Abstract

Background: Aflatoxins are potent carcinogens found in crops, such as peanuts, rice, maize, and other cereals that form the staple foods of people in developing countries. Epidemiological studies have linked dietary aflatoxin exposure with hepatocellular carcinoma (HCC) in humans and have shown that the risk of aflatoxin induced HCC is about 100 times greater in sub-Saharan Africa compared to other regions of the world. Aflatoxin ingestion is immunosuppressive and results in increased susceptibility to infections, activation of chronic infection and reduction of antibody responses to vaccines. Chronic aflatoxin exposure has also been shown to interfere with metabolism of proteins and a number of micronutrients that are critical to health and immune functioning. However, few studies have investigated the effect of aflatoxins on the health and immune status in humans.

Methods: We conducted a cross-sectional study in four villages in the Ejura Sekyedumase district of Ghana to measure the aflatoxin albumin adduct biomarker (AF-ALB) levels in the blood of the people and examine the association of AF-ALB levels with selected demographic and individual characteristics.

Results: AF-ALB were found in the plasma of all participants. By multivariate analyses, ethnic group, the village in which participants lived, the number of individuals in the household, and being at least one child in secondary school were significant predictors of AF-ALB. Participants who reported symptoms of acute aflatoxicosis, such as a history of yellow mouth, loss of appetite and, history and pattern of vomiting were more likely to have high AF-ALB levels. High proportions of the study group had abnormal levels of total protein (50%), low levels of albumin (40%) and high alanine aminotransferase (ALT) (45%). Approximately 31% of participants were positive for HBV and 11% were positive for HCV. The immune status of the participants was significantly associated with high AF-ALB. Thirty-one percent of participants were deficient in vitamin A and 71% deficient in vitamin E. Those with low AF-ALB had significantly lower values for vitamin A and E levels. Participants with high AF-ALB had significantly lower percentages of activated T and B cells (CD3+CD80+ and CD19+CD100+) and lower levels of CD4+ cells that expressed proliferation or both phenotypes in comparison to those with low AF-ALB levels. This is consistent with the observed increase in resistance to infections. There is a need for specifically targeted interventions to reduce aflatoxin exposure in Ghana.

Outbreaks of Acute Aflatoxicosis - Worldwide

- Other large outbreaks have occurred in India (1975) and Malaysia (1995).

Regional map of Ghana

Maize and peanuts in Ejura, Ghana

Maize after harvest in Ejura, Ghana

Study objectives

- Establish a baseline for aflatoxin exposure in the population.
- Examine sociodemographic factors associated with AF-ALB levels.
- Examine cellular immune status in relation to AF-ALB levels.
- Determine cytokine expression and antibody responses to different antibodies.

Sociodemographic factors associated with high AF-ALB

- Level of education (risk greater for those with primary or no education).
- Certain ethnic group (certain peas and peanuts as staples).
- Live in particular villages.
- Larger number of household members (risk increased at 5 household members).
- Children in secondary school (risk greater for 1 or more in secondary school).

Health indicators – study population

- Abnormal liver function, hepatitis, malaria & HIV infections:
  - Total protein (highly correlated): 30%
  - Albumin (low): 33%
  - Alanine transaminase (high): 40%
  - Hepatitis C: 40%
  - Hepatitis B: 14.3%
  - Malaria: 32%
  - HIV+:

Health factors significantly associated with high AF-ALB

- Experienced yellowing of the mouth, painful vomiting, swollen stomach.
- Hepatitis B positive.
- Serum ALT level (SD= 20.27 units for every unit increase in AF-ALB). The higher the AF-ALB levels, the higher the ALT level. (SD= 37.33 units for every unit increase in AF-ALB).
- Vitamin E deficiency (deficient in 71% (mean SD=0.44 vs. 0.28 mg/L; range=0.02-1.82 mg/L).

Percentages of activated T and B cells in relation to AF-ALB levels

Low AF-ALB

High AF-ALB

The percentages of CD3+CD80+ (2.164 vs. 3.065, p=0.137) and CD19+CD100+ (0.972 vs. 4.45, p=0.12) in each group were significantly lower (p<0.002) for those with high AF-ALB levels compared to those with low AF-ALB.

Perforin and Granzyme A positive CD8+ T cells and AF-ALB levels

The percentages of CD8+ perforin+ and CD100+ in participants with high AF-ALB are much lower (0.26% and 0.49% respectively) than in participants with low AF-ALB (2.72% and 1.77% respectively).

Summary:

- Immune status and high AF-ALB levels:
  - Significantly lower levels of T (CD3+), B (CD19+), and NK (CD16+CD56+) cells expressing the CD69 activation marker (present in cells from mounting appropriate immune responses).
  - Significantly lower levels of perforin and granzyme A expressing CD8+ T cells (perforin- and granzyme- cells, respectively).

Collaborators and Support

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