Cancer in the Sudan: An overview of the current status of knowledge on tumor patterns and risk factors

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1. Introduction

The Sudan, the largest and most diverse country in Africa, is experiencing a growing cancer problem, but little is presently known on tumor patterns, cancer epidemiology and ethnic or environmental cancer risk factors. The Sudan has no national population-based cancer registry. The main sources of cancer data are the hospital-based case series at the National Health Laboratory and the Radiation and Isotope Center in Khartoum, which published the latest Cancer Registry (SCR), which was based on histopathologically-confirmed cases diagnosed mainly at the National Health Laboratories in Khartoum, formerly known as Stack Medical Research.

While infectious diseases are still the main concern of the health care system, the Sudan, as most sub-Saharan African countries, needs to face a predicted increment in cancer incidence because of the progressively rising life expectancy, the wide diffusion of cancer-related infections, and the mounting pollution due to urbanization and spread of intensive agriculture and industrialization (Parkin et al., 2008; Sitas et al., 2008). As in other sub-Saharan African countries, the cancer patterns would be predicted to reflect population demography, such as shorter life expectancy and young population structure, and exposures to a variety of risk factors, associated with both traditional and new lifestyles (Ikpatt et al., 2002; Morris, 2003; Parkin et al., 2003; Gondos et al., 2005; Hamad, 2006; Kerr and Kerr, 2006; Porter, 2008). However, very little is known about cancer in Sudan (Morris, 2003; Hamad, 2006; Kerr and Kerr, 2006; Awadelkarim et al., 2010).

The Sudan has no national population-based cancer registry. The main sources of cancer data are the hospital-based case series at the only two oncological centers of the country, both located in the densely populated Central Sudan, i.e., the Radiation and Isotope Center in Khartoum (RIC), Khartoum State (Fig. 1), and the National Cancer Institute of the University of Gezira (NCI-UG) in Wad Medani, Gezira State (formerly “Institute of Nuclear Medicine Molecular Biology & Oncology”, INMO) (Fig. 1). In addition, from the early sixties (1960s) to the early eighties (1980s), there was the Sudan Cancer Registry (SCR), which was based on histopathologically-confirmed cases diagnosed mainly at the National Health Laboratories in Khartoum, formerly known as Stack Medical Research.
Laboratories. Until 1978, this was the only center providing histopathology services for the entire Sudan, and pathology reports were sent by telegraph to peripheral medical facilities contributing specimens from all the Sudanese states (Awadelkarim et al., 2010). This allowed to build up cancer series from the entire Sudan. Gradually regional histopathology laboratories were established, the first of them at the University of Gezira in 1978. The records of the SCR are now part of the National Health Laboratory (Hickey, 1959; INMO Annual Report, 2001, 2006; Awadelkarim et al., 2010).

In 2006 the NCI-UG, with the support of the International Agency for Research on Cancer (IARC), established the Gezira Cancer Registry, which is the first population-based cancer registry in the country. The Gezira Cancer Registry, located at the NCI-UG in Wad Medani, the capital city of Gezira State, covers only Gezira State (Central Sudan, 26,075 km²), serving about four million people (10% of the total Sudanese population). Most recently, in the year 2009, also the Sudanese Federal Ministry of Health established a population-based cancer registry named “Sudan Cancer Registry”.

During the year 2000, cancer was the third of the identified leading causes of death in Sudanese hospitals, after malaria and pneumonia, accounting for 5% of all deaths (Hamad, 2006). It must be underlined that this figure, which appears quite low, most likely reflects severe shortcomings in cancer diagnosis and data collection (Malik et al., 1976; Parkin et al., 2003; Awadelkarim et al., 2007; Awadelkarim et al., 2008). The recently-established population-based Gezira Cancer Registry should provide in the near future a more reliable basis for the assessment of cancer in Gezira State (Central Sudan).

2. Major environmental risk factors

Cancer incidence generally increases with age (Edwards et al., 2002; Weir et al., 2003; Parkin et al., 2008). Therefore, in the Sudan, as in other developing countries, low life expectancy and young population structure may be major reasons for differences in tumor patterns compared to Western countries. However exposure to environmental carcinogens, which may vary according to social, ethnic, geographic and occupational factors (Cardenas et al., 1997; Woodward and Boffetta, 1997), clearly impacts on cancer patterns in the Sudan, though this remains difficult to evaluate because of the scarcity of studies. We review in the following paragraphs the cancer-related environmental factors that are likely to play important roles.

2.1. Infections

The importance of infections as a major cancer risk factor in Africa is clearly evidenced by the fact that as many as 36% of the cancer cases in the continent are infection-related, which is double the world average (Parkin et al., 2008). With regard to the Sudan, malaria is endemic and actually spread in the last decades following the expansion of agriculture and irrigation. Epstein–Barr Virus (EBV)
infection and intense exposure to Plasmodium falciparum (hola-
edemic malaria) are recognized cofactors in the pathogenesis of
Burkitt’s lymphoma, one the most common pediatric cancers in
equatorial Africa (Chene et al., 2007). Furthermore, in immunocom-
promised hosts, EBV is causally associated with various other
malignancies that also appear to be frequent in the Sudan, including
nasopharyngeal carcinoma and B cell lymphoma.

Schistosomiasis is endemic in most of the Sudan. As discussed in
the section dealing with specific types of cancer, S. haematobium
is clearly associated with bladder cancer (Sitas et al., 2008).
Furthermore, Salim et al. (2010) recently reported one patient with sigmoid
colon adenocarcinoma coexisting with schistosomiasis, which may
suggest a possible causal relationship. S. mansoni ova were more often
seen in the tumor than in the normal tissue (Salim et al., 2010).

As discussed further on, infection with hepatitis B or C viruses
(HBV or HCV) is strongly associated with hepatocellular carcinoma
(HCC) in the Sudan (Omer et al., 2001a), while, unfortunately, little is
known about human papilloma viruses (HPVs), the causal agents of
cervical cancer, the second most common cancer in women
worldwide (Bradbeer, 1987; Henry et al., 1989; Frisch et al., 2000;
Chaturvedi et al., 2009b), also implicated in other epithelial cancers
(Ibrahim et al., 1998b; Herrera et al., 2003). Unsurprisingly, this
reflects the lack of cervical cancer screening programs. No information
regarding HPV subtypes in the Sudanese population is presently
available.

Human immunodeficiency virus (HIV)-related immunosuppres-
sion is a strong risk factor for two herpesviruses-associated cancers:
Kaposi’s sarcoma, associated with its specific herpesvirus, and non-
Hodgkin lymphoma, associated with Epstein–Barr virus (Franceschi
et al., 1999; Parkin et al., 1999; Dal Maso et al., 2001; Strickler, 2009).
The risks for both Kaposi’s sarcoma and non-Hodgkin lymphoma are
increased by at least 100-fold in individuals who develop AIDS
(Goedert et al., 1998; Frisch et al., 2001). HIV-associated cervical
carcinoma is also considered an AIDS-defining malignancy (Bradbeer,
1987; Maiman et al., 1988; Henry et al., 1989; Frisch et al., 2000;
Chaturvedi et al., 2009a; Strickler, 2009). In fact, HIV-infected women
with advanced immunosuppression seem to be particularly vulner-
able to persistent infection with high-risk HPV types that can lead to
cancer (Palefsky et al., 1999; Ahdieh et al., 2001; Denny et al., 2008).
A significant excess of AIDS-defining malignancies has been reported in
African countries such as Zimbabwe, Zambia, Uganda, Rwanda, and
South Africa (Wabinga et al., 1993; Newton et al., 1995; Sitas et al.,
2000; Newton et al., 2001; Mbulaiteye et al., 2003; Sissock and
Mayaud, 2005; Mbulaiteye et al., 2006). However, as anticipated
above for cervical carcinoma and discussed below in the section
dealing with specific cancers, these AIDS-defining malignancies are
still scarcely studied in the Sudan. Precise estimates of HIV prevalence
are lacking. According to the UNAIDS 2008 report on the global AIDS
erpidemic, there were at least 320,000 HIV-infected individuals in
Sudan and at least 25,000 people died of HIV in 2007 (UNAIDS, 2008).
A survey conducted by the Sudan National AIDS Program (SNAP) in
2002 estimated the prevalence rate of HIV in adults at 1.6%, with rates
ranging from 0.5% to 2.5% for specific population groups (the Sudan
plan for HIV/AIDS, including SNAP, is available at: http://www.fmoh.
gov.sd/English/St_Plan/doc/strategi%20plan%20and%20sectoral%20
plans%20on%20HIV-AIDS.pdf). At present, the register of HIV-
infected patients in 15 northern states in Sudan includes around
23,000 patients (Moszynski, 2006; Herieka et al., 2008).

