FOCUS

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Mycotoxin Exposure and Infant and Young Child Growth in Africa: What Do We Know?

by Martani J. Lombard

Key insights

The four main mycotoxins that influence human health are the aflatoxins, fumonisins, deoxynivalenol and zearalenone. These compounds are thought to alter the cellular and biochemical functions of the intestine, resulting in micronutrient deficiencies, systemic immune activation and impaired nutrient uptake. In Africa, the majority of the population are subsistence farmers who grow, store and prepare their own staple foods. Consequently, a large proportion of infants and young children receive these staple foods that are contaminated with mycotoxins.

Current knowledge

Regardless of high exposure levels and the burden of mycotoxins on the health economics of various low-income countries, mycotoxins have been largely overlooked from a public health perspective. Thus, knowledge of the effects of food-borne mycotoxins on the growth and health of infants and young children is critical for overcoming this public health challenge.

Practical implications

Results from aflatoxin studies indicate that this toxin can cross the placenta and is present in the umbilical cord and in breast milk. Furthermore, there are seasonal differences in the levels of aflatoxin in cord blood and breast milk. Due to low breastfeeding rates across Africa, there was a significant association between weaning status and aflatoxin exposure levels. Higher aflatoxin exposure (both in utero and in early life) was strongly associated with stunting and/or underweight. Children with fumonisin intakes exceeding the provisional maximum tolerable daily intake were significantly shorter and lighter. Very little is known about the effects of deoxynivalenol and zearalenone on childhood growth and development.

Mycotoxin exposure and infant growth impairment in Africa – what do we know?

Biomarker	Aflatoxin	Fumonisin	Deoxynivalenol	Zearalenone
Infant serum				
WAZ	SA	ND	ND	ND
HAZ	SA	ND	ND	ND
WHZ	SA	ND	ND	ND
Infant consumption				
WAZ	SA	SA	ND	ND
HAZ	NA	SA	ND	ND
WHZ	NA	NA	ND	ND
In utero (maternal serum)				
WAZ	SA	ND	ND	ND
HAZ	SA	ND	ND	ND
WHZ	NA	ND	ND	ND
Umbilical cord				
WAZ	NA	ND	ND	ND
HAZ	NA	ND	ND	ND
WHZ	NA	ND	ND	ND

SA = Significant association; NA = no association; DN = no data; WAZ = weight-for-age z-scores; HAZ = height-for-age z-scores; WHZ = weight-for-height z-scores.

Recommended reading

Wild CP, Gong YY: Mycotoxins and human disease: a largely ignored global health issue. Carcinogenesis 2010;31:71–82.

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Mycotoxin Exposure and Infant and Young Child Growth in Africa: What Do We Know?

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Key Messages

- There is limited information available on the presence of mycotoxins [aflatoxin (AF), fumonisin (FB), deoxynivalenol (DON) and zearalenone (ZEA)] and the exposure levels to these mycotoxins in infants and young children in Africa.
- Various animal and human studies indicate that AF cross the placenta during pregnancy, are present in the umbilical cord and are in breast milk; however, very little is known about the effects of other mycotoxins.
- AF influence infant and young child growth in various phases of growth, but it is not clear what the influence of other mycotoxins is on growth.

Key Words

Mycotoxin · Aflatoxin · Fumonisins · Deoxynivalenol · Zearalenone · Stunting · Wasting · Underweight · Africa · Infants · Children

Abstract

Introduction: Infant and young child (IYC) growth impairment remains a public health problem in Africa partly because infants are exposed to staple foods (contaminated with mycotoxins) at an early age. Understanding the role of mycotoxins in IYC growth is vital, and this paper systematically reviews the available knowledge. ***Methods:*** Studies were searched and included if they provided information on African IYC mycotoxin exposure rates and/or growth. Studies were excluded if subjects were older than 15 years, if they were animal studies or focusing on other mycotoxins. Relevant search words were included in search strings. Eight reviews were identified and reference lists scrutinised for additional studies. ***Results:*** Ten studies were included; 8 focused on aflatoxin (AF), 2 on fumonisin (FB) and none on deoxynivalenol (DON) and zearalenone (ZEA). AF exposure prevalence reached 100% with levels at 40.4 pg/mg. AF was present in umbilical cords indicating that AF crosses the placenta. Maternal exposure levels were correlated with breast milk levels. The highest levels of serum AF (mean 32.8 pg/mg) were measured in Benin and Togo with 5.4% reaching levels higher than 200 pg/mg. At the end of weaning, children had similar prevalence and exposure levels as adults. Results also indicated that infants with higher levels of maternal exposure had significantly lower height-for-age z-scores (HAZ scores), although there was no significant association between cord AF and infant HAZ scores or AF in cord blood and HAZ scores. Significantly higher mean maternal AF levels related to lower weight-for-age z-scores (WAZ scores) were reported, and infants with higher levels of maternal exposure had significantly lower WAZ scores that de-

