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EDITED BY
Hani El-Nezami,
The University of Hong Kong,
Hong Kong SAR, China

REVIEWED BY
Luis Abrunhosa,
University of Minho, Portugal
Wasiu Awoyale,
Kwara State University, Nigeria

*CORRESPONDENCE
Elisabetta Lambertini
✉ elambertini@gainhealth.org

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Quantitative assessment of aflatoxin exposure and hepatocellular carcinoma (HCC) risk associated with consumption of select Nigerian staple foods

Anthony Wenndt[1], Florence Mutua[2], Delia Grace[2,3], Lian F. Thomas[2] and Elisabetta Lambertini[1]*

[1]Global Alliance for Improved Nutrition (GAIN), Washington, DC, United States, [2]International Livestock Research Institute (ILRI), Nairobi, Kenya, [3]Natural Resources Institute, University of Greenwich, Greenwich, United Kingdom

Aflatoxin contamination of staple grains and legumes has been linked to hepatocellular carcinoma (HCC) and other adverse health outcomes, constituting a substantial public health concern globally. Low-resource food environments in sub-Saharan Africa are often under-regulated and are particularly vulnerable to adverse health and nutrition outcomes associated with aflatoxin exposure. This study identifies levels of HCC risk in the northern Nigerian adult population, leveraging a systematic review of available evidence on aflatoxin contamination in Nigerian maize, groundnut, rice, cowpea, and soybean. Estimated dietary intake (EDI) was computed using publicly available dietary consumption data and a probabilistic quantitative risk assessment was conducted to determine the relative risk of HCC associated with consumption of selected aflatoxin-contaminated commodities. In total, 41 eligible studies reporting aflatoxin contamination were used to model the distribution of aflatoxin concentrations in Nigerian commodities. EDIs for maize, groundnut, rice, and cowpea exceeded the provisional maximum tolerable daily intake (PMTDI) level of 1 kgbw-1 day-1, with maize yielding the highest mean EDI (36.7 kgbw-1 day-1). The quantitative risk assessment estimated that 1.77, 0.44, 0.43, 0.15, and 0.01 HCC cases per year/100,000 population were attributable to aflatoxin exposure through maize, groundnut, rice, cowpea, and soybean, respectively. Sensitivity analysis revealed that aflatoxin concentration, dietary consumption levels, consumption frequency, and other variables have differing relative contributions to HCC risk across commodities. These findings constitute a novel multi-study risk assessment approach in the Nigerian context and substantiate existing evidence suggesting that there is reason for public health concern regarding aflatoxin exposure in the Nigerian population.

KEYWORDS
aflatoxin, risk assessment, exposure, LMIC, mycotoxins, food safety, Nigeria, Africa

1. Introduction

Traditional food markets—also known as informal markets and comprising "wet" or public markets, small shops, vendors and other non-modern retail—are critical for ensuring access to safe, nutritious diets in many low- and middle-income countries (LMIC) (Wertheim-Heck et al., 2019). Food safety regulatory systems in many LMIC markets, formal and informal, are often insufficient for preventing exposures to contaminants that can jeopardize community health and offset the nutritive value of food. However, most of the poor obtain food from traditional markets so these are of especial interest (Grace, 2015). One such contaminant, aflatoxin, is widespread in informal grain value chains in LMICs and constitutes a food safety concern of burgeoning importance both for public health and economic prosperity in traditional market settings. Aflatoxin is a potent carcinogen, implicated in hepatocellular carcinoma (HCC) in humans, and, in some contexts, a leading risk factor for HCC (Liu and Wu, 2010). In addition to its carcinogenic properties, aflatoxin is associated with growth impairment in children (Khlangwiset et al., 2011) and may be an important driver of environmental enteropathy, resulting in compromised gut integrity and limited nutrient adsorption (Smith et al., 2012), although evidence for contribution to stunting is less strong (Hoffmann et al., 2018). The risk of dietary aflatoxin exposure is particularly pronounced in many sub-Saharan African food systems, where obsolete monitoring infrastructure, poverty, and weak beaurocratic structures coincide with high reliance on aflatoxin-susceptible staples, such as maize and groundnuts.

In the context of Northern Nigeria, the breadth and magnitude of aflatoxin exposure risk associated with foods sold in traditional markets are poorly understood, particularly for the most vulnerable consumers, limiting the capacity to identify and mobilize mitigation opportunities. Foods acquired at traditional markets have distinct characteristics compared to those produced on farms and consumed locally. Foods sold at these markets are usually subjected to various layers of informal and formal quality control, such as sorting, pest management, or visual inspection by supply chain intermediaries, which can in some circumstances measurably reduce the aflatoxin burden in food; for example, it was found that the prevalence of mycotoxins in traders' maize was lower than at other nodes of the value chain, even after a period of storage (Liverpool-Tasie et al., 2019). In addition, the consumer has direct control of quantity when purchasing food, enabling them to purchase quantities that they know will not spoil before consumption. On the other hand, with respect to purchased foods, the consumer has little control over pre-market nodes of the value chain, such as production, storage, and transport, which can all be critical control points for aflatoxin management (Massomo, 2020). Given that aflatoxin contamination is often not visibly identifiable without specialized technology, even grain that appears safe in the marketplace may be contaminated.

Northern Nigeria's traditional food markets cater to diverse populations, and supply communities with numerous food commodities. As in the rest of the country, maize and rice—both susceptible to aflatoxin contamination—are important staple grains in the region. Maize is commonly ground to flour and consumed as a stiff porridge (*tuwo masara*) or similar preparations. Rice is consumed either cooked as-is or ground to flour and consumed as cakes (*masa*). High-protein legumes such as cowpea and soybean are an important part of the local diet, but there has historically been little evidence on aflatoxin contamination in this crop. A steamed cowpea pudding, *moimoi*, is commonly consumed in the region. Soybean is commonly consumed as a curdled soymilk "cheese" or tofu-like product (*awara*) in the region. Groundnut, a major source of dietary aflatoxin globally, is an important crop in the region with production centered in the northern states of Niger, Kano, Zamfara, Kebbi, and others, contributing measurably to the Nigerian economy (Usman et al., 2013). Apart from whole groundnuts as a snack food, groundnut press cake (*kulikuli*)—a by-product of traditional or mechanical oil extrusion—is often shaped into various forms and consumed as a fried snack. Many of these commodities are available as raw ingredients or as ready-to-eat prepared foods sold at the marketplace.

