reach 36,163,778 in 2013. The age structure consisted of 40.8% below the age of 14 years, 52% aged between 15-54 years and 7.2% above 55 years. The average age was 58 years for males and 61 years for females. The population growth rate was 2.8% with equal distribution between genders (male:female ratio of 1.02:1). The urbanisation rate was 33.2% (www.cbs.gov.sd). Major ethnic groups are Arab, Fur, Beja, Nuba and Fallata living in 15 Sudanese states.

Data source. No population-based cancer study currently exists for Sudan. The cancer health facilities in Sudan consist of the governmental sector (RICK, National Cancer Institute of the University of Gezira, and National Health Laboratories), which provides broad services for patients with cancer, including diagnosis, hospitalisation, follow-up and treatment (chemotherapy, hormonal, palliative and radiotherapy treatment). The sector of private hospitals plays a minor role and is restricted to chemotherapy of patients with cancer. RICK was established in the early 1960s as the second African cancer treatment centre after South Africa. RICK is under direct auspices and supervision of WHO. The data of the present study were collected from RICK records. Our selection of RICK was based on the fact that it serves as referral cancer hospital for all of Sudan. Moreover, it is well-established and its facilities include cancer diagnosis and therapy using chemotherapy and radioactive isotopes, in addition to nuclear and clinical departments, with all necessary cancer expertise. Cancer cases were diagnosed and identified at RICK by standard pathological and radiological methods (histopathology, imaging techniques), immunohistochemistry and molecular markers.

Statistical analysis. Data were cross-checked for duplication and inaccurate entries. The cancer cases were summed into nine age groups: 0-15 years, 16-25 years, 26-35 years, 36-45 years, 46-55 years, 56-65 years, 66-75 years, 76-85 years and 86 years and older (days between age groups are counted within the years at the end of each interval). All patients were further categorized as follows: occupation (unemployed, students, housewives, employees in the governmental sector, workers, employees in the education sector, police/military, traders, drivers, farmers/shepherds, doctors, and medical assistants), education (not educated, primary school, secondary school, graduate, and post-graduate), marital status (not married, married, widow, and divorced) .

Regression analyses were carried-out for age, gender, occupation, education, marital status, tribe and resident state against cancer types using SPSS 21v (IBM Corporation, Armonck, NY, USA). Cross-tabulation analysis was used to calculate the prevalence rate using Excel 2013 (Microsoft, NNY, USA).

Results

A total of 33,201 patients with cancer were included in this study. The prevalence rate per year was in the range of 5,000-7,000 cancer cases for adults and 300-400 for children (Figure 1). Among adults, slightly more females were diagnosed with cancer than males (ratio 1.18:1; Figure 1A). By contrast, fewer girls than boys suffered from tumours (1:1.46; Figure 1B). During the investigated time frame (2009-2013), the annual number of newly-diagnosed tumours increased among adults, but remained more or less stable in children.

Figure 2 depicts the frequency of all diagnosed cases according to their tumour type in adults and children from 2009 to 2013. A total of 43 tumour types and locations were diagnosed by standard pathological and clinical procedures. Histological subtypes of tumours were summarised to the corresponding main tumour type. For example, Hodgkin and Non-Hodgkin lymphoma were listed as "lymphoma", acute/chronic myeloic/lymphoblastic leukaemia as "leukaemia", epithelial tumours at different locations in the head region as "head and neck tumours" and so on. The five most common tumour types in adults were breast cancer, leukaemia, prostatic carcinoma, lymphoma and colorectal carcinoma (Figure 2A). The top five tumour types in children were leukaemia, lymphoma, eye cancer, sarcoma, and brain tumour (Figure 2B).

Focusing on the age of patients with cancer at diagnosis revealed interesting gender-related differences. The median age of men at diagnosis was 56-65 years, while it was 36-45 years in women (Figure 3A). This may, at least in part, be due to the later onset of prostatic carcinoma (median age=66-75 years) compared to breast cancer (median age=36-45 years) and cervical and ovarian carcinoma (median age=56-65 years) (Figure 3B).