2.2. Pesticides

A total of over 200 active pesticide ingredients are registered in the
Sudan, either singly or combined in over 600 different formulat-
s. About 20% of these are mainly used for mosquito control. The
remaining 80% are used to control pests of cotton and other rotation
crops, besides considerable amounts used against desert locusts, birds
and rodents (El Hindi et al., 2003). Organochlorines were officially
banned in 1981, with the exception of endosulfan, and, after that year,
pyrethroids were used to substitute DDT (Waleij et al., 2004).

One significant problem with pesticides in the Sudan is connected
with the stockpiles of obsolete and banned pesticides. The conditions
of such stockpiles are in general very poor and pesticides stored in
corroded or otherwise damaged containers can be expected to have
entirely leaked in the environment (Fig. 2A). No facilities for local
disposal exist. An inventory made by the Food and Agriculture
Organization (FAO) has shown that there are about 666 tons of
obsolete pesticides in agricultural schemes all over the country, and
44 sites were identified as affected, with about 145 different
pesticides. It was estimated that 6000 m³ of soil were contaminated
(Jeyaratnama, 1990; El Hindi et al., 2003; Waleij et al., 2004).
Long-term exposures to pesticides and chronic disease-related effects
could have a great impact on public health, but this remains very difficult
to assess (Wong and Ng, 1984; Jeyaratnama, 1990; El Hindi et al., 2003).
No studies have been conducted as yet in the Sudan to evaluate
pesticides exposure in relation to cancer epidemiology. Furthermore,
the carcinogenic role of environmental pollution by synthetic
pesticides is still debated in the scientific community (Gold et al.,
1992; Ames and Gold, 1998; Tomatis et al., 2001; Richter and
Chlamtac, 2002), because of the lack of clear cause-and-effect relation
between any single type of pesticide/herbicide exposure and cancer.
This might reflect the influence of modifying factors, such as genetic
variation in the pathways of metabolic activation and detoxification,
rarely considered in pesticide-related cancer research (Zahm and
Ward, 1998; Infante-Rivard and Weichenthal, 2007). However, there is
evidence that common pesticides/herbicides induce oxidative stress,
and occupational or environmental exposures have been associated
with genotoxic effects (Lieberman et al., 1998; Garaj-Vrhovac
and Zeleznik, 2000; Abdollahi et al., 2004; Granot and Kohen, 2004).
Furthermore, based on the Hill causation criteria (Hill, 1965), recent
epidemiological studies suggest that repeated pesticide exposures
significantly increase the risk of cancer, particularly in children
(Zahm and Ward, 1998; Infante-Rivard and Weichenthal, 2007). Therefore,
in spite of the lack of data, it is probable that exposures to pesticides/
herbicides contribute to cancer in Sudan, and studies addressing this
issue should be promoted.

2.3. Other sources of pollution

Information concerning air pollution in the Sudan is scarce and it
is difficult to assess its possible role on disease. In rural areas, air
pollution can be expected to be low to moderate, whereas it could be
moderate to high in urbanized areas, such as Khartoum and other
larger cities. In general, air pollution can derive from industries and oil
producing facilities, and from traffic, but in the Sudan, as elsewhere in
Africa, fires lit for cooking within poorly ventilated mud huts, as well
as the habit of burning trash, should be considered. Ledated petrol
is still used in the country, which implies heavy metal exposure. In 1989,
the average total suspended particulate levels in Khartoum were
144 μg/m³, exceeding the World Health Organization (WHO) limit of
120 μg/m³ (Waleij et al., 2004), and levels are predicted to be
significantly higher at present, due to marked increase in road traffic.

As noted before, because of poor soil waste management
(Fig. 2B), trash is regularly burned in open pits at low temperature
fires (Fig. 2C). These fires receive little oxygen and produce heavy
smoke. Under these conditions a variety of toxic substances are
generated, depending on the type of waste burned. Virtually all
pollutants are released into the air close to ground level, where they
are easily inhaled. Among the environmental and health risks posed
by residential waste burning, dioxin exposure is a key concern (Waleij
et al., 2004). According to the United Nation Environment Program
(UNEP), waste burning could be the largest source of persistent toxic
substances such as dioxins and furans in Africa. In estimations made

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by UNEP, the Sudan ranked 5th, together with Tanzania, with respect to daily total toxicity equivalents (TEQ) emissions from uncontrolled domestic waste combustion (Waleij et al., 2004). Dioxin is a potent human carcinogen as well as an endocrine disrupter, and can cause reproductive, developmental, and immunological problems in humans and animals (Waleij et al., 2004). Its role in the etiology of endocrine-related cancers could be relevant in the Sudan.

Information about soil and water pollution is also scarce (Fig. 2A and D). However, the three Nile rivers (the Nile, the Blue Nile and the White Nile respectively) are the main transport lines and most industries and agricultural schemes are close to these rivers. Heavy pollution of soil and water can be expected in most industrial areas. Oil pollution is expected around petrochemical facilities and pipelines. Soil and water around agricultural schemes and pesticide storages facilities are likely to be contaminated with pesticides. Salinization, alkalisation and water logging resulting from irrigation are growing problems. Artisan gold mining by local populations is common, and may, depending on ore and extraction methods, pose serious environmental problems related to pollution with arsenic, mercury, grease and suspended small particles downstream of mining areas (Waleij et al., 2004).

3. Cancer patterns

3.1. Limitations of the published data

The majority of the studies reviewed here are descriptive reports of hospital/department records and provide valuable information about the cancer patterns seen and identified in Sudanese medical facilities. These studies may have obvious limitations in epidemiological research, such as: i) lack of population-related incidence data; ii) bias towards cancers that are more evident to patients and/or more easily diagnosed; iii) lack of power analyses for specific risk factors; and iv) overlapping across studies by different authors.

This is further complicated by the fact that no single institution, except the NCI-UG, provides a comprehensive annual report of the observed cancers. Given the fact that about 36% of the cancer cases occurring in sub-Saharan Africa are estimated to be infection-related (Parkin et al., 2008), it is also surprising that in Sudan there is a lack of studies focusing on infection-related tumors. This reflects the absence of a national policy for cancer research and treatment tailored to the specific Sudanese needs.

3.2. Major cancers reported in adults

Tables 1 and 2 and Figs. 3–5 summarize data on some of the published series of cancer cases in Sudanese adults. Early published information includes a historically important review of 1334 malignant epithelial neoplasms received in the Stack Medical Research Laboratories during the period 1935–54 (Hickey, 1959). The commonest tumor site was skin (32.8%, 437/1334), followed closely by breast (22.9%, 306/1334), which, quite interestingly, was the most frequent single tumor type (Hickey, 1959) (Table 2).