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creased over age. Cord AF levels had no effect on infant WAZ scores. One study investigated the association between FB and IYC growth and found that those with FB intakes greater than the provisional maximum tolerable daily intake were significantly shorter (1.3 cm) and lighter (328 g). No studies investigated the role of DON and ZEA. ***Conclusion:*** A limited number of epidemiological studies have been conducted, and available research indicates extreme exposures to AF. There are strong associations between AF exposure and stunting and wasting. However, more epidemiological research is urgently needed to understand the role of FB, DON and ZEA in IYC growth.

Introduction

Growth impairment is a large public health problem in Africa with many countries reporting a high prevalence of stunting and underweight in children (table 1) [1]. The combined effect of intrauterine growth restriction, infant and young child (IYC) stunting, underweight and wasting was responsible for millions of deaths in Africa during the last decade [2].

Growth faltering can have a detrimental impact on the long-term physical and cognitive development, and African children have for decades been especially vulnerable to growth faltering due to famine, drought, political instability and poverty. These factors inevitably lead to food insecurity resulting in poor nutritional intake. Infants are also often given complementary food at a young age, and weaning foods usually are household staples. Staple foods in the majority of African countries are predominantly maize and groundnuts which are vulnerable to fungi [3].

Mycotoxins are low-molecular-weight metabolites that are produced by fungi [4]. Although there are approximately 300–400 mycotoxins [5], four are known to influence human health [aflatoxin (AF), fumonisin (FB), deoxynivalenol (DON) and zearalenone (ZEA)] [6]. *Aspergillus* mold strains produce AF and ochratoxin, while *Fusarium* mold strains produce FB, DON and ZEA [6]. Table 2 summarises the most prevalent mycotoxins found in Africa.

Although various studies have been conducted to determine the effect of mycotoxin exposure on growth, a lack of suitable biomarkers has made it difficult to determine exposure and risk. However, various biomarkers have recently been tested and validated, potentially improving risk assessment [7].

The exact mechanisms by which mycotoxins influence IYC health are not currently known. A conceptual framework based on the known mechanisms of action and their effect on infant growth has been suggested; however, more research is urgently needed to completely understand the mechanisms and their individual downstream pathways [6]. It has been suggested that AF and DON inhibit protein synthesis leading to altered intestinal architecture, inhibition of intestinal regeneration, impaired tight junctions and glucose-galactose malabsorption [6]. DON exposure leads to an increase in systemic cytokines. FB lastly cause a decrease in complex sphingolipids. It is thus suggested that these mechanisms ultimately lead to zinc deficiency (AF), systemic immune activation (AF, DON and FB), impaired nutrient uptake (AF and DON) and food refusal (DON) [6].

Knowing the impact food-borne mycotoxins have on growth impairment and ultimately the health of infants and young children is of the utmost importance. This is especially true since the majority of the population in Africa are subsistence farmers and thus grow, store and prepare their own staple foods [3]. Unfortunately, a very limited number of epidemiological studies have been conducted, and little is known about the impact of food-borne mycotoxins on IYC health [3]. This paper systematically

Table 1. Summary of stunting and underweight prevalence in selected African countries [1]

Country	Stunting prevalence, %	Underweight prevalence, %
Algeria	15.9	3.7
Angola	29.2	15.6
Benin	44.7	20.2
Botswana	31.4	11.2
Burundi	57.7	35.2
Cameroon	36.4	16.6
Congo	31.2	11.8
DRC	45.8	28.2
Egypt	30.7	6.8
Ethiopia	50.7	34.6
Ghana	28.6	14.3
Kenya	35.2	16.4
Lesotho	45.2	16.6
Malawi	47.8	13.8
Niger	54.8	39.9
Nigeria	41.0	26.7
Rwanda	51.7	18.6
Sierra Leone	37.4	25.4
Sudan	37.9	31.7
Uganda	38.7	16.7

DRC = Democratic Republic of the Congo.

