Article

Hepatocellular carcinoma and aflatoxin in Sudan: The way forward

Moawia Mohammed Ali Elhassan

Author Affiliation: Oncology Department, The National cancer Institute, University of Gezira, Wad Madani, Sudan

Correspondence: Moawia Mohammed Ali Elhassan moawia2@gmail.com

Submitted: July 2023
Accepted: September 2023
Published: February 2024

Citation: Mohammed Ali Elhassan, Hepatocellular carcinoma and Aflatoxin in Sudan: The way forward, South Sudan Medical Journal, 2024;17(1):22-26 DOI: https://dx.doi.org/10.4314/ssmj.v17i1.5

ABSTRACT

Hepatocellular carcinoma (HCC) is the sixth most common type of cancer and the third leading cause of death worldwide. It is especially prevalent in developing countries, with around 80% of cases occurring in Asia and Africa. Aflatoxin B1 is a well-documented risk factor for HCC, among other factors. In Sudan, there is limited reliable and comprehensive data on cancer epidemiology, including HCC. This paper focuses on the current status of HCC in Sudan, specifically in relation to aflatoxin. Additionally, recommendations are provided to enhance the control measures for HCC in the country.

Keywords: hepatocellular carcinoma, aflatoxin B, mycotoxins, groundnuts, sub-Saharan Africa

Introduction

Primary liver cancer, which is the sixth most commonly diagnosed cancer and the third leading cause of death globally in 2020, is composed of several subtypes such as hepatocellular carcinoma (HCC), cholangiocarcinoma, hepatoblastoma, and angiosarcoma, but typically HCC accounts for 85-90% of cases.[1] Annually around 906 000 new cases of HCC are reported worldwide, with the highest incidence (>20 per 100,000) reported in countries in Eastern Asia, Southeastern Asia and North Africa. In contrast, South and Central America, as well as most of Europe, have low-incidence rates of less than 5 per 100,000.[1,2] The burden of HCC has been on the rise in developing countries, with approximately 80% of cases occurring in Asia and Africa.[1] Although several factors can increase the risk of developing HCC, the most documented ones are exposure to aflatoxin B1, heavy alcohol consumption and the hepatitis B and C viruses' infections, as well as iron overload.[1]

In Sudan, the incidence and mortality of HCC are difficult to determine as reliable and comprehensive data on cancer epidemiology are lacking since there is no functional national cancer registry. However, studies have suggested that HCC is amongst the 8th commonest cancer in Sudan with an age-standardized rate of 4.2 per 100,000.[3] Data from the National Cancer Institute, Sudan (Figure 1) revealed a sharp increase in HCC cases diagnosed between 2000 and 2018. This may be due to a combination of factors, including exposure to aflatoxin B1, alcohol consumption, and limited access to preventive measures such vaccination against hepatitis B virus. In Sudan, approximately 4.98% and 1.62% of the population in 2019 had chronic hepatitis B virus and chronic hepatitis C virus, respectively. Moreover, about 12% of liver cancer deaths are attributed to hepatitis B virus, whereas hepatitis C virus is responsible for 10% of these fatalities.[4] The implementation of screening for hepatitis B virus and hepatitis C virus in all blood banks nationwide, along with the addition of hepatitis B virus vaccination to the extended immunization program in 2006, represent significant milestones in the country's efforts to combat viral hepatitis. Total alcohol consumption per capita (litres of pure alcohol, projected estimates, 15+ years of age) in Sudan was reported at about 0.51 litres/year in 2018.[5]

Despite the high incidence of HCC in Sudan, there are few data regarding its burden in this region. This work highlights the current status of HCC in Sudan, specifically in relation to aflatoxin. Additionally, recommendations are provided to improve control measures for HCC in the country.

Aflatoxin as a risk factor for HCC

Aflatoxins are toxic secondary metabolites produced by fungi belonging to Aspergillus family, with *Aspergillus flavus* and *Aspergillus parasiticus* being the major producers. These toxins are classified into four major types: B1, B2, G1 and G2, with B1 being considered as the most hepatotoxic and hepatocarcinogenic. Aflatoxins can be found in variety of grains but most often occur in peanuts and maize. An estimated 4.5 to 5.5 billion individuals worldwide are at risk of exposure to these toxins.[6] The optimal environmental conditions for fungal growth and toxins production are temperatures between 24 and 35°C, and the moisture content exceeding 7% (10% with ventilation).[7] As a result, aflatoxin contamination predominantly impacts regions situated between 40° north and 40° south of the equator. Consequently, this issue is more prevalent in developing countries within the tropical region.[7] With the impact of climate change, it is expected that the contamination of food crops with aflatoxins will increase, as these conditions are favourable for proliferation of Aspergilli. In Sudan, like most sub-Saharan African countries, the high temperature and humidity are highly suitable for growth of Aspergillus fungi and production of mycotoxins.[6]