Despite a substantial body of survey evidence regarding aflatoxin contamination in Nigerian food commodities, including in marketplace environments, there has hitherto not been any comprehensive risk assessment that has focused on this context. The aim of this study, implemented as part of the United States Agency for International Development (USAID) Feed the Future Initiative program, EatSafe: Evidence and Action Toward Safe, Nutritious Food (EatSafe), is to elucidate the extent of aflatoxin exposure risk associated with commodities commonly purchased from traditional food markets in Nigeria. At the start, a systematic review was conducted of aflatoxin contamination in five aflatoxin-susceptible local commodities, namely maize, groundnut, rice, cowpea, and soybean, reported in surveys from Nigeria. We used these aflatoxin occurrence data, in conjunction with secondary data on local dietary consumption, to estimate exposure and risk of HCC using a probabilistic quantitative risk assessment methodology. Based on these findings, the relative risk associated with local consumption of each commodity was determined and key recommendations identified for aflatoxin management in northern Nigerian traditional food markets.

2. Materials and methods

2.1. Literature review of aflatoxin contamination and prevalence in Nigerian commodities

A systematic review of peer-reviewed literature was conducted in Web of Science to ascertain reported data on aflatoxin contamination in Nigerian maize, groundnut, cowpea, soybean, rice, and other food products derived therefrom. Each search included three keywords, (1) "aflatoxin," (2) the commodity name, and (3) the geographic focus, "Nigeria." Articles were first assessed for relevance based on a title and abstract screening, followed by full text review of relevant articles. Eligibility for inclusion in the study was assessed using the following inclusion criteria: (1) publication date 1980—present, (2) aflatoxin, either total aflatoxin or aflatoxin B1 (AFB1) concentration determined for raw commodity (not cooked or prepared), (3) samples are reasonably intended for human consumption (not for livestock feed, etc.), (4) fungal growth is naturally-occurring, not artificially inoculated, (5) aflatoxin is detected in at least one sample (studies with 0% detection retained for modeling prevalence, but excluded from the contamination model), (6) reported means reflect batches of several distinct samples, not replicates of the same pooled sample(s), (7) the number of total samples analyzed is reported, and (8) an estimate of batch variance (standard deviation, range, etc.) is reported. Additional studies were identified by the authors *via* non-systematic searches in Google Scholar using similar keywords.

Data extracted from eligible studies included: mean, standard deviation, median, and range of aflatoxin concentration (ng/g); study year; country; sub-national division; commodity type; sample source (household, market, or prepared food); metabolite (total aflatoxin or aflatoxin B1); total number of samples; number of positive samples or detection rate; limit of detection. Individual batch means reported within studies were extracted separately, when possible. Risk modeling was done based on the aflatoxin B1 (AFB1) metabolite, in accordance with the known carcinogenic potency associated with the hepato-carcinogenic effects of AFB1 in conjunction with hepatitis B infection (JECFA, 1999). Whenever available, reported estimates of AFB1 concentration were extracted from the included studies. To be as conservative as possible (i.e., to prevent under-estimation of exposure) in risk assessment when only total aflatoxin concentration was reported, the reported total aflatoxin levels were treated as AFB1 in the subsequent risk assessment. When only the concentration range (minimum and maximum) was reported, the midrange (e.g., min+max/2) was used for analysis in place of the mean, as previously reported (Andrade and Caldas, 2015).

The spatial distributions of available aflatoxin contamination data for each commodity were visualized using GIS mapping. Batch-wise estimates of mean aflatoxin concentration were grouped by state of sample origin. Studies wherein multiple (>2) states/regions were pooled, and therefore geographic origin indistinguishable, were omitted from GIS analysis. If a study's reported batches encompassed two states but state origins were not reported on a batchwise basis, the study was classified as the majority-sampled state for GIS mapping if >2/3 of batches were from that state; otherwise, the study was omitted from the maps. Maps were generated with the 'ggspatial' package in R using open-access GIS datasets (Global Administrative Areas, 2022).

2.2. Risk modeling approach

A quantitative risk assessment model was developed to estimate exposure to AFB1 associated with consumption of staple foods in Nigeria, as well as the risk of HCC, a key adverse health outcome associated with aflatoxin dietary exposure. The model considers a "market to table" scenario to assess absolute and relative exposure associated with different food commodities and does not aim to include pre-harvest or supply chain risk factors upstream of retail. The model takes as key input the distribution of aflatoxin prevalence and concentration in the product at the point of purchase, and follows portions of each food through home handling, preparation, and consumption. Parameters included in the model and their distributions are summarized in Table 1 and described in the following sections. The model was programmed and executed in the R software environment (R Core Team, 2021). A second-order Monte-Carlo approach was used to account for both variability and uncertainty (using 1,000 iterations in each dimension) in input parameters and implemented using the "mc2d" package in R. The model included several key assumptions: (1) no fungal growth or additional toxin accumulation occurs during storage, before consumption; (2) aflatoxin concentration is stable at normal cooking temperatures, i.e., no concentration reduction occurs during cooking (Kabak and Var, 2008); (3) no detoxification procedure is implemented by the consumer, i.e., no "inactivation" of the toxin is accounted for.