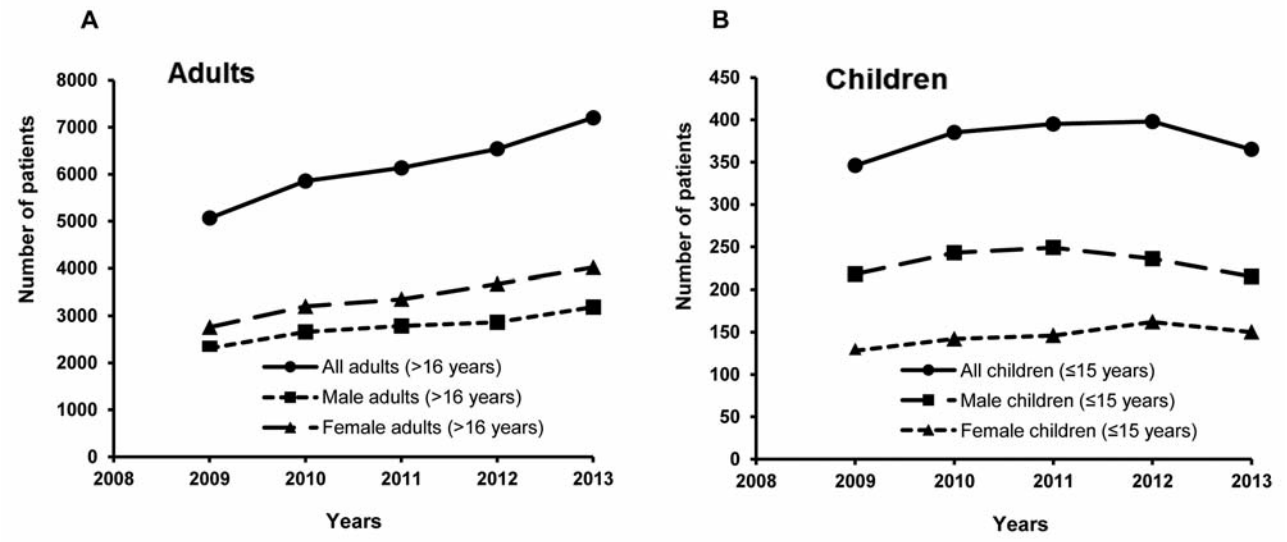

Figure 1. *Cancer prevalence from 2009 to 2013 in (A) adults and (B) children.*

When the tumour distribution was specified according to gender, the gender-related tumour types were top ranked, *i.e.* prostatic carcinoma as most frequent male tumour (Figure 4A) and breast, cervical and ovarian carcinomas as leading female tumours (Figure 4B). These tumour types were followed by leukaemia, lymphoma and colorectal carcinoma in men and leukaemia, oesophageal carcinoma and lymphoma in women. The frequency distribution of tumour types did not differ much between boys and girls (≤15 years of age). Taking leukaemia as an example, we investigated the distribution of tumour subtypes and found that chronic myeloid leukaemia was the most frequent haematopoietic malignancy among adults and acute lymphoblastic leukaemia among children (Figure 4, insets). This distribution was independent of gender.

Taking the numbers of the total populations of the different Sudanese states for the year 2009 into account (www.cbs.gov.sd), we calculated the percentage of cancer diagnoses per state. Remarkably, the cancer incidence differed considerably between the states. Northern Sudan, River Nile and Khartoum had much higher incidence rates than Al Gedarif, Southern Dafur and Blue Nile. For example, the percentage of cancer diagnoses in the total population was 8-fold higher in Northern Sudan than in Blue Nile.

Next, we analyzed whether the proportional frequency of tumour types in the Sudanese states differed from those in Sudan as a whole. Oesophageal cancer occurred proportionally more frequently in Kassala (rank 3, Figure 5B) than in the whole of Sudan (rank 7, see Figure 2).

In addition to the relationship between the number of patients with tumour and their age (see Figure 4), we found a significant correlation between the number of cancer cases, marital status and the occupation of patients. Four categories of marital status and 12 categories of occupations were recorded at the time of diagnosis. Cancer was significantly more frequently diagnosed among those who were married, whereas housewives and labourers (workers and farmers/shepherds) were more frequently diagnosed than among any other occupation for females and males, respectively. We surmised that these sub-groups of marital status and occupation significantly correlated with cancer cases were not social or professional risk factors but rather could be due to highly dominant classes in Sudanese society.