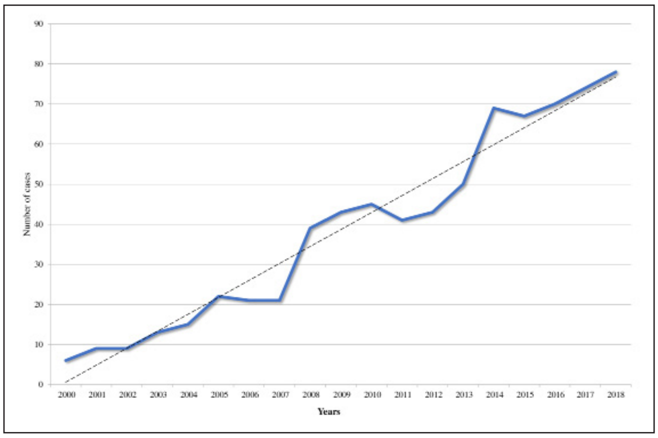

Figure 1. Number of hepatocellular carcinoma cases treated at the National Cancer Institute, Sudan between 2000 and 2018 Source: Annual Reports, Oncology Department, National Cancer Institute, Sudan

Humans can be at risk of exposure to aflatoxin either directly by consuming aflatoxin-contaminated products like maize and peanuts or indirectly by consuming animal-produced food such as milk, eggs, and liver, wherein animals were fed aflatoxin-contaminated feed.[6,8] The European Commission and the United States (USA) have different maximum limits for aflatoxins in human food commodities. The European Commission sets a maximum limit of 4 μg/kg, while the USA allows a higher limit of 20 μg/kg. However, the USA has stricter limits for specific commodities like milk and milk products, which have an action level of 0.5 μg/kg for aflatoxin M1, a metabolite of aflatoxin B1 found in milk.[9] The maximum levels for aflatoxins set by the Codex Alimentarius Commission, established by FAO and WHO, in various nuts, grains, dried figs and milk are in the range of 0.5 to 15 μg/kg.[10]

Many studies have demonstrated the association between the ingestion of aflatoxin-contaminated foods and the risk of HCC. The International Agency for Research on Cancer (IARC) has categorized aflatoxins as a group 1 carcinogens. They have also confirmed the link between food contamination, specifically with aflatoxin B1, and the increased risk of HCC.[8] It has been estimated that aflatoxins may be responsible for 28.2% of all HCC cases worldwide.[11] Omer et al. investigated the combined effects of hepatitis B virus infection and aflatoxin B1 exposure on the development of HCC in Sudan.[12] They found that Hepatitis B virus and aflatoxins exposure account for approximately 80% of HCC cases, whether alone or in combination.

Aflatoxin and HCC in Sudan

Populations in developing countries especially those in tropical and subtropical areas are almost universally exposed to moderate to high levels of aflatoxins. Aflatoxins can contaminate a wide range of food commodities, such as cereals, oilseeds, spices, nuts, and milk products, posing a potential health hazard for both humans and animals along with huge economic losses. Sudan, the leading producer of peanuts (groundnuts) in the world, primarily cultivates peanuts in Western Sudan and the irrigated schemes of the Gezira State. Homemade peanut butter, locally called "dakwa," is a popular dish throughout the country, particularly among impoverished communities. Omer et al. evaluated aflatoxin levels in peanut butter samples collected from the Western and Central Sudan. In this study, contamination of peanut butter samples with aflatoxins was defined as levels exceeding 10 μg/kg. The authors reported that peanut butter contains aflatoxins 5-20 times higher than the WHO safety guidelines. Furthermore, aflatoxin contamination in peanut butter samples was higher in Western Sudan (63%) compared to Central Sudan (50%).[12] Another study examined traditionally prepared and distributed peanut butter samples sold by street vendors in the Khartoum State, Sudan. The study found high levels of aflatoxin B, which is above the internationally regulated tolerance levels, in all screened peanut butter samples.[13]

Younis and Malik investigated aflatoxin contamination in Sudanese groundnuts and groundnut products (excluding oil). They discovered that the percentage of aflatoxin contamination was as follows: 2% for kernels, 64% for butter, 14% for cake, and 11% for roasted groundnuts. Their findings indicated that aflatoxin B1 was predominant in all samples.[14]