A subsequent study reported data on 2234 malignant tumors of all types, collected from the same source and from the Department of Pathology, University of Khartoum, during the period 1954–61 (Lynch et al., 1963). This series was later compared with another series of 1578 malignant tumors of all types from the Khartoum district, examined at the Department of Pathology in 1957–65 (Daoud et al., 1968). The University Pathology Laboratories serve mainly the Khartoum Civil Hospital (KCH) which has 900 beds and where diagnostic facilities and specialists are more readily available than elsewhere in the country (Daoud et al., 1968). The comparison intended to assess the influence of diagnostic contexts on cancer patterns. The patterns of malignant disease in the two series analyzed

Fig. 2. Examples of pollution in the Sudan. A, fissured cement-lined pit containing an obsolete pesticide stockpile; B, plastic litter, often burned with wood in home fires, is a major problem in the countryside around towns and villages in Northern and Central Sudan; C, industrial waste burning on vacant land in Khartoum state; and D, raw sewage flowing towards the White Nile near Khartoum.
Table 1
Reported cancer series from the Sudan. The table details period of registration, number of reported cases, institution, location, type of registration and corresponding reference.

<table>
<thead>
<tr>
<th>Period</th>
<th>Number of cases</th>
<th>Institution</th>
<th>Location</th>
<th>Type of registration</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1954–1961</td>
<td>2234</td>
<td>Stack Medical Research Laboratoriesa and Department of Pathology, University of Khartoum</td>
<td>Khartoum</td>
<td>Pathology-basedb</td>
<td>Lynch et al. (1963)</td>
</tr>
<tr>
<td>1957–1965</td>
<td>1578</td>
<td>Department of Pathology, University of Khartoum</td>
<td>Khartoum</td>
<td>Pathology-basedb</td>
<td>Daoud et al. (1968)</td>
</tr>
<tr>
<td>1962–1973</td>
<td>8212</td>
<td>Departments of Pathology, University of Khartoum and National Health Laboratory, Ministry of Health</td>
<td>Khartoum</td>
<td>Pathology-basedb</td>
<td>Malik et al. (1976)</td>
</tr>
<tr>
<td>1978</td>
<td>1036</td>
<td>Sudan Cancer Registry (SCR)</td>
<td>Khartoum</td>
<td>Pathology-basedb</td>
<td>Mukhtar (1986)</td>
</tr>
<tr>
<td>1999–2006</td>
<td>3547</td>
<td>Institute of Nuclear Medicine, Molecular Biology and Oncology (INMO), University of Gezira</td>
<td>Wad Medani</td>
<td>Hospital-basedd</td>
<td>Awadelkarim et al. (2008)</td>
</tr>
<tr>
<td>2003–2006</td>
<td>260</td>
<td>Histopathology Department, Almawani Hospital</td>
<td>Port Sudan</td>
<td>Pathology-basedb</td>
<td>Ageek et al. (2007)</td>
</tr>
</tbody>
</table>

a Currently referred to as “National Health Laboratories” Khartoum.
b Based on pathology records.
c Based on records at cancer hospitals.
d Based on records at cancer hospitals.

Table 2
Relative frequencies of cancer types/sites in the reported case series of adult Sudanese cancer patients.

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>131 9.8</td>
<td>217 9.7</td>
<td>176 11.2</td>
<td>454 5.5</td>
<td>55 5.3</td>
<td>821 7.9</td>
<td>1854 7.4</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4 0.3</td>
<td>–</td>
<td>13 0.1</td>
<td>17 0.1</td>
<td></td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>240 2.9</td>
<td>30 2.9</td>
<td>726 7.0</td>
<td>996 4</td>
<td></td>
</tr>
<tr>
<td>Other pharynx</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>8 0.8</td>
<td>185 1.8</td>
<td>193 0.8</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>1 0.1</td>
<td>–</td>
<td>–</td>
<td>44 2.8</td>
<td>106 1.3</td>
<td>37 3.6</td>
<td>347 3.3</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>5 0.4</td>
<td>–</td>
<td>–</td>
<td>24 1.5</td>
<td>72 0.9</td>
<td>21 2</td>
<td>44 0.4</td>
<td></td>
</tr>
<tr>
<td>Colon/rectum</td>
<td>74 5.5</td>
<td>–</td>
<td>–</td>
<td>53 3.4</td>
<td>345 4.2</td>
<td>41 4</td>
<td>223 2.1</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>38 2.8</td>
<td>–</td>
<td>–</td>
<td>35 2.2</td>
<td>–</td>
<td>39 3.8</td>
<td>62 0.6</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>8</td>
<td>115 1.1</td>
<td>2 0.8</td>
<td>125 0.5</td>
</tr>
<tr>
<td>Skin</td>
<td>437 32.8</td>
<td>414 18.5</td>
<td>218 13.8</td>
<td>1179 14.4</td>
<td>107 10.3</td>
<td>428 4.1</td>
<td>21 8.1</td>
<td>2804 11.2</td>
</tr>
<tr>
<td>Small intestine</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>22 0.3</td>
<td>–</td>
<td>22 0.1</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>306 22.9</td>
<td>261 11.7</td>
<td>214 13.6</td>
<td>937 11.4</td>
<td>149 14.4</td>
<td>2084 20</td>
<td>54 20.8</td>
<td>4005 16</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>91 6.8</td>
<td>–</td>
<td>–</td>
<td>510 6.2</td>
<td>82 7.9</td>
<td>812 7.8</td>
<td>1534 6.1</td>
<td></td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>165 0.7</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>23 1.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>38 3.7</td>
<td>206 2.0</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>18 1.3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>19 1.8</td>
<td>40 0.4</td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>54 4.0</td>
<td>–</td>
<td>–</td>
<td>15 1.0</td>
<td>263 3.2</td>
<td>24 2.3</td>
<td>292 2.8</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>6 0.4</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>14 1.4</td>
<td>179 1.7</td>
<td></td>
</tr>
<tr>
<td>Eye</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>115 5.1</td>
<td>27 1.7</td>
<td>–</td>
<td>441 1.8</td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>1 0.1</td>
<td>8 0.4</td>
<td>9 0.6</td>
<td>–</td>
<td>–</td>
<td>3 0.3</td>
<td>178 1.7</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>19 1.4</td>
<td>34 1.5</td>
<td>39 2.5</td>
<td>–</td>
<td>–</td>
<td>16 1.5</td>
<td>209 2</td>
<td></td>
</tr>
<tr>
<td>Lymphomas (all types)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>732 8.9</td>
<td>71 6.9</td>
<td>956 9.2</td>
<td>11 4.2</td>
<td>1770 7.1</td>
</tr>
<tr>
<td>Penis</td>
<td>26 1.9</td>
<td>–</td>
<td>–</td>
<td>8 0.5</td>
<td>–</td>
<td>–</td>
<td>34 0.1</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>32 3.1</td>
<td>435 4.2</td>
<td>479 1.9</td>
</tr>
<tr>
<td>Vagina/vulva</td>
<td>43 3.2</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>43 0.2</td>
<td></td>
</tr>
<tr>
<td>Testis</td>
<td>16 1.2</td>
<td>–</td>
<td>–</td>
<td>18 1.1</td>
<td>–</td>
<td>–</td>
<td>6 0.3</td>
<td></td>
</tr>
<tr>
<td>Other types</td>
<td>45 3.4</td>
<td>1185 53</td>
<td>694 44</td>
<td>3352 40.8</td>
<td>188 18.1</td>
<td>1645 15.8</td>
<td>110 42.3</td>
<td>7219 28.8</td>
</tr>
<tr>
<td>Total (all sites)</td>
<td>1334 100</td>
<td>2234 100</td>
<td>1578 100</td>
<td>8212 100</td>
<td>1036 100</td>
<td>10,410 100</td>
<td>260 100</td>
<td>25,064 100</td>
</tr>
</tbody>
</table>

(Hickey, 1959), included only epithelial tumors from Stack Medical Research Laboratories, Khartoum, 1935–54; (Lynch et al., 1963), Stack Medical Research Laboratories and Department of Pathology, University of Khartoum, 1954–1961; (Daoud et al., 1968), Department of Pathology, University of Khartoum, 1957–1965; (Malik et al., 1976), Departments of Pathology of the University of Khartoum and of the National Health Laboratory, Khartoum, 1962–1973; (Mukhtar, 1986), Sudan Cancer Registry, 1978; (Hidayatalla and Rahman, 1986), Radiation and Isotope Center, Khartoum, 1967–84; (Ageek et al., 2007), Almawani Hospital, Port Sudan, 2003–06.