The exposure model was based on Estimated Daily Intake (EDI) of aflatoxin attributable to per-capita consumption of each commodity. EDI was estimated for the study population using an equation adapted from that described previously (Udovicki et al., 2021):

$$EDI\ (ng\ kg^{-1} bw\ day^{-1}) = \frac{C \times S \times i \times f_{cons}}{BW} \quad (1)$$

Where C = concentration of aflatoxin per kg sample (ng/g), S = g consumed per person per day on a day the product is consumed, i = the frequency of contamination among portions, f_{cons} = the frequency of maize consumption in the population, and BW = body weight (kg). An exposure model was constructed for each commodity using the probability distributions of C, S, i, f_{cons}, and BW, following the EDI equation described above, and incorporated into a Monte-Carlo simulation model for risk assessment. Exposure model input parameters for each commodity are summarized in Table 1.

2.3. Probability distributions of input parameters

2.3.1. Aflatoxin prevalence in samples (i)

To account for the fact that not all samples (and, thus, not all portions consumed) are contaminated with detectable levels of aflatoxin, the probability of consuming a contaminated portion (i) was approximated by aflatoxin prevalence, or detection rate, in the model. The prevalence data reported by the literature considered were fit to a beta distribution and uncertainty around the parameter estimates was modeled using parametric bootstrapping (1,000 iterations) using the 'bootdist' function in the 'fitdistrplus' R package (Delignette-Muller and Dutang, 2015). In addition to its representation of the probability of consuming a contaminated portion, the 'i' parameter was also used to correct for possible overestimation of exposure attributable to the tendency in the literature to report means only for contaminated samples (i.e., excluding non-detects). Due to the small number of studies reporting detection rate for soybean, it was not possible to fit a beta distribution to the data; instead, the mean detection rate reported in the available literature (7.3%; see reference in Table 1) was used in the exposure model.

2.3.2. Aflatoxin concentration in samples (C)

To select an appropriate probability distribution to describe the observed aflatoxin concentrations (C) reported by the included studies, for samples where aflatoxin was detected, the empirical distribution of study means was examined, and a series of goodness-of-fit tests were performed. Concentration estimate data were assumed to be derived using assays of the same sensitivity and precision; in other words, the initial mass of samples collected and analyzed was ignored. Given the expected skewedness of aflatoxin data, three probability distributions suitable for skewed data were considered: gamma, Weibull, and log-normal, in addition to the normal distribution. Q–Q plots, P–P plots, and cumulative distribution functions (CDFs) were examined for model fit. Three Goodness-of-Fit statistics (namely the Kolmogorov-Smirnov statistic, the Cramer-von Mises statistic, and the Anderson-Darling statistic) were estimated for each of the probability distributions and compared (Supplementary material S1). As a final test of Goodness-of-Fit across the candidate distributions, uncertainty in the parameters of the fitted distributions was estimated using parametric bootstrapping (1,000 iterations). To ensure adequate fit of the selected distributions, Q–Q plots and P–P plots were examined for the final distributions before proceeding with exposure assessment and risk analysis (see Supplementary material S2). For use in quantitative risk

TABLE 1 Summary of exposure model input parameters for each commodity.

Variable	Sym.	Value or distribution[a]	Source
Maize			
Aflatoxin concentration (ng/g)	C	~TWeibull (l = 93.6, k = 0.75, 0, 1874)	Included studies: (Adebajo et al., 1994; Atawodi et al., 1994; Bankole and Mabekoje, 2007; Atehnkeng et al., 2008; Ayejuyo et al., 2011; Onilude et al., 2012; Perrone et al., 2014; Bandyopadhyay et al., 2019; Keta J. et al., 2019; Keta J. N. et al., 2019; Oyeka et al., 2019; Ayeni et al., 2020; Mbaawuaga et al., 2020; Onyedum et al., 2020; Shehu et al., 2020; Ekpakpale et al., 2021; Ezekiel et al., 2021)
Contamination frequency (%)	i	~ Beta (a = 1.11, b = 0.54)	
Consumption Frequency (portions/day)	f_{cons}	~ Empirical ({days consumed per week}, {proportion of population}) = ~ Empirical ({0, 1/7, 1}, {0.104, 0.150, 0.746})	(Olayiwola et al., 2012)
Mass conversion rate (g/g)	m	$\frac{1\ g\ maize}{5.15\ g\ tuwo\ masara}$	(Fadupin, 2009)
Consumption Level (g/portion)	S	~ TN (200*m, 86.6*m, 150*m, 300*m)	(Sanusi and Olurin, 2014)
Mean adult body weight (kg)	BW	~ N (63.7, 10.28)	(Akinpelu et al., 2015)
Groundnut			
Aflatoxin concentration (ng/g)	C	~TlnN (m = 2.72, s = 1.47, 0, 1281)	Included studies: (Bankole et al., 2005; Jimoh and Kolapo, 2008; Odoemelam and Osu, 2009; Ayejuyo et al., 2011; Afolabi et al., 2015; Oyedele et al., 2017; Adetunji et al., 2018; Ekhuemelo and Abu, 2019; Odeniyi et al., 2019; Vabi et al., 2020; Ezekiel et al., 2021; Adefolalu et al., 2022)
Contamination frequency (%)	i	~ Beta (a = 3.31, b = 0.61)	
Consumption Frequency (portions/day)	f_{cons}	~ Empirical ({days consumed per week}, {proportion of population}) = ~ Empirical ({0, 1/30, 1/7, 3/7, 1}, {0.100, 0.64, 0.0407, 0.0358, 0.0331})	(Maziya-Dixon, 2004; Ezekiel et al., 2013)
Groundnut oil yield (for mass conversion	δ	~ TN (0.283, 0.0865, 0, 1)	(Nkafamiya et al., 2010)
Mass conversion rate (g/g)	m	$\frac{1}{1-\delta}$	
Consumption Level (g/portion)	S	~ TN (121.45*m, 60.59*m, 30*m, 300*m)	(Sanusi and Olurin, 2014)[b]
Mean adult body weight (kg)	BW		(Akinpelu et al., 2015)
Rice			
Aflatoxin concentration (ng/g)	C	~TN (m = 52.1, s = 36.7, 0, 372)	Included studies: (Ibeh et al., 1991; Ayejuyo et al., 2011; Makun et al., 2011, 2014; Adejumo et al., 2013; Olorunmowaju et al., 2014; Rofiat et al., 2015; Awuchi et al., 2020; Onyedum et al., 2020; Ekpakpale et al., 2021; Ezekiel et al., 2021; Wartu, 2021)
Contamination frequency (%)	i	~ Beta (a = 1.28, b = 0.39)	
Consumption Frequency (portions/day)	f_{cons}	~ Empirical ({days consumed per week}, {proportion of population}) = ~ Empirical ({0, 2/7, 4/7, 1}, {0.837, 0.0709, 0.0511, 0.0378})	(Maziya-Dixon, 2004)
Mass conversion rate (g/g)	m	$\frac{1\ g\ rice}{3\ g\ cooked\ rice}$	Assumed
Consumption Level (g/portion)	S	~ TN (420*m, 182.23*m, 100*m, 1,000*m)	(Sanusi and Olurin, 2014)
Mean adult body weight (kg)	BW	~ N (63.7, 10.28)	(Akinpelu et al., 2015)
Cowpea			
Aflatoxin concentration (ng/g)	C	~TlnN (m = 3.29, s = 1.38, 0, 200) truncation upper bound (200 ng/g) is the highest batch maximum reported	Included studies: (Houssou et al., 2009; Afolabi et al., 2019; Awuchi et al., 2020; Ogungbemile et al., 2020; Ezekiel et al., 2021)
Contamination frequency (%)	i	~ Empirical ({1, 0}, {0.367, (1-0.367)})	
Consumption Frequency (portions/day)	f_{cons}	~ Empirical ({days consumed per week}, {proportion of population}) = ~ Emp ({1/7, 3/7, 5/7, 1}, {0.474, 0.363, 0.009, 0.153})	(Odogwu et al., 2021)
Mass conversion rate (g/g)	m		(Akuso and Kiin-Kabari, 2012)