Discussion

We report on 33,201 cancer cases recorded at RICK between 2009 and 2013. This is the largest study yet on the burden of cancer in Sudan. It extends an older study on more than 10,000 patients at RICK from 1967-1984 (4). The most frequent types of cancer in adults were breast cancer, leukaemia, prostatic carcinoma, lymphoma and colorectal carcinoma. The prevalence of these tumour types in Sudan is partly different from that of developed countries. While breast and prostatic carcinoma belong to the top leading cancer types worldwide and in the U.S.A. (8, 9) leukaemia and lymphoma occurred much more frequently than in the U.S.A. On the other hand, lung cancer as the second leading cause of morbidity and top leading cause of mortality in the U.S.A. (9) ranks only 13th in Sudanese men and 27th in Sudanese women.

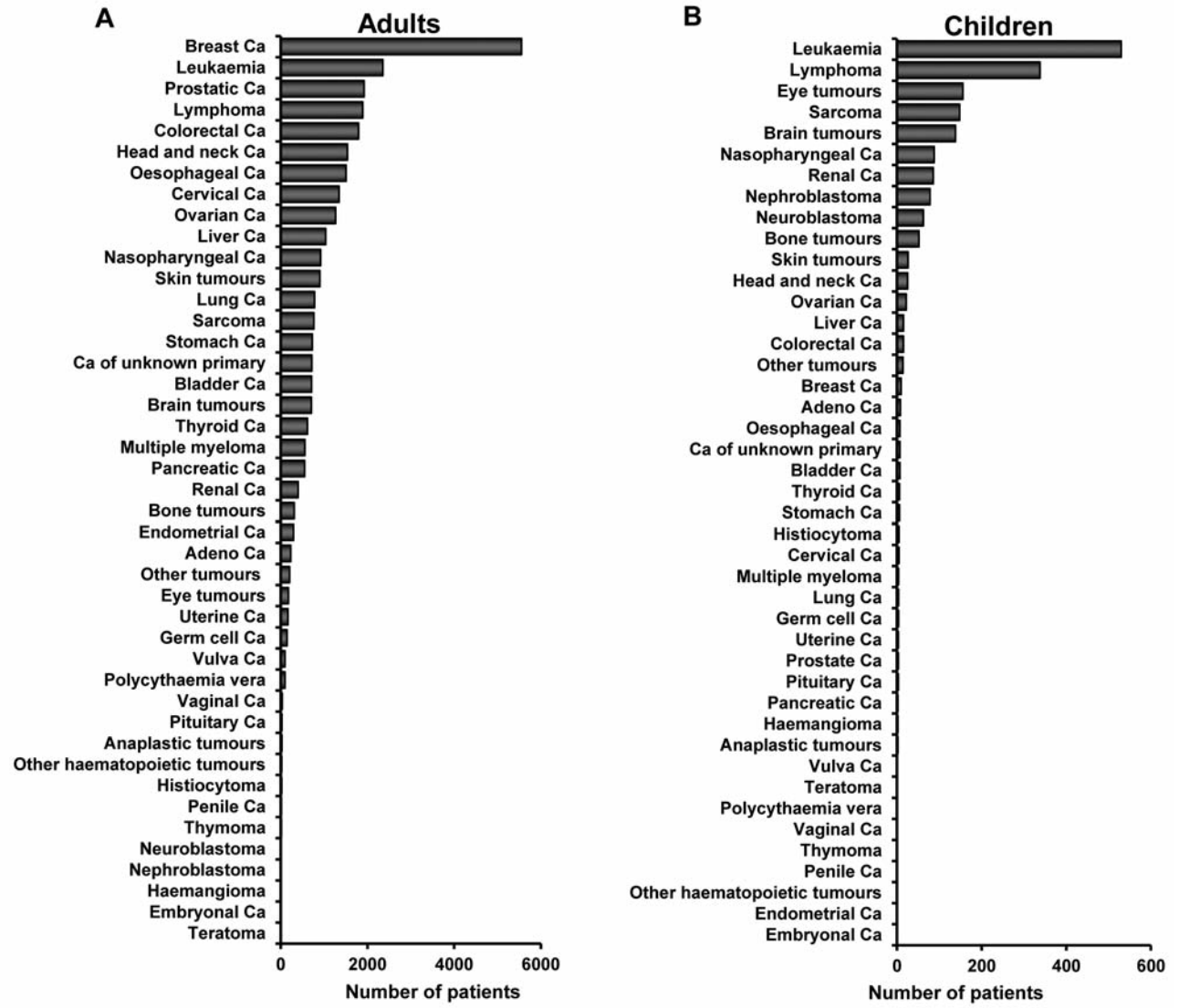

Figure 2. *Prevalence of different tumour types from 2009-2013.*

Although some risk factors for breast cancer may be similar in Sudan and industrialised countries (*e.g.* obesity, early menarche, increased detection awareness, late and few births), which may be attributed to increase in urbanization rate and economic development in developing countries, breast cancer occurs one decade earlier in Arab countries and is frequently more advanced at diagnosis than in western countries (10, 11). Risk factors for the high prevalence of prostatic carcinoma and colorectal carcinoma may be obesity, a fat-rich diet *etc*. Interestingly, human papillomavirus (HPV) infection may also be involved in the development of breast and colorectal carcinoma (12). The reason for the low frequency of lung carcinoma may be that cigarette smoking is not that common in Sudan compared to the U.S.A. and other developed countries. This result in accordance with the low frequency of lung cancer in the Arab world (13). On the other hand, epithelial head and neck cancer (including oral tumours) and oesophageal carcinoma ranked 6th and 7th in Sudan and were more frequent than in the U.S.A. (9). Rather than cigarette smoking, tobacco is traditionally used in Sudan in a moist form called *toombak*, with widespread use among Sudanese males (14, 15). Tobacco nitrosamines may be released during consumption and may account for the high numbers of oral and oesophageal tumours (16). HPV also contributes to head and neck tumours in Sudan (12, 15). The uncommonly high prevalence of leukaemia and lymphoma is difficult to explain. Although some haematopoietic malignancies are