The pathology-based SCR tumor series for the year 1978 was reported (Mukhtar, 1986). It included 1036 malignant tumors. Breast cancer was the most frequent tumor, accounting for 142/1036 cases (13.7%), followed by skin cancer, which accounted for 107/1036 cases (10.3%). Other cancers of particular interest in this series were nasopharyngeal carcinomas, oral cancers and eye tumors, the latter represented mainly by conjunctival carcinomas (Mukhtar, 1986), as also reported previously (Malik et al., 1974) (Table 2).
Hidayatalla and Rahman published a series of 10,410 cancer cases seen in the RICK hospital between 1967 and 1984. The distribution of tumor types was somewhat biased towards more radiosensitive tumors (such as breast and nasopharynx) (Hidayatalla and Rahman, 1986). The commonest cancers in males were those of the nasopharynx, which appeared to be more frequent in patients from southern and Sudanic tribes, as noted in an earlier report (Hidayatalla et al., 1983), non-Hodgkin lymphoma, also as reported previously (Malik et al., 1974), cancers of the mouth, especially gingival carcinomas, again as reported previously (Lynch et al., 1963), and carcinomas of the urinary bladder. Importantly, Kaposi sarcoma, which, regardless of ethnic origin, comprised 1.2% of all tumors in male patients, was much more common in patients from the South and West, as noted in 1967, i.e., well before the onset of the AIDS epidemics (Wasfi et al., 1967). In male patients from Southern and Western Sudan Kaposi sarcoma strikingly accounted for 7.2% of all treated cancers (Hidayatalla and Rahman, 1986). In females, the commonest cancers were, in order of frequencies, those of the breast, as previously noted in 1969 (Hidayatalla and Rahman, 1986) and mouth (Hidayatalla and Rahman, 1986). The tumor types was somewhat biased towards more radiosensitive tumors such as breast and nasopharynx (Hidayatalla and Rahman, 1986). The distribution of tumor types was somewhat biased towards more radiosensitive tumors such as breast and nasopharynx (Hidayatalla and Rahman, 1986). The distribution of tumor types was somewhat biased towards more radiosensitive tumors such as breast and nasopharynx (Hidayatalla and Rahman, 1986).

A recent and unique report from Port Sudan, on the Red Sea coast, described diagnosed cancer cases (n = 260) accessioned at the Histopathology Department of Almawan Hospital from November 2003 to November 2006 (Ageek et al., 2007). In this series female patients were more represented than males [females, 67.3% (175/260); males, 32.7% (85/260)]. The mean age at cancer diagnosis was 48 years. The most common cancers were those of the breast, cervix, head and neck, gastrointestinal tract and skin. In female patients the most common cancers were those of the breast, cervix, head and neck. The most common cancers in males were those of head and neck, skin, soft tissue and gastrointestinal tract, in order of frequency. Unsurprisingly, given the sex bias, the two major cancers of women, breast and cervical carcinomas, were also the most commonly observed malignancies overall (Ageek et al., 2007).

Based on referral data from RICK, in the 18 years to 1984 nasopharyngeal carcinoma was the most common of the treated tumors diagnosed in males, whereas non-Hodgkin lymphoma ranked second. In the 20 years from 1984 to 2004, chronic myeloid leukemia became the predominant cancer, while lymphomas (Hodgkin and non-Hodgkin combined) remained the second most common cancer observed in men. In women, breast, cervical and ovarian cancer, in ranking order, were the three most common cancers treated over both time periods, but there was also an increase in the frequency of chronic myeloid leukemia. As recently reported, carcinomas of the breast and of the uterine cervix accounted for about 50% of all treated cancers in women (Hamad, 2006). Thus, based on hospital series, cancer patterns appeared to be quite different in males and females and, in males, included tumors very rare in Western countries such as nasopharyngeal carcinoma. It must be stressed, however, that these data are most likely biased by differences in detection and hospitalization rates.

3.3. Childhood cancer

Table 3 and Fig. 6 summarize the published childhood cancer series from the Sudan. Childhood cancer cases in the RICK’s registry for the period 1967–84 were described by Hidayatalla (1988). This series, which consisted of 775 cases, was divided into two broad ethnic groups: “Arabs”, including Arabs and Mowalad, Nubians and Bejas, 558 cases; and “Sudanics”, including Nilotic and Sudanic tribes, as well as Beggara, 217 cases. The spectrum of tumor types was similar in the two groups (Hidayatalla, 1988). The commonest tumors were lymphomas (Hodgkin and non-Hodgkin combined); with a frequency of 175/775 (22.6%) overall (both groups). For Hodgkin disease, the frequencies were similar in “Arabs” (52/558, 9.3%) and “Sudanics” (19/217, 8.8%), while Burkitt lymphoma was more frequently observed in “Sudanics” (15/217, 6.9% versus 16/558, 2.9% in

“Arabs”). Leukemia was uncommon in both groups, particularly in “Sudanics” (10/217, 4.6% versus 63/558, 11.3% in “Arabs”). Surprisingly, a large proportion (21/73, 29%) of all leukemias were classified as chronic myeloid, a rare hematological malignancy in childhood (Hasle, 2007). Overall, after hematological malignancies, the most common tumor was retinoblastoma, which accounted for 121/775 cases (15.6%, both groups). However, in the “Sudanic” group retinoblastoma accounted for 49/217 cases (22.6%), versus 72/558 (12.9%) in “Arabs”. Therefore in “Sudanics” retinoblastoma was more frequently diagnosed than lymphomas. The proportions of brain tumors, neuroblastomas and Ewing sarcomas were low in both ethnic groups. Nasopharyngeal carcinomas were frequent, accounting for 78/101 (77%) cases in the “Arabs” versus 57/104 (55%) in “Sudanics”. Therefore in both groups combined, nasopharyngeal carcinoma accounted for 121/775 cases (15.6%, both groups). However, in the “Arabs” group nasopharyngeal carcinoma accounted for 72/217 cases (33.4%), versus 49/558 (8.9%) in the “Sudanics”. Therefore in the “Arabs” group nasopharyngeal carcinoma was more frequently observed than lymphomas.

Burkitt lymphoma cases seen and diagnosed historically in Khartoum during the period 1962–73 (29 cases overall) accounted for (20%) of all childhood lymphomas treated in that period. Age at presentation was 6.8 years, with male to female ratio of 3.8:1. Clinical features, anatomical localizations and histological appearances corresponded to those reported in the literature. The geographical origin of the patients closely correlated with that of holo- or hyper-endemic malaria (Veress et al., 1976).

All pediatric patients treated at INMO (now NCI-UG) in Wad Medani from May 1999 to June 2007 were recently reviewed (Haroun et al., 2008c). Consistently with the late age at diagnosis, the clinical stage was generally high and abdominal mass was the commonest symptom.