(Continued)

TABLE 1 (Continued)

Variable	Sym.	Value or distribution[a]	Source
Consumption Level (g/portion)	S	~ *TN (198.3*m, 122.4*m, 50*m, 780*m)*	(Sanusi and Olurin, 2014)
Mean adult body weight (kg)	BW	~ *N (63.7, 10.28)*	(Akinpelu et al., 2015)
Soybean			
Aflatoxin concentration (ng/g)	C	~ *TlnN (1.88, 0.91, 0, 4)*	(Ogunsanwo et al., 1989; Atawodi et al., 1994; Fapohunda et al., 2018) (concentration); (Niyibituronsa et al., 2019) (truncation upper bound)
Contamination frequency (%)	i	~ *Empirical ({1, 0}, {0.073, (1-0.073)})*	(Fapohunda et al., 2018)
Consumption Frequency (portions/day)	f_{cons}	~ *Empirical ({days consumed per week}, {proportion of population}) = ~ Emp ({0, 1/7, 2/7 3/7, 1}, {0.1875, 0.1667, 0.2083, 0.239})*	(Adewale, 2005)
Mass conversion rate (g/g)	m	$\frac{1\ g\ soyben}{1.927\ g\ awara}$	(Noh et al., 2005)
Consumption Level (g/portion)	S	~*TN (94*m, 44*m, 0, ∞)*	ILRI consumption data
Mean adult body weight (kg)	BW	~ *N (63.7, 10.28)*	(Akinpelu et al., 2015)

[a]Distribution shorthands N = "normal", lnN = "log normal", T = Truncated. Aflatoxin concentration and contamination frequency parameters represent bootstraps on observed values reported in included studies.
[b]No distribution for *kulikuli* portion size was identified; the values used are for *akara*, another legume-based local snackfood with assumed similar portion size.

assessment, a distribution simulating variability conditional on the uncertainty bootstraps was generated using the 'mcstoc' function in the 'mc2d' R package. The upper bound used for truncation of the distribution was the maximum batch aflatoxin concentration reported for each commodity in the included studies.

Given that there were very few ($n = 1$) observations of detectable aflatoxin in soybean batches in the included studies, it was not possible to compute Goodness-of-Fit statistics for the candidate distributions, for this commodity. Instead, a log-normal distribution (truncated between 0 and the highest observed sample maximum) was assumed and fit to the available data. As the one included study reporting detectable aflatoxin in Nigeria reported a sample maximum of only 2 ng/g, a higher (i.e., more conservative) value of 4 ng/g, reported in a Rwandan study (Niyibituronsa et al., 2019) was used as the upper bound of the truncated distribution. Similarly, as there were scant records of aflatoxin contamination in Nigerian cowpea samples, one record from a neighboring country (Benin) that was identified in the systematic literature review was included in the dataset (Houssou et al., 2009).

2.3.3. Commodity consumption (f_{cons} and S)

Two food consumption parameters were included as inputs in the exposure assessment model: (1) the frequency of consumption events (f_{cons}), and (2) the quantity of product consumed per consumption event (S). For all commodities, f_{cons} and S were derived from previously reported consumption data for key prepared food consumed in the study region. Local foods selected for the estimation included *tuwo masara* (maize), *kulikuli* (groundnut), cooked rice, *moi-moi* (cowpea), and *awara* (soybean), each of which is a common local preparation of the focus commodity. Empirical distributions were fit to f_{cons} data (consumption events/week) for each commodity, based on reported values in the literature (Table 2). To account for the fact that aflatoxin data were reported for raw (unprepared) commodities, mass conversion rates (m) were applied to portion sizes to determine the equivalent of raw commodity consumed per portion (Table 2). Consumption amount S was assumed normally-distributed, and means (±SD) from prior studies were used to fit a probability distribution truncated at the lower bound of 0 (e.g., no negative consumption).