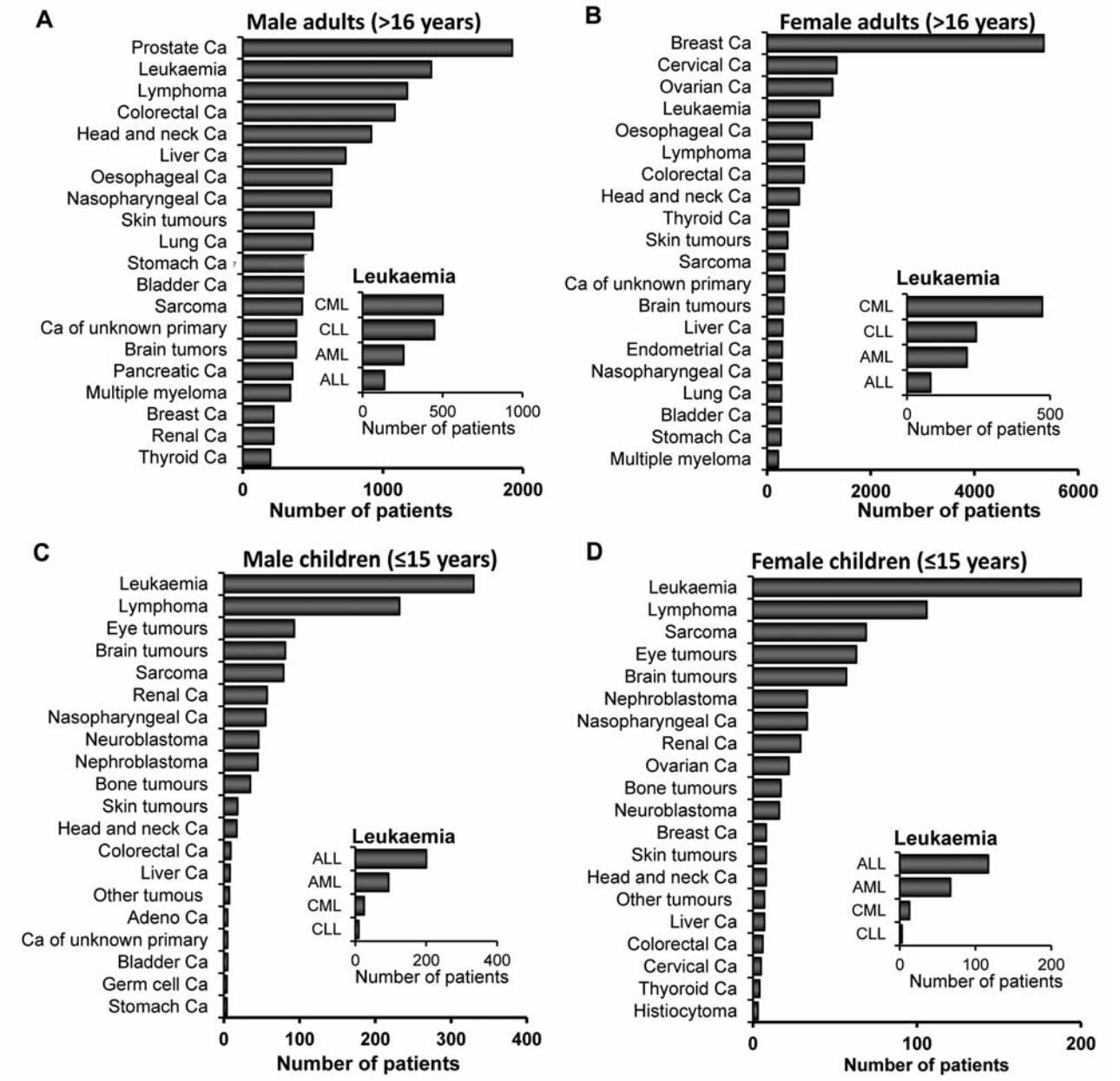

Figure 3. *Age-adjusted cancer prevalence in males and females (A) and of gender-related tumour types (prostatic, breast, cervical, and ovarian carcinoma) (B).*

virally induced, *e.g*. Burkitt lymphoma by Epstein-Barr virus (EBV) and non-Hodgkin lymphoma by HIV, the aetiology of the majority of leukaemia and lymphoma types is unknown (17). Among leukaemia, chronic myeloid leukaemia was the most frequent haemoblastosis in Sudan. This is different from industrialized countries (9). Breakpoint cluster region–ABL proto-oncogene 1 (*BCR–ABL*) rearrangements are well-known genetic aberrations in chronic myeloid leukaemia. Interestingly, the frequencies of BCR–ABL rearrangements in the Sudanese population demonstrated distinct profiles compared to other geographical regions (18).

HPV contributes to the development of cervical carcinoma, being among the most frequent tumour types in females in sub-Saharan Africa (19). High-risk HPV genomes have also been identified in patients with cervical carcinoma from Sudan (20-22). In the present study, it ranked second after breast cancer. Screening and prevention programs may help reduce the number of patients with cervix carcinoma in the