4. Specific cancer types

Few studies performed in the Sudan provide data on specific cancer types and their associated risk factors. The following paragraphs will review available information on breast cancer, cervical carcinoma, nasopharyngeal carcinoma, tumors of the eye and adnexa, oral cancer, alimentary tract tumors, hepatocellular carcinoma, Hodgkin’s disease, thyroid cancer and urinary bladder cancer. Other cancers are not treated here mainly because of lack of information.

4.1. Breast cancer

Overall, breast cancer appears to be the most frequent hospital-treated malignancy in the Sudan, accounting for about one fifth of all cancers reported in males and females combined (RICK 17%, i.e., 2395/13,924; INMO 21%, i.e., 732/3547) (INMO Annual Report, 2001; Ferlay et al., 2004; Parkin et al., 2005; Hamad, 2006; INMO Annual Report, 2006; Awadelkarim et al., 2007; Awadelkarim et al., 2008). This may partly reflect awareness bias, as breast masses or ulcerated lesions typical of advanced disease are readily evident to the patients...
European-American breast cancer patients found associations between onset breast cancer, particularly in parous women, could be magnified due to environmental factors responsible for male breast cancer and for early demographic factors resulting in low post-diagnosis (Fig. 7); (d) high grade; (e) poor prognosis (INMO Annual Report, 2001; Khairy et al., 2005; INMO Annual Report, 2006; Awadelkarim et al., 2007; Awadelkarim et al., 2008). Many factors could contribute to these differential characteristics including: i) demographic factors (Ikpat et al., 2002; Okobia and Bunker, 2005; Parkin et al., 2005; Adesunkanni et al., 2006; Okobia et al., 2006); ii) lifestyle, environmental and socio-economic factors, including reproductive factors and access to medical care (Ikpat et al., 2002; Parkin et al., 2005; Adesunkanni et al., 2006; Okobia et al., 2006); and iii) intrinsic ethnic/genetic factors (Ijaduola and Smith, 1998; Mbonde et al., 1998; Fregene and Newman, 2005; Okobia and Bunker, 2005).

Overall the features of breast cancer in the Sudan may reflect population structure and reproductive factors resulting in low post-menopausal breast cancer incidence. This would imply that the role(s) of etiological factors responsible for male breast cancer and for early onset breast cancer, particularly in parous women, could be magnified in Sudanese breast cancer series (Awadelkarim et al., 2007).

Studies that compared extensive series of African-American and European-American breast cancer patients found associations between aggressive estrogen receptor (ER)-negative breast cancer and both younger age at diagnosis and black ethnicity (Carey et al., 2006; Porter, 2008). These data raise the possibility that genetic factors could contribute to a higher burden of aggressive ER-negative breast cancer in indigenous African women. Possible differences between breast cancer in Sudanese and European patients were investigated by Awadelkarim et al. (2008), who compared two breast cancer case series, one from Central Sudan (Khartoum) and one from Northern Italy (Milan), for clinicopathological characteristics, expression of estrogen receptor (ER), progesterone receptor (PR), Her-2/neu, basal cytokeratins (CK) 5/6 and CK17, and breast cancer subtypes. Compared with the Italian patients, the Sudanese patients were younger (P<0.0001) and their tumors were larger (P<0.0001), more advanced in stage (P<0.00001), of higher grade (P<0.00001) and more frequently positive for nodal metastases (P<0.00001). ER expression varied between the two series (P<0.0008), but no significant differences were found for PR (P=0.32), combined hormone receptors (ER/PR) (P=0.12), Her-2/neu (P<0.09), CK5/6 (P<0.1), CK17 (P=0.4), combined basal CK status (CK5/6/CK17) (P=1) or breast cancer subtypes (P=0.12). The differences between the Sudanese and the Italian breast cancer series seemed to reflect stage at diagnosis rather than intrinsic biological characteristics (Awadelkarim et al., 2008).

As in industrialized countries, strong genetic factors contribute to a subset of breast cancer cases in the Sudan. Pilot studies at INMO (NCI-UG) showed that mutations in the two major susceptibility genes, BRCA1 and BRCA2, accounted for variable but significant fractions of the premenopausal cases (Awadelkarim et al., 2007). Awadelkarim et al. (2007) characterized for germline BRCA1/2 mutations a one-year series of patients (34 females and 1 male) selected by diagnosis within Central Sudan (Khartoum) and one from Northern Italy (Milan), for clinicopathological characteristics, expression of estrogen receptor (ER), progesterone receptor (PR), Her-2/neu, basal cytokeratins (CK) 5/6 and CK17, and breast cancer subtypes. Compared with the Italian patients, the Sudanese patients were younger (P<0.0001) and their tumors were larger (P<0.0001), more advanced in stage (P<0.00001), of higher grade (P<0.00001) and more frequently positive for nodal metastases (P<0.00001). ER expression varied between the two series (P<0.0008), but no significant differences were found for PR (P=0.32), combined hormone receptors (ER/PR) (P=0.12), Her-2/neu (P<0.09), CK5/6 (P<0.1), CK17 (P=0.4), combined basal CK status (CK5/6/CK17) (P=1) or breast cancer subtypes (P=0.12). The differences between the Sudanese and the Italian breast cancer series seemed to reflect stage at diagnosis rather than intrinsic biological characteristics (Awadelkarim et al., 2008).
The 55 non-truncating variants included 3 unclassified variants predicted to affect protein product and not co-occurring with a truncating mutation in the same gene. Patients were from different tribes but most BRCA1/2 variation was among individuals (86.41%) and patients clustered independently of tribe of origin. Cluster analysis based on age at cancer diagnosis and reproductive variables split female patients in two groups that, by factor analysis, were explained by low versus high scores of the total period occupied by pregnancies and lactation. The cluster with low scores comprised all 4 patients with truncating pathogenetic mutations and 3/4 carriers of unclassified variants predicted to affect the protein product. This suggests that BRCA1/2 could represent an important etiological factor of breast cancer in males and young women less exposed to pregnancy and lactation, and poses the major problem of the identification of at-risk families and disease prevention. Factors other than BRCA1/2 could contribute to breast cancer in young highly multiparous women who breast-fed for prolonged periods (Awadelkarim et al., 2007).

Hereditary breast cancer tends to present with synchronous or metachronous bilateral disease. A study from Khartoum Teaching Hospital examined the frequency and features of bilateral breast cancer. Medical records of patients treated for breast cancer during the 5-year period 1994 to 1999 were reviewed. Bilateral breast cancer cases were analyzed focusing on individual information, family history, menstrual status, surgical and chemo-radiation therapy, staging and histopathological characteristics. Of 521 patients treated for breast cancer, 90 (17.2%) were reported to have advanced breast carcinoma (stages III and IV) and 7 (1.3%) revealed bilateral breast cancers, which in 5 cases (0.9%) were synchronous and in 2 (0.4%) metachronous. The median age at diagnosis was 47.3 years (range, 24–81 years). Four of the seven patients (57.1%) had positive breast

![Fig. 6. Relative frequencies of cancers reported in Sudanese children, obtained by pooling data from the published sources (Hidayatalla, 1988; Haroun et al., 2006; Abuidris et al., 2008a). Numbers and percentages are given for each cancer type (n; %).](image-url)
Possible joint effects of Her-2/neu Ile655Val and ESR1 C325G on breast cancer risk were also investigated. The frequency of these polymorphic variants varied with ethnic origin. A significantly higher risk of breast cancer was observed among carriers of homozygous ESR1 325 CC and heterozygous Her-2/neu 655 Ile/Val (P = 0.05; adjusted OR = 4.9, 95% CI: 1.0–24) (Siddig et al., 2008b). These results suggest that an interaction between the ESR1 325C and Her-2/neu Ile655Val variants could contribute to breast cancer risk in Sudanese women (Siddig et al., 2008b).