Table 2. Summary of the most prevalent mycotoxins in Africa

	Mycotoxins			
	AF	FB	DON	ZEA
Origin	*Aspergillus flavus* and *Aspergillus parasiticus* [9]	*Fusarium verticillioides* [31]	*Fusarium culmorum* and *Fusarium graminearum* [31]	*Fusarium graminearum* and *Fusarium crookwellence* [30]
Types	B_1, B_2, G_1, G_2, M_1, M_2	FB_1, FB_2, FB_3		
Accumulation	accumulate after harvest	location, climate, susceptibility of the plant to fungal invasion, insect damage, crop stress		
Primary food sources	nuts, spices, maize (corn), cacao, coffee, rice, milk	maize (corn)	wheat, barley, maize (corn)	maize (corn), wheat, barley, sorghum
Solubility	fat soluble	water soluble [16]	partially water soluble	
TDI, μg/kg bw/day	none	2 [32]	100 [33]	
PMTDI, μg/kg bw/day		2	1	0.5
Urine biomarker	AF-guanine adduct, AFM_1, AFP_1, AFQ_1 and AFB_1-mercapturic acid [34]	FB_1	DON glucuronide, DON + de-epoxydeoxynivalenol (DON-1)	ZEA + α-zearalenol (α-ZOL) + β-zearalenol (β-ZOL)
Blood biomarker	Serum/plasma AF-alb adduct [34]			
Breast milk biomarker	AFM_1 [5]			

TDI = Tolerable daily intake; bw = body weight.

reviews the current available knowledge regarding the different mycotoxins in terms of growth retardation of infants and young children living in low- and middle-income countries in Africa. Gaps are identified and further research is suggested.

Methods

A systematic search was conducted in four major databases including Medline (PubMed), EBSCOhost Online Research Databases, Google Scholar and HighWire Press. Studies were included if they provided information on mycotoxin exposure rates (AF, FB, DON and/or ZEA) in one or more African countries (regardless of the region). Studies were further included if research was conducted on IYC mycotoxin exposure and growth faltering.

Studies were excluded if the research was conducted in non-African countries, if they were conducted before the year 2000 and if they were conducted on parameters other than child growth faltering. Animal studies and those that investigated the effect of other mycotoxins were also excluded.

The following search words (amongst others) were included in the search strings: mycotoxin, aflatoxin, fumonisins, deoxynivalenol, zearalenone, Africa, sub-Sahara, growth, stunting, wasting, underweight and malnutrition. In addition to this, 8 recent reviews conducted on related topics were identified and their reference lists were scrutinised for additional studies.

Results on different exposure levels for the four mycotoxins and their effect on IYC growth faltering were tabulated.

Results

A total of 55 studies were initially identified (fig. 1). Of these, 41 studies were excluded for the following reasons: (1) not conducted in Africa; (2) not focusing on growth impairment; (3) animal study, and (4) subjects too old for inclusion. In total, 10 studies were included; 8 focused on AF, 2 on FB and none investigated DON and ZEA.

Aflatoxin

There are six major types of AFs (table 2), of which AFB_1 is the most toxic [5, 6]. It is estimated that approximately 4.5 billion of the world's population is exposed to AF [8]. This mycotoxin occurs in tropical regions where the humidity and the temperature are high [9].