2.3.4. Adult body weight

Previously reported estimates of adult body weight (men, women, and the general population) for a Nigerian population (Akinpelu et al., 2015) were used to fit a probability distribution of this parameter for the exposure assessment. A mean (±SD) adult body weight of 63.17 (±10.28) kilograms (Akinpelu et al., 2015) was used for exposure assessment. Adult body weight was assumed to follow a normal distribution as per the approach previously described by Sirma et al. (2019).

2.3.5. Risk characterization: HCC

The risk of aflatoxin B1-associated hepatocellular carcinoma (HCC) attributable to consumption of each commodity was estimated based on probability distributions of exposure (i.e., EDI), the constituent aspects thereof, and the carcinogenic potency of aflatoxin. The carcinogenic potency of aflatoxin, defined as the probability of HCC ("r") per 100,000-individual population was estimated using the equation (Udovicki et al., 2021):

$$r = \left(0.3\ \times HBsAG^{+}\right) + \left(0.01\ \times \left(1 -\ HBsAG^{+}\right)\right)$$

It has been demonstrated that the probability of HCC attributable to aflatoxin exposure is greater for individuals with Hepatitis B surface antigen (HBsAG) positivity by a factor of 30. A HBsAG positivity rate of 13.2% has been reported for the Nigerian population (Garba et al., 2021). Thus, the carcinogenic potency was estimated as: (0.3 × 0.132) + [0.01 × (1–0.132)] = 0.04828. The risk of disease (HCC cases/year per 100,000 population) was estimated by multiplying the EDI by the carcinogenic potency (Udovicki et al., 2021), using the equation:

$$HCC\ Risk = EDI \times r$$

TABLE 2 Summary of batch-wise aflatoxin concentrations reported in reviewed literature.

	Maize $N^* = 40^a$	Groundnut $N = 26^a$	Rice $N = 36^a$	Cowpea $N = 5^a$	Soybean $N = 3^a$
Metabolite					
AFB1	18 (45%)	17 (65%)	27 (75%)	4 (80%)	2 (67%)
Total aflatoxin	22 (55%)	9 (35%)	9 (25%)	1 (20%)	1 (33%)
% Positive samples	68.8 (27.4, 0.0–100.0)	84.5 (17.8, 39.3–100.0)	74.3 (29.3, 0.0–100.0)	31.1 (46.1, 3.7–100.0)	7.3 (12.7, 0.0–22.0)
(Missing)	8	10	1	1	0
Mean concentration (ng/g)[b]	104.4 (154.1, 0.0–611.8)	78.8 (219.2, 3.4–939.0)	46.6 (37.8, 0.0–157.3)	53.5 (54.6, 3.6–122.0)	0.6 (1.1, 0.0–1.9)

*N = number of batches reported across included studies.
[a] n (%); Mean (SD, Min-Max range of batch means).
[b] All samples of both metabolites were averaged together. Observations of total aflatoxin were treated as AFB1 for the risk assessment to prevent under-estimation of risk, as described in the Methods section.

Sensitivity analyses were performed for each commodity-wise risk model in order to determine the relative contributions of the input parameters to the level of HCC risk. Spearman's rank-order correlation coefficient (ρ) was computed and tornado graphs generated for each model. This coefficient takes values between −1 and 1, where values nearer to 1 are more highly correlated with the outcome (HCC risk). Mean and median values of Spearman's ρ were computed and assessed together with 95% uncertainty intervals around the estimates.

3. Results

3.1. Occurrence of aflatoxin in Nigerian food products

Results of the systematic literature review are presented in Figure 1. The search strategy yielded 285 studies from the Web of Science search. An additional 14 studies were identified by the authors using Google Scholar and other sources, yielding a total of 300 studies, eligible for title and abstract screening. Among these records, 244 were found to be irrelevant and were excluded from full-text review. The remaining 55 records were subjected to full-text screening for eligibility against the inclusion and exclusion criteria. A total of 41 studies satisfied all criteria and were included in the analysis, including 18, 12, 12, 5, and 3 studies each for maize, groundnut, rice, cowpea, and soybean; five of the included studies reported on more than one of the target commodities (see Table 1).

The included studies reported 40, 26, 36, 5, and 3 estimates of batch-wise aflatoxin contamination in Nigerian maize, groundnuts, rice, cowpea, and soybean, respectively, including 4 batches in which aflatoxin was not detected. A batch is here defined as a mean representing several (>2) distinct samples, not replicate measures of the same pooled sample. Aflatoxin contamination data reported in the included studies are summarized in Table 2. Of the 41 studies included in the analysis, 16 (39%) reported only total aflatoxin, while the remaining studies included estimates of AFB1. Among the batches included in the study, AFB1 estimates were available for 62%, while the remaining 38% of batches yielded estimates of total aflatoxins only. Prevalence data (% positive samples reported within a given batch) were available for 81.8% of reported batches, where "positive" is here used interchangeably with "detected". Prevalence

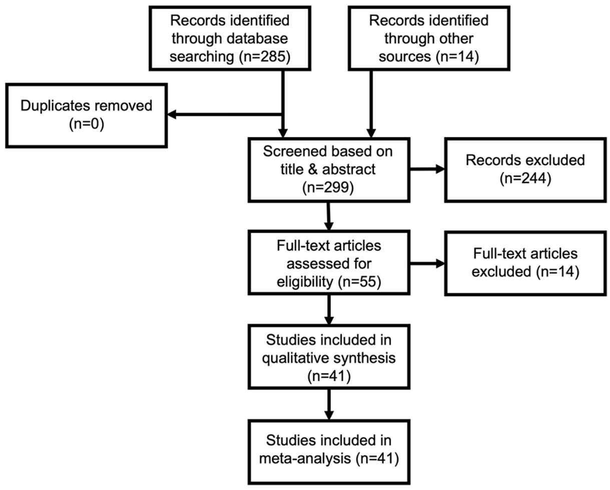

FIGURE 1
PRISMA flow diagram illustrating the systematic literature review process.

was highest in groundnut (84.5% ± 17.8) and rice (74.3% ± 29.3) batches, and lowest in soybean (7.3% ± 12.7). However, very few observations available for soybeans and cowpea make results for these two commodities not generalizable.