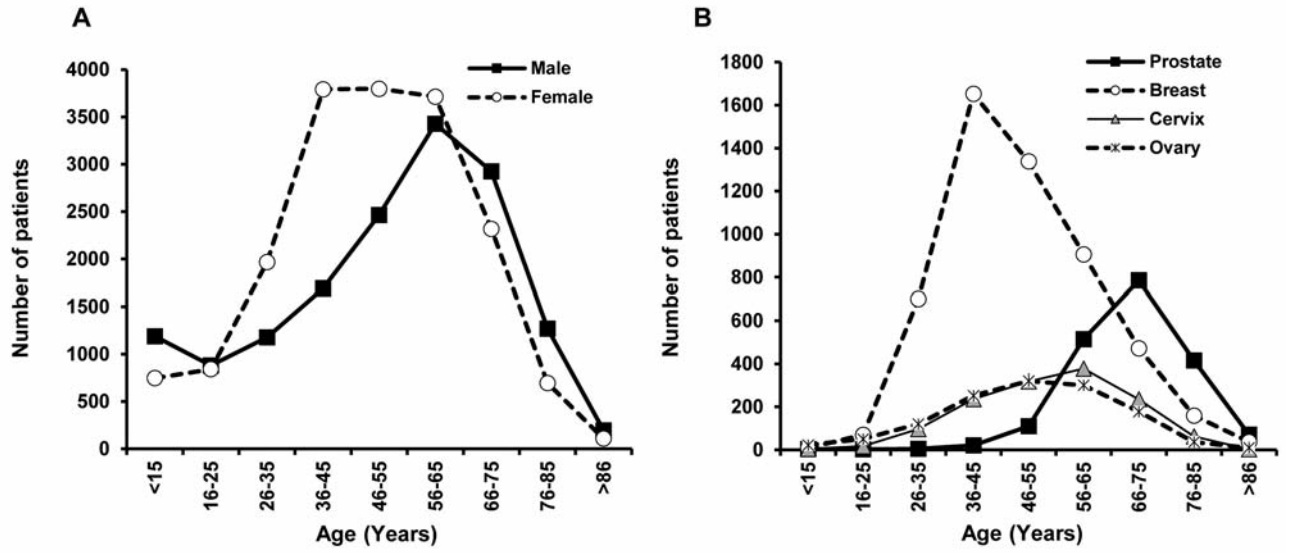

Figure 4. *Gender-related cancer distribution in adults (A, B) and children (C, D). ALL: Acute lymphoblastic leukaemia; AML: acute myeloid leukaemia; CLL; chronic lymphocytic leukaemia; CML: chronic myeloid leukaemia.*

future (23, 24). Other tumour types with viral involvement are liver cancer (hepatitis B virus and hepatitis C virus) and nasopharyngeal carcinoma (HPV and EBV) (25, 26). Causal agents in addition to viruses for liver cancer are aflatoxin and contaminated foods, as well as schistosomal infections (27).

A striking result was that the onset of cancer in women occurred on average at earlier ages than in men, a result that was correlated with the earlier onset of breast, cervical, or ovarian cancer compared to prostatic carcinoma. Comparable observations have been published for several Arab nations. Najjar *et al*. found that the average age at presentation of breast cancer in Arab countries is a decade earlier than in Western countries (28).

The most frequent childhood cancer types were leukaemia, lymphoma, eye cancer, sarcoma and brain tumours. Typical childhood tumours, such as nasopharyngeal carcinoma, nephroblastoma and neuroblastoma, were also among the top 10 frequent tumour types. These data are in accordance with older Sudanese data from 1967-1984 (29). The role of viral carcinogenesis also has to be considered for paediatric tumours, *e.g*. EBV for leukaemia and HPV for nasopharyngeal carcinoma (20).

The reason for some Sudanese states (*e.g*. Northern Sudan, River Nile, Khartoum) having higher percentages of cancer diagnoses in the total population than other states (*e.g*. Blue Nile) remains unknown. It can be speculated that the degree of urbanisation accompanied by changes in lifestyle and environmental pollution might play a role. More detailed analyses are required to identify the corresponding risk factors. We found a high prevalence of oesophageal cancer in Kassala, while other authors reported predominance of this tumour type among females in Gezira (30). Risk factors for oesophageal tumours include alcohol intake and maize-based diet contaminated with fungi that produce mycotoxins (fumonisins), which are known carcinogenic agents since they produce nitrosamines (31).

In Arabian culture, marriages between cousins are not uncommon. Therefore, it was interesting to observe that marriage among cousins was not associated with higher tumour prevalence.

Despite the large number of patients included in our study, several limitations have to be discussed: The study was based on data of one single Sudanese hospital (RICK) and a bias in patient recruitment cannot be excluded. Therefore, our data should be confirmed by population-based studies in the future. Another disadvantage is that data on cancer mortality were not available. This should be considered by future follow-up studies to allow comparisons between survival prognoses in Sudan and in industrialized countries. Deficiencies in current treatment protocols will be a starting point to improve survival times of patients with cancer in Sudan. Finally, we cannot exclude that some patients suffering from cancer did not present at RICK, giving cause for data bias. Stigmatization of patients with cancer as well as severe poverty among the Sudanese population may prevent consultation of physicians at RICK. This is a potentially unresolved problem that has to be addressed by educational and healthcare programmes in the future.