4.2. Cervical carcinoma

Cervical carcinoma is the most common cancer in sub-Saharan Africa (30–40 per 10^5 females) (Parkin et al., 2008). In western countries its incidence is relatively low, but, prior to the introduction of screening programs, was in the range of that currently estimated in Africa (38.0 per 10^5 females in the USA at the time of the Second US National Cancer Survey in 1947) (Dorn and Cutler, 1959; Parkin et al., 2008). According to GLOBOCAN 2002, the impact of cervical cancer in the Sudan is in the range of that registered in other sub-Saharan African countries, with age-adjusted mortality estimated at 12.7 per 10^5, compared to 2.3 per 10^5 in USA, and 3.4 per 10^5 in Western, Northern and Southern Europe (Ferlay et al., 2004). Overall 78% of the Sudanese cervical cancer patients seen in hospitals presented with stage III or IV disease (Hamad, 2006; Ageek et al., 2007). Based on the Sudanese hospital cancer series, the disease appears to rank second (after breast carcinoma) among the cancers treated in females (INMO Annual Report, 2001; Hamad, 2006; INMO Annual Report, 2006).

HPV infection is the major causal agent of cervical cancer (Herrero et al., 2003; Galloway, 2000; zur Hausen, 2000), however, quite strikingly, no single report about HPV infection and cervical carcinoma from the Sudan was found in PubMed (search: HPV and Sudan). The primary approach to the control of cervical carcinoma should be through prevention by screening for precancerous cervical lesions, but no effective cytology screening programs are currently available in the Sudan, due to competing health needs and lack of infrastructures and trained personnel. Facilities for diagnosis and treatment of cervical cancer are available only in well-organized centers in Khartoum, i.e., Khartoum Teaching Hospital and Soba University Hospital (Hamad, 2006; Ageek et al., 2007). The only available treatment is surgery or radiotherapy, which are expensive and not accessible to most patients.

The HPV vaccine, though far from being used in the developing world due to costs and other social factors, could be the only effective tool to protect adolescent girls from cervical cancer (Pollack and Tsu, 2005). In this regard it is worth mentioning that the obstetrical and gynecological society of Sudan (http://www.rho.org/files/dossier14_-Sudan_Obst_Gyn_Society.pdf) is committed to work in partnership with the international community in the effort to combat cervical cancer through vaccination.

4.3. Nasopharyngeal carcinoma

Nasopharyngeal carcinoma (NPC) is frequent in the Sudan, accounting for 5.8% (n = 374) of all cancer cases reported from the SCR and for 7.2% (n = 512) of those reported from RICK (Hidayatalla et al., 1983); these are among the highest NPC frequencies in cancer series worldwide. With male/female ratio of 3:1, NPC was the commonest in the SCR (9.2%). It seems to occur in young patients (the youngest reported case was 3-year-old), with 14% and 12.1% of the cases within 14 years of age in the SCR and RICK series respectively (Hidayatalla et al., 1983). However, a lower frequency of NPC in children has been reported recently at INMO (now NCI-UG), where between 1999 and 2007 NPC accounted for about 3.4% of all childhood cancers (Abuidris et al., 2008a). The ethnic and
geographical distribution of the treated NPC cases suggests that racial susceptibility could play a significant role, while environmental factors were not identified; however, as elsewhere, Epstein–Barr virus is most likely associated with this malignancy also in the Sudan (Hidayatalla et al., 1983). A recent report describes the NPC patients treated at INMO (now NCI-UG) during the period 2000–2005. The total number of patients was 103. Age ranged from 11 to 82 years, with a median of 41 years, and a mean of 45.5 years. Male:female ratio was 2:1. The WHO histology type-3 accounted for 73.8% of cases, WHO type-2 for 26.2%, and no WHO type-1 cases were found in the series. Neck swelling was the most common presenting symptom. This pattern of NPC presentation resembles that seen in other endemic areas, such as South China. Identifying risk factors for NPC in the Sudan is a research priority (Abuidris et al., 2008b).

4.4. Tumors of the eye and adnexa

Malik and El Sheikh (1979) studied surgical biopsy material of lesions affecting the eye and eye adnexa submitted from 1970 to 1975 to the Department of Pathology of the Faculty of Medicine, University of Khartoum (serving mainly the teaching and reference hospitals in the Khartoum Province), and to the National Health Laboratory, Khartoum (serving provincial and district hospitals in the rest of the country). The combined cases from these two sources may provide a view of the pattern of neoplasms of the eye and adnexa in the Sudan, with the well-recognized limitations of referral bias and of biopsy material. Overall 854 lesions were reviewed, of which 718 (84%) were primary and 136 (16%) secondary to pathological conditions outside the orbit. The 718 primary lesions of the eye and adnexa included 279 malignant tumors, which accounted for 4.3% of the total cancer cases recorded at the two institutions during the study period (6489 cases overall). Conjunctival squamous carcinoma was the commonest tumor type (141/279, 50.4%), retinoblastoma accounted for 57/279 cases (20.8%), basal cell carcinoma for 17/279 (6.1%) and malignant melanoma for 13/279 (4.6%). Conjunctival carcinomas were more predominant in Northern than in Southern Sudanese patients, and no basal cell carcinoma of the eyelids was recorded in the latter. Retinoblastoma and melanoma also seemed to show ethnic patterns. Burkitt's lymphomas involving the eye were more frequent in patients from Southern Sudan. Environmental factors, infections, nutritional disorders (particularly vitamin A deficiency), genetic factors and differences in pigmentation between Afro-Arabs and Sudanics could contribute to the observed ethnic differences in eye tumor patterns (Malik and El Sheikh, 1979).

4.5. Oral cancer

Snuff, locally known as toombak, was introduced in the Sudan approximately 400 years ago, and toombak dipping is widespread, especially among males. Tobacco used for toombak preparation derives from locally grown Nicotiana rustica, a very potent tobacco variety with high nicotine concentration. The fermented ground powder is mixed in an aqueous solution of sodium bicarbonate and presents in a loose, moist form. The pH is in the 8–11 range, moist content varies from 6% to 60% and nicotine content from 8 mg to 102 mg/g of dry weight (Idris et al., 1998). Tobacco-specific N-nitrosamines (TSNAs) were quantified in snuff extracts: N′-nitrosonornicotine (NNN), N′-nitrosodentabine (NAT), N′-nitrosoanabasine (NAB) and 4-(methyl-nitrosoamo)-1-(3-pyridyl)-1-butanone (NNK). Unusually high levels of these TSNAs (mean; range in mg/g of dry weight) were detected; NNN (1.13; 0.50–3.08); NAT (0.08; 0.02–0.29); NAB (0.22; 0.02–2.37); and NNK (2.31; 0.62–7.87) (Idris et al., 1991; Idris et al., 1998). During dipping, TSN concentrations reached μm/ml levels (NNN: 0.6–2.1; NAT: 0.6–0.5; NAB: 0.05–1.9; NNK: 0.06–6.7; NNAL: 0.05–3.3; iso-NNAL: 0.07–0.4) (Idris et al., 1992; Idris et al., 1998).