Maize and groundnut were observed to have the highest mean aflatoxin contamination levels (106.4 ± 154.1 and 78.8 ± 219.2 ng/g, respectively) among the considered commodities. Mean AFB1 concentrations exceeded Nigerian regulatory legal limit of 2 ng/g AFB1 in maize and 20 ng/g total aflatoxin in groundnuts, respectively (Chilaka et al., 2022). Aflatoxin is presently not regulated in Nigeria for rice, cowpea, and soybean, but concentrations observed in rice and cowpea exceeded all limits for aflatoxins in regulated commodities. Groundnut yielded the highest batch-wise maximum aflatoxin concentration, with a concentration of 939 ng/g in the most contaminated batch. The mean values for all batches with at least one contaminated sample are shown in Figure 2.

The aflatoxin data identified in the systematic review were not representative of the entire Nigerian context, but rather were concentrated in certain regions (Figure 3). Of the individual batches

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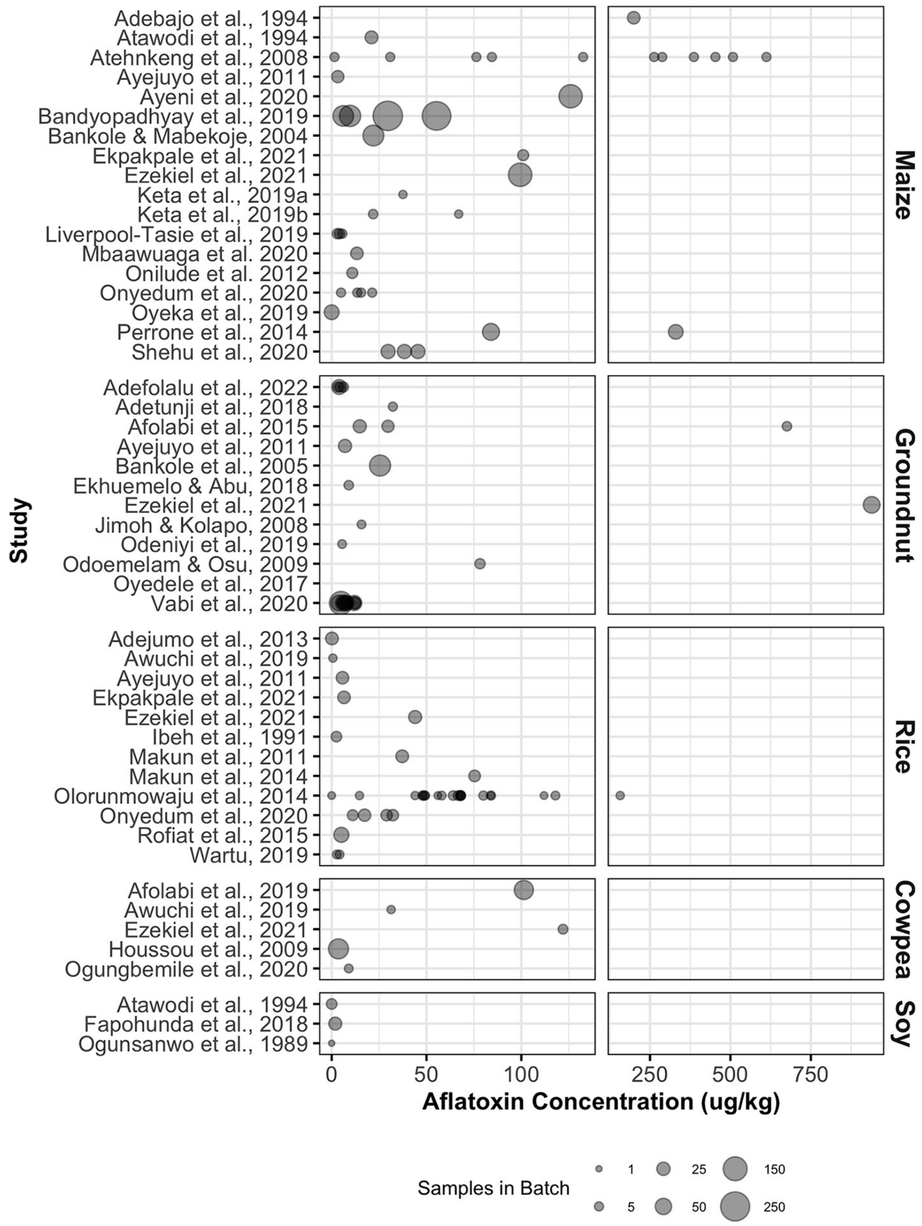

FIGURE 2
Summary of mean aflatoxin concentrations reported for batches of raw commodity samples in the included studies. Point size corresponds to the number of samples within each batch.

reported, the geographical origins were specified at State-level for 70%, while the remaining 30% of batches were geographically specified only at the regional level. By far, the greatest sampling effort at State-level was Kaduna State, which yielded 20% of the batches included in this study. Other states with relatively high sampling efforts included Niger State (8%), Kebbi State (7%), Oyo State (6%), and Lagos (5%). There was a conspicuous lack of available data reporting aflatoxin concentrations in the northeastern and southern regions of the country. The geographical breadth of sampling effort across commodities corresponded to the overall abundance of each commodity in the dataset; the geographical distributions of maize and groundnut batches (the most abundant reported commodities) were greater than those of the other commodities.