In conclusion, the present study demonstrates that cancer is an increasingly serious problem. On the one hand, governmental programmes should focus on identification and assessment of risk factors in order to

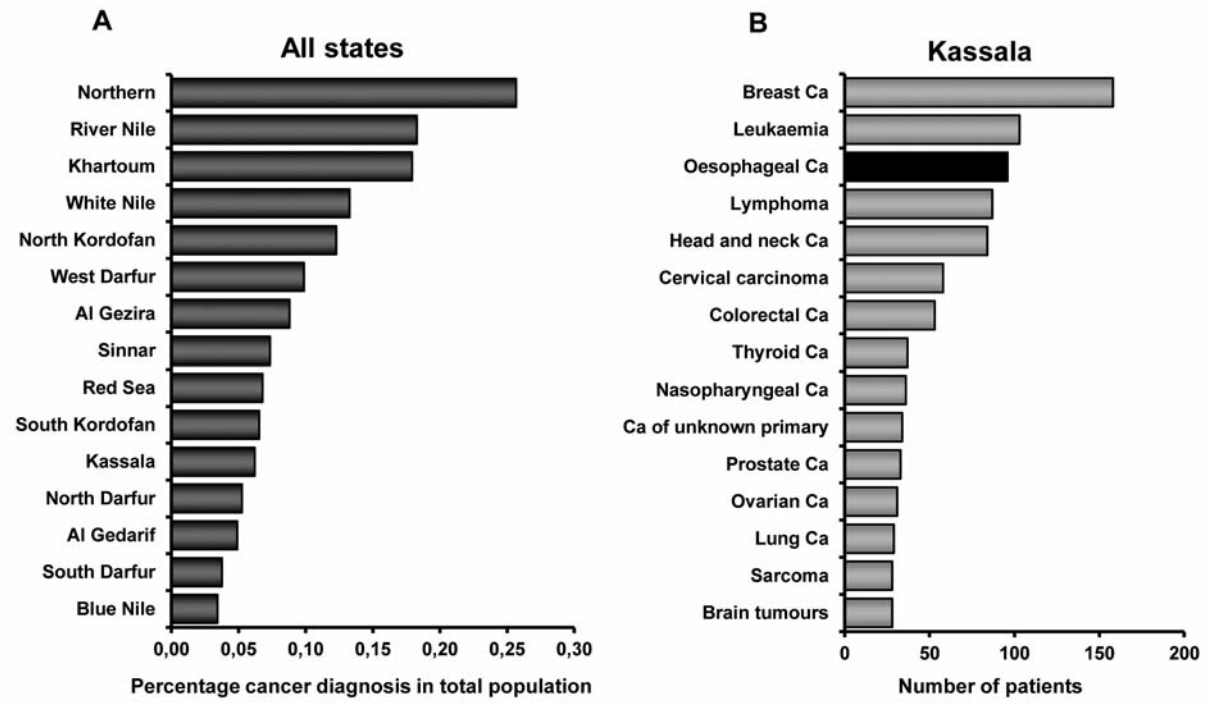

Figure 5. *Cancer prevalence in Sudanese states in 2009. A: Prevalence of all tumour types; B: the tumour types in Kassala (highlighting that oesophageal tumours were more frequent in Kassala than in the entire Sudan, see Figure 2).*

improve cancer prevention. Vaccination programmes will reduce the incidence of virally-induced tumours such as those of the cervix, liver, nasopharynx, and others. Educational programmes will further support preventive endeavours to change unhealthy lifestyles. On the other hand, treatment options for patients with cancer should be improved to prolong their survival times. This is especially true for the significant killers such as breast cancer, leukaemia, lymphoma, prostatic cancer and colorectal carcinoma.

Conflicts of Interest

The Authors declare that there is no conflict of interest with regard to this study.

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