The Aflatoxin Hazard and the Associated Health Effects

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Abstract

Aflatoxins are a family of fungal toxins that possess acute life threatening toxicity, carcinogenic properties and other potential chronic adverse side effects. Dietary exposure is considered a major public health concern especially for subsistence farming communities in sub-Saharan Africa and South Asia where staple dietary foods such as maize and groundnuts are often highly contaminated with aflatoxins due to the hot and humid climates and poor storage of food materials coupled with low awareness of risk and lax enforcement of regulatory limits. Aflatoxin exposure can occur at any stage in life and is a major risk factor for hepatocellular carcinoma especially when Hepatitis B infection is present. Recent evidence suggests that aflatoxin may be a causative factor in stunted child growth as well as lowering of immunity increasing susceptibility to diseases. However, a causative relationship has not been established between exposure to aflatoxins and these latter health defects has not been conclusively established. This paper addresses the various health effects of aflatoxin exposure and examines the effects of co-exposure of aflatoxins with other mycotoxins.

The Aflatoxin Hazard and the Associated Health Effects

Aflatoxins are secondary metabolic products of Aspergillus flavus and Aspergillus parasiticus fungi. They contaminate major food crops including maize, tree nuts and groundnuts. They are highly prevalent in tropical regions especially in sub-Saharan Africa and South Asia where the hot and humid climates that stimulate fungal growth allow them to flourish. The main types of aflatoxins are aflatoxin B1(AFB1), aflatoxin B2(AFB2), aflatoxin G1 (AFG1) and aflatoxin G2(AFG2) which are found in food materials. Aflatoxin M1(AFM1) and aflatoxin M2(AFM2) which are products of hydrolyzed metabolisis of aflatoxin M1 and M2 respectively can be found in milk. AFB1is the most common type of aflatoxin and the most toxic has been labelled by the International Agency for Research on Cancer as a human carcinogenic while AFM1 is considered a ‘possible carcinogen’.

Aflatoxin is a global food safety concern as recognized by the World Health Organization (WHO) with rural subsistence farming communities in the developing world being the population most at risk of exposure to aflatoxins. This is due to factors like a majority of their staple foods being susceptible to aflatoxin contamination, issues of food insecurity, low aflatoxin awareness in the communities and lack of enforcement of regulatory limits on food consumption.

# Health Effects

The main route through which humans are exposed to aflatoxins is through direct consumption of contaminated food. Aflatoxin exposure can occur throughout the life course beginning in utero through trans placental exposure, through breast milk amongst young children during breastfeeding. However, the type of aflatoxin exposure that occurs during breastfeeding is the aflatoxin AFM1 which is less toxic than the type of aflatoxin found in food (AFB1). Exposure to aflatoxins also occurs during weaning especially in sub-Saharan Africa and Southern Asia where weaning foods are cereal and legume based, both of which are susceptible to aflatoxin contamination and children’s exposure increases during weaning.

Exposure to high doses of aflatoxins in a short period of time is known as acute aflatoxicosis. Although acute aflatoxicosis occurs on a case to case basis, large outbreaks have been known to occur for instance in Kenya in 2004, 317 individuals were diagnosed with acute liver failure of which 125 (37%) died as a result of acute aflatoxicosis. The trigger was hypothesized to be consumption of contaminated home grown maize. Tests ran on maize samples from patients with acute aflatoxicosis was found to have eight times the amount of aflatoxin contamination that maize from those from patients without aflatoxicosis.

Chronic aflatoxicosis, on the other hand is caused by exposure to low dose aflatoxins over a long period of time. This type of aflatoxicosis is more prevalent than acute aflatoxicosis. The most established effect of chronic exposure is hepatocellular carcinoma (HCC). Other effects include impaired child growth and immune suppression.

## Hepatocellular Carcinoma(HCC)

Hepatocellular carcinoma was in 2012 classified as the sixth most common cancer worldwide with 83% of cases in less developed regions in the world. The highest incident rates were observed in Asian and African countries. Owing to its mutagenic and carcinogenic properties, aflatoxin has been classified as a major risk factor alongside the Hepatitis B virus (HBV) and the Hepatitis C virus (HCV). In fact, it has been shown that aflatoxins and HBV, which are both highly prevalent in Africa and South Asia, can synergistically interact, resulting in an increased risk of HCC.

A systemic review and meta- analysis of 17 case control and cohort studies carried out in sub-Saharan Africa, China and Taiwan examined the Population Attributable Risk (PAR) of aflatoxin related HCC. The population attributable rate is the number or proportion of patients that would not occur if a risk factor is removed. The PAR of aflatoxin related HCC was 17% but was higher in HBV positive populations (22%) in comparison to HBV negative populations (8.8%). This highlights the potential reduction reduction in HCC that could be achieved by significantly reducing aflatoxin exposure.