3.2. Exposure levels and risk assessment

The probability distribution of the EDI was estimated for each commodity based on the distributions of aflatoxin concentrations, commodity consumption, and adult body weight. There is no tolerable daily intake (TDI) level for aflatoxin, because it has been classified as a Class 1 carcinogen, and thus exposure is considered unsafe at any dose (van de Perre et al., 2015; Saha Turna and Wu, 2022). However, a proposed provisional maximum tolerable daily intake level (PMTDI) of 1 ng/kg bw/day has been used as a reference value for judging risk associated with aflatoxin exposures (Kuiper-Goodman, 1998; Magrine et al., 2011). The commodity with the highest estimated EDI in the exposure model was maize, with a value of 36.7 (95% CI: [22.7–54.8]) ng/kg bw/day, substantially higher than

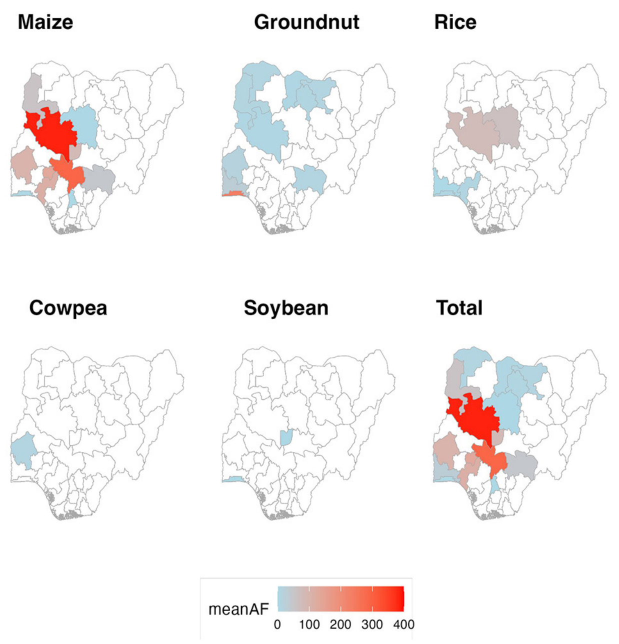

FIGURE 3
Geospatial overview of aflatoxin contamination reported in reviewed literature, reflecting sampling effort and detected levels.

the PMTDI level. The estimate of EDI in the groundnut, rice and cowpea models also exceeded the PMTDI level, but more modestly, with estimates of 9.12 (95% CI: [4.41–19.21]), 8.85 (95% CI: [6.91–11.09]), and 3.14 (95% CI: [1.25–7.22]) ng/kg bw/day, respectively. Dietary aflatoxin exposure attributable to soybean consumption in the study population is much less than the other commodities, with an EDI of 0.28 (95% CI: [0.24–0.32]) ng/kg bw/day, below the PMTDI level. The mean risk of HCC attributable to consumption of maize, groundnut, rice, cowpea, and soybean in the target population was estimated as 1.77 (95% CI: [1.10–2.65]), 0.44 (95% CI: [0.21–0.93]), 0.43 (95% CI: [0.33–0.54]), 0.15 (95% CI: [0.06–0.35]), and 0.01 (95% CI: [0.01–0.02]) HCC cases per year/100,000 population, respectively.

Sensitivity analysis of the relative impacts of variability in the model's input parameters on HCC risk indicated that variability in aflatoxin concentration (C) in a consumed portion has the greatest impact on HCC risk attributable to maize consumption (Spearman's $\rho = 0.64$), followed closely by variability in the frequency of maize consumption ($\rho = 0.58$). Variability in S, i, and BW had comparatively low impact on risk in the maize model. In the rice model, the frequency of rice consumption (f_{cons}) had a very large impact on the level of HCC risk ($\rho = 1.00$), whereas estimates for the other parameters did not exceed 0.1. In both the cowpea and soybean models of HCC risk, the most impactful parameter on risk level was the frequency of contamination (i), for which Spearman's ρ was estimated at 0.97 and 1.00 for cowpea and soybean, respectively, indicating a near-perfect correlation. While this suggests that contamination frequency may be a contributory factor, it should be acknowledged that the estimated exposure attributable to these commodities was relatively low, and that the limited data available for these commodities may have obscured contributions from other factors in the sensitivity analysis.

4. Discussion

This study presents novel evidence that dietary consumption of several key commodities found in Nigerian traditional food marketplaces, particularly in the northern regions, may lead to aflatoxin exposures sufficient to cause adverse health outcomes. HCC incidence rate in Nigeria, from all causes, was previously estimated as 2.6 cases per 100,000 individuals (Kedar Mukthinuthalapati et al., 2021); thus, our findings suggest that a substantial proportion of total HCC incidence in the region may be attributable to dietary aflatoxin exposure *via* the consumption of the considered commodities, particularly maize and groundnut.

The estimates presented here are above the chosen PMTDI levels but below prior risk estimates for aflatoxin-associated HCC attributable to single-commodity consumption for infants and children in Nigeria (Adetunji et al., 2017). The relative ranking of these products observed in this study is consistent with existing evidence that cereals (maize and groundnuts in particular) are more susceptible to aflatoxin accumulation than pulses. For both maize and rice in the study area, the higher estimated risk levels are reflective of both high consumption levels and high contamination levels, whereas cowpea and soybean, despite moderate consumption levels in the population, harbor low concentrations of aflatoxin and therefore pose lower risk of aflatoxin-associated HCC. Despite having aflatoxin concentrations comparable to those of maize samples, the HCC risk associated with groundnut consumption is relatively lower, owing to low overall levels of groundnut consumption in the target population.