A study on vegetable oil samples collected in Khartoum state reported that nearly all (98.8%) samples were contaminated with aflatoxins, with a mean level of 57.5 μg/kg. Notably, all sesame oil was found to contain aflatoxin levels that exceeded the United States FDA acceptable limit of 20 μg/kg.[15] Similarly, another study in Sudan aimed to measure aflatoxin levels in groundnut, sesame, and cottonseed oils. Aflatoxin was detected in 14.3% of samples, the highest incidence of aflatoxin contamination occurred in sesame followed by groundnut while no aflatoxin contamination was detected in cottonseed oil. All aflatoxin contaminated samples are unrefined, highlighting the importance of refining processes for eliminating aflatoxins from edible oils. The higher incidence of aflatoxin contamination in sesame oil warrants further investigation, considering its wide consumption in Sudan without refining.[16] In their study, Mariod et al. found that the concentration of aflatoxin B1 in groundnut oil samples collected from various regions in Sudan showed a range of 0.5 to 70 μg/kg. Similarly, in samples of sunflower oil, the range was found to be 0.7 to 35 μg/kg. The study also highlighted that unrefined samples had significantly higher levels of contamination. As a result, it was concluded that inadequate practices during the cultivation, harvesting, handling, and storage of crops were contributing factors to the elevated levels of aflatoxin B1 in the oil samples.[17]

The prevalence of aflatoxins in animal feed in Khartoum State was investigated. The results showed higher levels of aflatoxin B1 contamination, which was detected in 32.14% of the samples. The average concentration was found to be 109.68 μg/kg, with a concentration range of 5.94–327.73 μg/kg. Additionally, the aflatoxin M1, major metabolite of aflatoxin B1, was found to be prevalent in the samples of dairy cattle milk in the Khartoum State.[18] Several studies conducted in Africa have also reported high concentrations of aflatoxin M1 in raw milk.[19]

The above-mentioned literature from the Sudan revealed that aflatoxin B1 contamination in food commodities is alarmingly high. Climatic conditions, poor storage conditions and ineffective food regulations favour the occurrence of mycotoxins in the Sudan.

The Way Forward

The following measures are proposed to different stakeholders to effectively prevent and control aflatoxin contamination.

Recommendations to farmers:

• Empower farmers to implement aflatoxin prevention and control measures, including:

- Conduct regular inspections of whole grains (especially maize, sorghum, rice) and nuts such as peanuts, which are commonly contaminated with aflatoxins.
- Discard any items that show signs of mould.
- Avoid causing damage to grains during drying and storage, as damaged grains are more prone to fungal invasion and mycotoxin contamination.
- Store grains properly in dry and well-aerated storage facilities.

Recommendations to the public:

• Raise public awareness about aflatoxin prevention and control through effective communication, including:

- Purchase grains and nuts as fresh as possible.
- Ensure proper storage of food, keeping it free from insects, dry, and not exposed to excessive warmth.
- Minimize the time interval between purchase and consumption of food products.
- Encourage a diverse diet, which not only reduces mycotoxin exposure but also improves overall nutrition.

Recommendations to local authorities:

- Demonstrate the political will to address the issue of aflatoxin exposure.
- Disseminating information on proper storage, handling, and processing techniques.
- Strengthen the coverage of the hepatitis B vaccination program to reduce the prevalence of the virus, as it can compound the effects of aflatoxin exposure and contribute to cancer development.
- Support the development and accreditation of laboratories at the national level for mycotoxin testing.
- Enforce regulations to ensure that the concentration of aflatoxins in traded foods is minimized and comply with the globally recognized standards.
- Promote the use of crop varieties with a lower risk of aflatoxin contamination.
- Ensure the implementation of refining processes to eliminate aflatoxins from edible oils. Additionally, authorities should conduct regular inspections and testing of edible oils to check for aflatoxin levels. If oil samples exceed the maximum limits, they are considered unsafe for consumption and are removed from the market.

Recommendations to scientific communities:

- Conduct epidemiological studies to identify the risk factors for HCC in Sudan, as there is a limited amount of research in this field.
- Perform more research to investigate the dietary habits, farming methods, food storage conditions, and environmental factors that can decrease the risk of aflatoxin exposure in Sudan.
- Develop affordable and accessible methods for detecting aflatoxin contamination.
- Gain a better understanding of the true cost of aflatoxin contamination, as this information can potentially drive policy changes and a shift in attitudes toward the issue.