A study in the Nile River Province, Northern Sudan, showed that toombak dipping is common in 40% and 10% of adult males and females, respectively (Idris et al., 1995a,b). Toombak dippers develop clinically and histologically characteristic lesions at the site of dipping (Idris et al., 1996). Oral squamous cell carcinoma (OSCC) was found to be associated with toombak dipping (Elbeshir et al., 1989; Idris et al., 1991; Idris et al., 1995a,b; Idris et al., 1998). Mutations in the p53 gene have been studied in relation to toombak dipping. A much higher proportion of p53 mutations was found in OSCCs from toombak dippers (93%, 13/14) relative to those from non dippers (57%, 8/14) (Ibrahim et al., 1999). However mutation types were similar, showing an excess of transversions in both groups, which suggests exposure to similar carcinogenic factors, while OSCCs from Scandinavia, analyzed in comparison, showed an excess of transitions. No p53 mutations were found in non-malignant oral lesions. The mutations detected in Sudanese toombak dippers were similar to those induced by tobacco-specific N-nitrosamines (TSNAs) in experimental animal models (Ibrahim et al., 1999). Further studies are necessary to validate target codons of p53 as biomarkers of malignant transformation in toombak-addicted individuals (Ibrahim et al., 1999). The importance of such studies is underlined by the fact that in the Sudan toombak is also suspected to be associated with esophageal and salivary gland carcinomas.

Human papillomavirus (HPV), the major etiologic agent of cervical cancer, appears to be involved in OSCC (Herrero et al., 2003), but may not play an important role in OSCC from Sudanese snuff dippers (Ibrahim et al., 1998b). However, co-infection with HPV types 6 and 11 was found in association with mild oral epithelial dysplasia in 2 Sudanese toombak dippers, suggesting that these viruses could be associated with the early stages of carcinogenesis (Ibrahim et al., 1998a).

4.6. Alimentary tract tumors

A study reported by Malik et al. (1976) focused on malignant alimentary tract tumors seen between 1962 and 1973 at the Departments of Pathology of the University of Khartoum and of the National Health Laboratory, Ministry of Health (Tables 1 and 2). Overall a total of 8212 cancer cases in Sudanese patients were analyzed. Primary malignant alimentary tract tumors, which accounted for 546 cases (6.6%), were much less frequent in this case series than in Western case series. Based on hospital data, alimentary tract tumors were less common in patients from the South than from the North. Most patients were in the sixth and seventh decades of life. Esophageal cancer was relatively common, especially in patients from Northern Sudan, and was more frequently observed in females. Rectal cancer was more frequent than colon cancer per se and was detected more often in males. The oldest affected patients were in the fourth to sixth decades of life, and of those cases for which the age was known, about 80.0% were under age 60. Colon cancer was more frequently observed in the caecum, which is consistent with the fact that it occurred in relatively young patients. The authors noted that alimentary tract cancer in general did not seem to be related to intestinal schistosomiasis or other chronic infections (Malik et al., 1976).

Cancers of the esophagus (n = 141), stomach (n = 88), small intestine (n = 19), colon and rectum (n = 126), accounted for 19.1% (374/1958) of all tumors seen at El Zahrawi histopathology laboratory in Khartoum during 2000 to 2004. Cancers of the esophagus were mainly squamous cell carcinomas of the upper and middle third. Gastric tumors ranked third in frequency. Carcinomas accounted for 87% (74/88) of all malignant gastric tumors, gastric lymphomas for 6/88 (7.1%) and gastrointestinal stromal tumors (GIST) for 5/88 (5.9%) (El Hassan et al., 2008). The majority of the cases (i.e., 52/74, 70%) were documented only by endoscopic biopsy (El Hassan et al., 2008), most tumors being advanced and inoperable, as reported previously.
(El Masri et al., 1975). Only 22/74 cases (30%) of all stage II or III, were represented by surgical resections. Male to female ratio was 3:3.1. Most patients were above 50 years of age. *Helicobacter pylori* infection could be implicated in gastric lymphomas and gastric carcinomas arising in Sudanese patients. In this respect evidence of *H. pylori* infection was recently assessed in gastric biopsies from 127 patients (92 males and 57 females), who reported symptoms suggestive of gastritis. The mean age was 47.2 years for males and 52.1 years for females. Chronic gastritis was detected in 125/127 cases and 89 had histologic evidence of *H. pylori* infection. The two patients negative for *H. pylori* had no pathological changes (El Hassan et al., 2008). This suggests that the association between *H. pylori* and gastric cancer should be further investigated in the Sudan.

### 4.7. Hepatocellular carcinoma

In the Sudan strong positive associations were found between infections with hepatitis B virus (HBV) or hepatitis C virus (HCV) and hepatocellular carcinoma (HCC), with odds ratios (ORs) of 9.8 (95% CI 5.1–18.9) and 8.3 (95% CI 2.3–29.9), respectively (Omer et al., 2001a). Given the estimated prevalences of HBV and HCV infections of 7.0% and 1.5%, respectively, at least 57% of all Sudanese HCC cases could be attributed to these viral infections (Omer et al., 2001a). Some studies highlighted synergisms between aflatoxin exposure and chronic HBV infection in the causation of HCC (Ross et al., 1992; Qian et al., 1994; Yu et al., 1997). In Sudan a case-control study was conducted in 1996–98, based on 150 HCC patients recruited from 5 of the 6 hospitals in Khartoum (i.e., Tropical Medicine Hospital, Oumdurman Hospital, Khartoum Hospital, Soba Hospital and Ibn Sena Hospital) and 295 controls from West and Central Sudan. Demographic characteristics and food habits were investigated. Thirty-seven peanut butter and peanut samples were collected from local markets. Aflatoxin concentrations were significantly higher in West Sudan (87.4 ± 197.3 μg/kg), a higher risk area, than in Central Sudan (8.5 ± 6.8 μg/kg), a lower risk area. Peanut butter consumption was identified as a strong risk factor for HCC in West Sudan. The association was mainly for subjects with GSTM1 null genotype, which would entail deficient aflatoxins detoxification (Omer et al., 1998; Omer et al., 2001b; Omer et al., 2004).

According to Omer et al. (2001b) the odd ratio for high versus low peanut butter consumption was 1.2 (0.7 ± 2.0) and 1.5 (1.1 ± 1.9) for hepatitis-positive versus hepatitis-negative subjects. Thus, hepatitis and peanut butter consumption seemed to be statistically independent factors, affecting risk of HCC in a multiplicative fashion. Being hepatitis-positive subjects at 10-fold increased HCC risk, the attributable risk of peanut butter consumption among this subjects far exceeds the attributable risk among hepatitis-negative subjects (Omer et al., 2001b). Regarding the population-attributable risk due to aflatoxin-contaminated peanut butter, it appears that almost 50% of all HCCs could be avoided if peanut butter consumption could be limited to the lowest quartile, or if aflatoxin intake could be reduced correspondingly. Among the subjects with GSTM1 null genotype this could even entail an 80–90% reduction (Omer et al., 2001b).

### 4.8. Hodgkin disease

Hodgkin disease accounted for 30.6% (n = 105) of all lymphomas and for 2.0% of all cancers seen in patients presenting to RICK during the period from January 1984 to January 1989. The median age of the patients was 30 years, and the majority of the cases fell within two age groups, above 25 years and above 50 years, following the classical bimodal pattern. Males were more commonly affected, particularly among children (M:F = 4.7:1.0). Two striking differences were observed between this series and those from the western world. The first was the high frequency of late clinical stages (III and IV) (70%), despite the moderate duration of the reported symptoms. The second was the predominance of the mixed cellularity and lympho-cytic predominant subtypes (65%), versus 42% in the western world (Ravel, 1994). The high frequency of late clinical stages with favorable histological subtypes is quite unusual and deserves further investigation (AbuElHassan et al., 1993).