Another study in China that considered the impact of agricultural reforms during the 1980s, involving the change from a maize based diet to a rice based diet, which is lower in aflatoxin contamination, and implementation of mass HBV immunization program in that country, on the prevention of primary liver cancer. With the use of the Qidong Cancer Registry data and the measurement of the albumen contaminated with aflatoxins (AF-alb) in serum samples collected from 7 different cohorts between 1982 and 2012. It was found that the PAR for reduction in primary liver cancer due to these changes was estimated to be 65%. AF-alb concentrations were found to have declined from a mean of 19.3 pg/mg to undetectable levels of 0.5pg/mg between 1989 and 2012. This study highlights that a reduction in aflatoxin exposure by changing diet coupled with control of HBV can achieve a large reduction in liver cancer prevalence.

Aflatoxin has also been implicated in the aetiology of other liver diseases including cirrhosis and hepatomegaly. A study in Kenya conducted by Gong et al. reported that the prevalence of hepatomegaly, a firm form of liver enlargement increased in children with higher aflatoxin exposure. This is consistent with the fact that the liver is the key target organ for aflatoxin toxicity.

## Impaired Child Growth

The first 1000 days of life from conception to 24 months presents acritical period for healthy growth and development, hence dietary intake during pregnancy plays a fundamental role in the child’s future health status. In sub-Saharan Africa, malnutrition and child growth impairment are major public health concerns.

WHO defines stunting as a height-for-age Z score (HAZ) of -2 and being underweight as having a weight-for-age Z score (WAZ) of-2 and wasting as having a weight-for-height Z score of -2. The impact of aflatoxin on growth at different time points has been investigated

In Utero Exposure

A number of studies have demonstrated that aflatoxin exposure can occur in utero through trans placental transmission and that higher exposure levels have been associated with lower birth weights and stunted child growth. It has been suggested that epigenetic changes which may occur as a result of aflatoxin exposure, are the causative agents of lower birth weights heir and stunted growth.

Exposure via Breast Milk

Although breast milk is full of nutritional and immunological components, it is a potential source of aflatoxin exposure for very young infants. AFM1 the hydroxylated metabolite of AFB1 is typically detected in breast milk 12 to 24 hours following ingestion of food contaminated with AFB1. Only a few epidemiological studies have investigated the relationship between AFM1 in breast milk samples and impaired child growth. Mahdavi et al. () reported that AFM1 concentrations measured in breast milk samples of lactating Iranian women who were exclusively breastfeeding their children were negatively associated with their infants HAZ scores. The number of positive AFM1 samples in this study, however, was very small and insufficient information is provided on how the data collected was used, making interpretation difficult.

Magoha et al. examined the relationship between AFM1 measured in breast milk samples of 143 lactating mothers and growth impairment in their infants under 6 months of age in Northern Tanzania. Breast milk samples along with anthropometric data was collected in the first third and fifth months after birth. All of the breast milk samples had detectable AFM1 concentration.

Significant inverses were found between AFM1 exposure and HAZ and WAZ but not WHZ. It is not possible to measure individual levels of breast milk consumption in such a study therefore AFM1 exposure estimates were based on age-specific average intakes stated by the United States Environmental Protection Agency. This study highlights the potential for exposure of AFM1 from breast milk contributing to child growth impairment.

Although significant inverses were found by the studies, further research is necessary to draw reasonable conclusions regarding this complex relationship. Breastfeeding, should, therefore not be discouraged based on this limited evidence. The WHO recommendation of exclusive breastfeeding until 6 months of age should be encouraged owing to the high nutritional content and immunological properties of breast milk. Furthermore, infants who are exclusively breastfed appear to have lower AF-Alb concentrations compared to those partially breastfed and fully weaned. It must therefore be remembered that prolonged breastfeeding is protective to child health

Exposure via weaning food

Children of weaning age in developing countries especially in sub-Saharan Africa are considered a high-risk population group for aflatoxin exposure. Maize and groundnuts, which are typical constituents of weaning foods are highly susceptible to aflatoxin contamination. Furthermore, exposure levels relative to body weight are higher for children than for adults and the rapid growth that occurs and the additional nutrients required during this time period, mean that this is a critical time for the impact of aflatoxin on growth. It is evident that stunted growth is highly prevalent in parts of Africa and South Asia. For instance, in East and West Africa approximately 42% and 36% respectively, of the children under the age of 5 years have stunted growth. This is similar to the rates observed in South Central Asia where approximately 36% of children under the age of 5 years have stunted growth.

There is evidence to suggest that aflatoxin exposure during this critical period of weaning may be an underlying determinant of impaired child growth. In a study done in Benin and Togo, it was seen that aflatoxin exposure levels increased when children started on weaning foods, peaking at 3 years of age. Multivariate regression analysis suggested that aflatoxin exposure was inversely correlated with HAZ, WAZ and WHZ after adjustment of confounding factor.

# Conclusion

Aflatoxin exposure as a result of contamination of staple cereal crops is a significant food issue, especially for developing regions like South Asia and sub-Saharan Africa. Very high exposure can lead to acute toxicity which can be very lethal. Chronic exposure to aflatoxins can occur at any age including in utero and typically increases during weaning. Aflatoxin is an established risk factor for liver cancer especially when HBV infection co-exists and there is increasing evidence of other impacts including child growth impairment and immune suppression.