Moreover, while the present estimate of maize-associated HCC risk is very similar to what was estimated for aflatoxin exposure *via* groundnuts in a Nigerian population (1.38 HCC cases year^{-1} 100,000 pop^{-1}) (Adetunji et al., 2018), the estimate of risk associated with groundnut consumption in the present study was substantially lower. The discrepancy in risk associated with groundnut consumption between the present study and the study conducted by Adetunji et al. could be attributable to the fact that point estimates, rather than probability distributions, of groundnut consumption and aflatoxin concentration were used in their exposure assessment, and that detection rates were not accounted for. This illustrates the potential utility of an exposure modeling approach that accounts for population-specific probability distributions in exposure-related variables. Another Nigerian study (Garba et al., 2021) estimated AFB1-associated HCC risk levels much higher (3.06 cases per 100,000 population) than what was observed in this study; this illustrates the importance of taking a multi-commodity approach in risk assessment.

The risk estimates presented here are on par with other estimates in Nigeria, but they are higher than what was observed in a European population with lower maize consumption and contamination levels (Udovicki et al., 2021). This is consistent with the observation that our EDI estimates for maize and groundnut alone far exceed the average upper bound exposure level for adults reported by EFSA [EFSA Panel on Contaminants in the Food Chain (CONTAM), 2020]. In many sub-Saharan African food system contexts, optimal conditions for fungal growth and aflatoxin accumulation are often coupled with poor food monitoring and regulatory systems. In Nigeria, regulation and enforcement of food safety policy and standards is impeded by outdated infrastructure and insufficient expertise (Okoruwa and Onuigbo-Chatta, 2021).

While the present study offers important insights into the exposure and health risks associated with aflatoxin contamination of key foods in Nigerian traditional food marketplaces, several data gaps and limitations need to be considered. First, the models presented in this study were populated using secondary data sources, which necessitates some assumptions about their applicability to the target population. For instance, data from different Nigerian states were pooled together, unweighted—hence implicitly weighted by sampling effort in reported literature; estimates should therefore be considered representative of current evidence in the country, but not of specific regions or states or of the country as a whole. The systematic review methodology used to compile comprehensive regional aflatoxin contamination data was sufficient for commodities with well-established aflatoxin literature (i.e., maize, groundnut, and rice), but was much more limited for cowpea and soybean, which have scarcer published evidence on aflatoxin contamination levels, in all sub-Saharan Africa. Further risk assessments using primary data from more susceptible commodities, and applying context-specific sampling, would contribute invaluably to the knowledge base around aflatoxin exposure risk in specific regions, as the basis for targeted interventions.

Second, the heterogeneity in reporting formats for aflatoxin prevalence and concentrations hinders the characterization of concentration distributions in meta-analysis. An approach based on batch means was implemented here, capturing the variability across batches, while deprioritizing within-batch variability due to data limitations. In addition, some assumptions were made on consumption amounts and body weight, in the absence of more precise national consumption data. Overall, data were sufficient to support a sound preliminary assessment, but estimates are less accurate than assessments conducted using primary data. Following agreed-upon best reporting practices for aflatoxin detection rate, limits of detection, and concentrations would improve estimate accuracy. However, the level of detail included in this study—if applicable to the specific local context—is sufficient to inform intervention decisions and to highlight critical data gaps that prevent such decisions (e.g., here for cowpea or soybean and derived foods).

Third, this study focused specifically on risk of HCC, which is just one of several possible health outcomes of interest (Gong et al., 2016). HCC was selected based on its severity and its relatively well-defined dose-response relationship with aflatoxin. However, aflatoxin-associated malnutrition and growth impairment outcomes are increasingly a focus of the research community and are critically in need of comprehensive risk assessment as studies to date have not conclusively shown a causal linkage (Turner et al., 2007; Leroy et al., 2018) and the biological mechanisms have not been elucidated (Tessema et al., 2021). As these outcomes often arise as a result of several environmental factors in combination (Moore et al., 2001), it is challenging (and ethically dubious) to articulate dose-response relationships for these outcomes (Turner, 2013).

Our findings indicate substantial reason for concern regarding the risk of aflatoxin exposure in Nigeria, but this is set against a backdrop of promising management efforts in the country that have potential for further scalability and contextualization. For example, Nigeria has been a pioneer in Africa in the development and use of biocontrol agents to combat aflatoxin-producing fungi (Bandyopadhyay et al., 2019; Ortega-Beltran and Bandyopadhyay, 2021). Additionally, value chain approaches to mycotoxin management have been initiated in the country. For example, one recent study found that aflatoxin-safe labeling programs influence willingness to pay for actors across the value chain and may incentivize consumption of certified aflatoxin-safe products (Sanou et al., 2021). These efforts and others illustrate that there are practical control strategies in place that could leverage risk assessments to ensure that intervention is appropriately directed to populations with the greatest need.

Overall, this study provides a comprehensive quantitative synthesis of published evidence (as of 2022) on aflatoxin contamination in key staple commodities in Nigeria, national-level exposure and risk estimates based on such data, and a novel approach leveraging secondary data that can be adapted by other researchers to conduct similar assessments. Findings point to a non-negligible potential HCC risk associated with maize and groundnut, in alignment with previous estimates that highlight the specific contributions of maize and groundnut to HCC risk. Clear data gaps exist for cowpea and soybean, preventing a meaningful risk assessment; however, because of moderate consumption and less implication in aflatoxin exposure, cowpea and soybean are of less concern than maize and groundnut. The heterogeneity in aflatoxin levels, and hence risk estimates, across the country warrants attention if using these findings to inform localized intervention decisions; complementing country-scale findings with local primary data is encouraged.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

AW and EL designed the study and developed the methodology. AW synthesized input data, coded, and run the model. EL oversaw all study steps and provided guidance. FM, LT, and DG provided input on study approach, input data, and result interpretation. AW led manuscript writing and graphics, with inputs and review from EL. All authors reviewed the final draft. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsufs.2023.1128540/full#supplementary-material

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