### 4.9. Thyroid cancer

Goiter, mainly attributable to iodine deficiency, is endemic in the Darfur region of West Sudan. Of 7134 subjects examined, mainly school children, 85.5% had goiter, which in 23.9% was large (stage II or III). Goiter prevalence was high in pre-pubertal children of both sexes and in adult females. Large goiters were more frequent in rural than in urban areas (40.9 and 11.4%, respectively) (Eltom et al., 1984). Even in Port Sudan, on the Red Sea Coast of East Sudan, goiter rate was 13.5% among 7697 school children (Eltom et al., 1984), and the prevalence of visible goiter in the population was 17% (Izzeldin et al., 2007). Goiter appears to be also frequent in Central Sudan (Eltom et al., 1985).

Bashier et al. (1996) reported 94 patients with solitary and significantly dominant thyroid nodules treated in Khartoum. Inadequate sampling was reported in 5 cases (5.9%). Of the remaining 89 patients, 64 had simple goiters (72%), 12 follicular adenomas (13.5%), 12 malignant nodules (6 follicular, 5 papillary and one anaplastic carcinoma) (13.5%) and one patient had Hashimoto’s thyroiditis. Malignancy was detected in 14% of the clinically solitary nodules (10/70), compared to 10% (2/19) of the dominant nodules (Bashier et al., 1996).

One hundred and twelve patients with thyroid malignancy were seen at RICK during the period 1982–1989. Female: male ratio was 2.5:1.0, with a higher frequency of cases between 40 and 70 years of age. Follicular carcinoma was the commonest histotype (42%), followed by papillary (22.3%) and anaplastic (21.4%). Goiter was the main presenting symptom (92.9%). Most patients (40%) presented with advanced disease, limiting the option of total thyroidectomy. Metastases were detected in 32 (28.6%) patients. Follicular carcinoma had the highest frequency of blood-borne metastasis (21/47 follicular cancer cases), mostly osseous (16 cases). Anaplastic and squamous cell carcinoma showed locally aggressive behavior, indicating advanced disease. These studies clearly point to the need of improving the detection and treatment of thyroid cancer, as well as the prevention and treatment of goiters, in the Sudan (Omran and Ahmed, 1993).

### 4.10. Bladder cancer

Bladder cancer, one of the most prevalent cancers in most African countries, ranked 6th among cancers in men (224/4721 cases, 4.7%) and 16th among cancers in women (68/5689, 1.2%) at RICK during the period between 1967 and 1984 (Hidayatalla et al., 1986), and 9th among cancers in men (20/489, 4.1%) and 18th among cancers in women (4/547, 0.7%) at the SCR in 1978 (Mukhtar, 1986). Daoud et al. (1968) reported carcinoma of the bladder as the commonest tumor of the urinary tract, accounting for 2.6% of all malignancies (41/1578). Bladder cancer seems to be more frequent in Central Sudan where urinary schistosomiasis by *S. haematobium* is highly endemic. Bladder carcinogenesis may be promoted by bacterial and/or HPV infection on a background of schistosomiasis (El-Mawla et al., 2001). The frequency of the different histological types of bladder cancer was similar to that reported from Egypt and supports the relationship with schistosomiasis. In fact, squamous cell carcinoma, the commonest histological variant of bladder cancer in the Sudan, is distinctly uncommon in England and America, whereas it is frequent in countries with endemic schistosomiasis, like Egypt, Kenya and Uganda (Daoud et al., 1968; Sitas et al., 2008). Tumors are usually advanced at diagnosis.
In 1975 an early study analyzed age, sex, geographical origin, morphological features and association with urinary schistosomiasi in 255 urinary bladder cancer patients from Central Sudan. It was concluded that the pattern of bladder cancer conformed to that reported from regions with endemic schistosomiasi (Malik et al., 1975). More recently, a series of 52 patients with squamous cell carcinoma of the urinary bladder were studied in Khartoum. These cases accounted for 52/193 (27%) of all bladder tumors studied over a 6-years period. Male:female ratio was 12:1; 62% of the patients were below 50 years of age (mean 47) and only 31% reported a previous history of urinary schistosomiasi. However associated stigmata of S. haematobium infestation, such as sandy patches, were detected in 69% of the cases. Fourteenth had schistosoma ureteric strictures and most tumors were in the region of the trigone; 60% was clinically staged T3N0M0 at presentation, i.e., there was evidence of locally aggressive disease while metastases were not documented (Sharfi et al., 1992).

Four hundred and fifty patients with haematuria were also studied in Khartoum. Their mean age was 35 years and 103 (23%) had past history of urinary schistosomiasi. The commonest causes of haematuria were urinary calculi, found in 206 patients (46%), to which other 16 cases with resident bladder stones should be added, and carcinoma of the bladder, detected in 47 patients (10%). Twenty of the bladder cancer patients had squamous cell carcinoma in association with urinary schistosomiasi, and all these patients were under 40 years of age. Other causes of haematuria included glomerular diseases in 31 patients, malignant renal tumors in 11, benign renal cysts in 5, benign prostatic hyperplasia in 31, cystitis in 9, and urethritis also in 9 patients (Sharfi and Hassan, 1994).

4.11. Prostate cancer

Prostate cancer is estimated to be a major cancer of men in several sub-Saharan African countries, and African-Americans have higher rates of prostate cancer incidence and mortality compared to men of other ancestries, particularly in the younger age groups (Brawley, 1998; Delongchamps et al., 2007). In the year 2008 at NCI-Ug, prostate cancer ranked first among all cancer types in males (34.4%, 96/271). This reflected the current improvement of the diagnostic facilities (INMO Annual Report, 2008). Despite this, no published data are currently available for prostate cancer in the Sudan. No single report was retrieved by searching PubMed (prostate cancer and Sudan), and prostate cancer is not included in the major cancer series from Central Sudanese hospitals. This is most probably the consequence of multiple combined factors, including little attention to prostate cancer screening, lack of diagnostic facilities, scarce disease awareness, comparatively low life expectancy and young population structure.

5. Conclusion

The Sudan appears to be experiencing a growing cancer epidemic, which carries many challenges characteristic of developing countries. These include high frequency of advanced, difficult-to-treat cancers at presentation, a high burden of cancers related to infectious diseases and/or associated with reproductive risk factors in women, as well as cancers linked to traditional lifestyles. Furthermore increasing pollution may pose new threats, which still need to be evaluated and addressed. However, public concern about cancer is increasing. The Federal Ministry of Health in Khartoum has formed a committee to draft a proposal for a cancer control program. Furthermore, the Federal Ministry of Health issued a National Strategy for Reproductive Health for the years 2006–2010 (Maternal and Newborn Health “MNH”, 2006–2020), that aims at establishing a screening program for breast cancer and cancer of the cervix; [http://www.mnoh.gov.sd/English/St_Plan/doc/SudanNationalStrategyforReproductiveHealth%5D.pdf].

The challenges of implementing such programs are nonetheless formidable, and, even if fully implemented, many problems would remain open. In order to insure more effective interventions these efforts could be at first focused on geographically defined areas better served by central cancer institutions.

The data we reviewed in this work can be in many ways biased and are certainly incomplete. Important forms of cancer not treated here might in fact be frequent in the Sudan, but might remain under-diagnosed and under-reported, while more easily detectable forms are probably over-represented in hospital series. Nonetheless, our purpose was to provide an overview of the present state of knowledge, and to highlight some remarkable efforts directed to shed light on cancer in the Sudan. Cancer appears to pose a major threat to the health of the Sudanese population. To address this threat it is necessary to act at different and complementary levels, starting from the ex novo development of cancer management facilities and from proper training of personnel, while research on the epidemiological, pathobiological and genetic characteristics of the most common cancers should be promoted, together with investigations addressing their relationships with environmental risk factors. These are very difficult tasks that require time, dedicated manpower, continuous political and financial support as well as scientific, educational and sanitary cooperation, both at the national and, necessarily, at the international level. Hopefully, this review will contribute to raise interest on cancer problems in the Sudan and, more generally, in other sub-Saharan African countries.

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