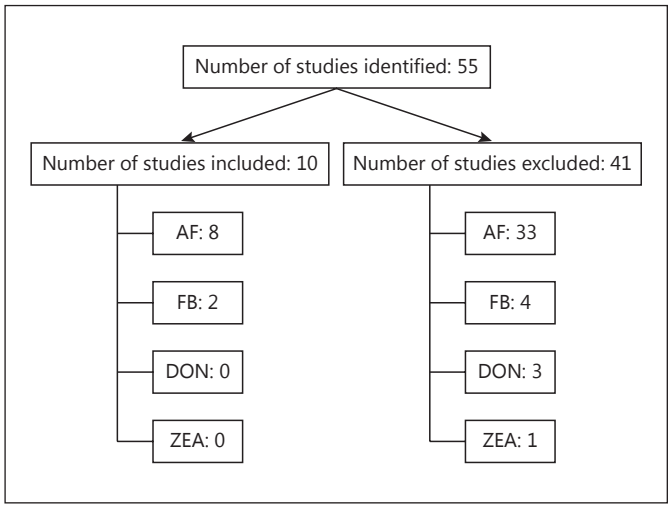

Fig. 1. Included and excluded studies.

Maternal and infant exposure occurs at extremely high levels in various African countries, including Ghana [10], Benin [11, 12], Togo [11], Egypt [13, 14], Guinea [14] and the Gambia [15] (table 3). Various aspects of exposure were studied including maternal consumption [10, 15], umbilical cords [15], breast milk [13, 14] and IYC consumption [11, 12, 14–17].

Exposure

Two studies investigated maternal AF exposure in Ghana (n = 755) [10] and the Gambia (n = 119) [15] (table 3). Although both reported 100% exposure prevalence, maternal serum AF exposure was much higher in the Gambia (40.4 pg/mg) compared to Ghana (10.9 pg/mg).

Another study [15] measured serum AF levels in umbilical cords to determine if AF crosses the placenta. The study reported lower serum AF levels in cord samples compared to mothers' serum AF levels (10.1 pg/mg and 40.4 pg/ml, respectively). It was, however, clear that AF is transported from the mother to the infant, increasing the already vulnerable infant's exposure [15]. Lastly, the authors identified significantly increased serum AF levels in cord blood during April to July compared to December to March or August to November [15] (table 3).

Because AF are lipophilic, maternal AF consumption can result in the accumulation of AF and its metabolites in breast milk [13]. It is, however, difficult to determine the average daily infant AF exposure from breast milk because maternal exposure varies daily, and fat content and total milk volume consumed per feed and within feeds vary [14]. Polychronaki et al. [14] found AFM_1 (13.5 pg/ml) in the breast milk of 36% (n = 138) of their participants in Egypt. They further found an increase in AFM_1 breast milk levels during different seasons (April to July) [14], indicating the importance of seasonal differences.

Infants and children are especially vulnerable to mycotoxin exposure, mostly because of a lower detoxification capacity, rapid growth and high intake of food and water per kg body weight [18]. In a study conducted in Benin and Togo (West Africa), extremely high levels of serum AF were measured (table 3) amongst children [16]. The geometric mean exposure of these children was 32.8 pg/mg, with at least 1 child exposed to 1,064 pg/mg [16]. Also, 5.4% of the participating infants had exposure levels higher than 200 pg/mg. Serum AF levels were lowest among infants (<12 months) but increased as age increased to 24–36 months of age, when exposure levels reached a plateau [16].

Because of poor exclusive breastfeeding rates reported all over Africa, it is important to understand the impact of complementary feeding and weaning on the exposure levels of these infants. Gong et al. [16] conducted a multivariable analysis to determine the impact weaning status has on exposure levels. Results indicated a significant association with serum AF and that exposure was at least two-fold higher amongst those not breastfed compared to those exclusively or partially breastfed. This suggests that weaning status rather than age is associated with high exposure levels [16].

Infants and children are especially vulnerable to mycotoxin exposure, mostly because of a lower detoxification capacity, rapid growth and high intake of food and water per kg body weight.

In their study, Gong et al. [16] also found a weak positive correlation between child maize consumption and serum AF levels [16]. The authors concluded that this was due to a number of reasons including (1) poor maize intake quantification methods, (2) the influence of AF reduction practices such as maize washing and sorting; (3) other AF dietary components, and (4) the fact that the AF-alb marker integrates exposure over a different period than the dietary assessment method reflects [16].