Conclusion

Sudan is witnessing an increasing incidence of HCC, possibly due to food contamination by aflatoxins. Further research is crucial to provide evidence for taking policy action. The results obtained from such studies would provide policymakers with valuable evidence to develop a control programme for HCC in the Sudan that is based on scientific evidence. Additionally, there is a high need for a comprehensive aflatoxin control programme that raises awareness about the disease and prompts the government, regulatory bodies, and the food industry to establish and enforce strict guidelines and standards to combat aflatoxin contamination. The ultimate goal is to reduce the impact of this life-threatening disease on the populations.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71: 209- 249. https://doi.org/10.3322/caac.21660
2. Rumgay H, Arnold M, Ferlay J, et al. Global burden of primary liver cancer in 2020 and predictions to 2040. J Hepatol. 2022;77(6):1598-1606. https://doi.org/10.1016/j.jhep.2022.08.021.
3. Saeed IE, Weng HY, Mohamed KH, et al. Cancer incidence in Khartoum, Sudan: first results from the Cancer Registry, 2009-2010. Cancer Med. 2014;3(4):1075-84. https://doi.org/10.1002/cam4.254.
4. The Coalition for Global Hepatitis Elimination; Sudan Data. https://www.globalhep.org/country-progress/sudan.
5. The World Bank; Total alcohol consumption per capita (Liters of pure alcohol, projected estimates, 15+ years of age) – Sudan. https://data.worldbank.org/indicator/SH.ALC.PCAP.LI?locations=SD
6. Benkerroum N. Aflatoxins: Producing-moulds,

structure, health issues and incidence in Southeast Asian and Sub-Saharan African countries. International journal of environmental research and public health. 2020 Feb;17(4):1215. https://doi.org/10.3390/ijerph17041215

7. Williams JH, Phillips TD, Jolly PE, et al. Human aflatoxicosis in developing countries: a review of toxicology, exposure, potential health consequences, and interventions. The American journal of clinical nutrition. 2004 Nov 1;80(5):1106-22. https://doi.org/10.1093/ajcn/80.5.1106

8. Ostry V, Malir F, Toman J, et al. Mycotoxins as human carcinogens—The IARC Monographs classification. Mycotoxin Res. 2017, 33, 65–73. https://doi.org/10.1007/s12550-016-0265-7

9. Kumar P, Gupta A, Mahato DK., et al. Aflatoxins in Cereals and Cereal-Based Products: Occurrence, Toxicity, Impact on Human Health, and Their Detoxification and Management Strategies. Toxins 2022, 14, 687. https://doi.org/10.3390/toxins14100687

10. Food and Agriculture Organization of the United Nations (FAO); The World Health Organization (WHO). Codex Allimentarius International Food Standards. General standard for contaminants and toxins in food and feed. (Last amended 2019). CODEX STAN. 193–1995. http://www.fao.org/fao-who-codexalimentarius/codex-texts/list-standards/en/.

11. Liu Y, Wu F. Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment. Environ Health Perspect. 2010 Jun;118(6):818-824. https://doi.org/10.1289/ehp.0901388

12. Omer RE, Kuijsten A, Kadaru AM, et al. Population-attributable risk of dietary aflatoxins and hepatitis B virus infection with respect to hepatocellular carcinoma. Nutr Cancer. 2004;48(1):15-21. https://doi.org/10.1207/s15327914nc4801_3

13. Elshafie SZ, ElMubarak A, El-Nagerabi SA, et al. Aflatoxin B1 contamination of traditionally processed peanuts butter for human consumption in Sudan. Mycopathologia. 2011 Jun;171(6):435-439. https://doi.org/10.1007/s11046-010-9378-2

14. Younis YMH, Malik MK.TLC and HPLC assay of aflatoxin contamination in Sudanese peanuts and peanut products.Kuwait J. Sci. Eng. 2003;30(1):79–93.

15. Elzupir AO, Suliman MA, Ibrahim IA, et al. Aflatoxins levels in vegetable oils in Khartoum State, Sudan. Mycotoxin Res. 2010 May;26(2):69-73. https://doi.org/10.1007/s12550-010-0041-z

16. Idris YM, Mariod AA, Elnour IA, et al. Determination of aflatoxin levels in Sudanese edible oils. Food Chem Toxicol. 2010 Aug-Sep;48(8-9):2539-41. https://doi.org/10.1016/j.fct.2010.05.021

17. Mariod AA, Idris YM. Aflatoxin B1 levels in groundnut and sunflower oils in different Sudanese states. Food Addit Contam Part B Surveill. 2015;8(4):266-70. https://doi.org/10.1080/19393210.2015.1082511

18. Elzupir AO, Elhussein AM. Determination of aflatoxin M1 in dairy cattle milk in Khartoum State, Sudan. Food Control 2010:21(6):945-946 https://doi.org/10.1016/j.foodcont.2009.11.013

19. Min L, Li D, Tong X, et al. The challenges of global occurrence of aflatoxin M1 contamination and the reduction of aflatoxin M1 in milk over the past decade. Food Control. 2020; 117:107352. https://doi.org/10.1016/j.foodcont.2020.107352.