Table 3. Mycotoxin exposure studies conducted in various African countries in the last decade

Reference	Country	Sample size, n	Mycotoxin tested	Method	Age group	Exposure levels	Prevalence n/total n (%)
10	Ghana	755	AF	Serum AFB_1-lysine adducts	Mothers	Mean (range), pg/mg: 10.9 (0.44–268.7)	755/755 (100.0)
11	Benin and Togo	480	AF	Serum AF-alb adducts	Children (9–60 months)	Geometric mean (range), pg/mg: 32.8 (5.0–1,064.0) Fully weaned infants: 45.6 (38.8–53.7)* Partially breastfed infants: 18.0 (15.2–21.3)	475/479 (99.2)
16	Benin and Togo	479	AF	Serum AF-alb adducts	Infants and children (0–60 months)	Geometric mean (range), pg/mg: 32.8 (25.3–42.5)	475/479 (99.0)
12	Benin	200	AF	Serum AF-alb adducts	Infants (16–37 months)	Geometric mean AF-alb, pg/mg: February October Weaned 54.4 99.4 Not weaned 8.9 24.0	
14	Guinea	50	AF	Urinary AF metabolites (AFM_1, AFB_1, AFB_2, AFG_1, AFG_2)	Infants (24–48 months)	Geometric mean (95% CI), pg/ml: AFB_1: 13.2 (11.8–14.6) AFB_2: 0.2 (0.2–0.3) AFG_1: 26.0 (24.5–27.7) AFG_2: 0.57 (0.46–0.70) AFM_1: 2.7 (2.5–2.8)	AFB_1: 1/50 (2.0) AFB_2: 5/50 (10.0) AFG_1: 2/50 (4.0) AFG_2: 12/50 (24.0) AFM_1: 4/50 (8.0)
17	Kenya	242	AF	Maize consumption	Children (3–36 months)		198/242 (82)
14	Egypt	50	AF	AFM_1 levels in breast milk	Lactating mothers	Mean (range), pg/ml: January: 8.0 (4.2–108.0) February: 12.0 (4.8–275.0) March: 18.0 (5.0–181.0) April: 36.0 (5.7–889.0) May: 40.0 (4.6–609.0) June: 28.0 (4.5–228.0) July: 60.0 (6.3–497.0) August: 15.0 (4.5–127.0) September: 14.0 (4.3–63.0) October: 13.0 (5.3–110.0) November: 28.0 (4.9–360.0) December: 12.0 (9.2–61.0)	12/50 (24.0) 8/49 (16.3) 28/50 (56.0) 20/50 (40.0) 23/26 (88.5) 25/26 (96.2) 24/26 (92.3) 22/29 (75.9) 24/29 (82.3) 22/29 (75.9) 21/29 (72.4) 16/50 (32.0)
14	Egypt	50	AF	Urinary AF metabolites (AFM_1, AFB_1, AFB_2, AFG_1, AFG_2)	Infants (24–48 months)	Geometric mean (95% CI), pg/ml: AFB_1: 26.6 (16.3–42.9) AFB_2: 0.8 (0.5–1.3) AFG_1: 26.6 (23.3–30.6) AFG_2: 1.1 (0.7–1.7) AFM_1: 16.3 (10.1–26.6)	AFB_1: 8/50 (16.0) AFB_2: 29/50 (58.0) AFG_1: 1/50 (2.0) AFG_2: 18/50 (36.0) AFM_1: 32/50 (64.0)
13	Egypt	388	AF	AFM_1 levels in breast milk	Lactating mothers	Median (IQR), pg/ml: 13.5 (10.3–21.43)	139/388 (36.0)

Table 3 (continued)

Reference	Country	Sample size, n	Mycotoxin tested	Method	Age group	Exposure levels	Prevalence n/total n (%)
15	The Gambia	(1) 119 (2) 99 (3) 118	AF	(1) Maternal blood, AF-alb during pregnancy (2) Cord AF-alb (3) Infant blood AF-alb at 16 weeks of age	(1) Pregnant women (2) Cord (3) Infants (16 weeks)	Geometric mean (IQR), pg/mg: (1) Maternal: 40.4 (4.8–260.8) (2) Cord: 10.1 (5.0–189.6) (3) Infant: 8.7 (5.0–30.2) Samples collected: December–March: 70.8 (43.8–106.7)** April–July: 37.7 (24.3–66.0) August–November: 26.6 (16.1–46.5) Spearman correlation coefficient: Maternal AF-alb and cord blood: r = 0.383** Maternal AF-alb and week-16 infant AF-alb: r = 0.151 Cord blood and week-16 infant AF-alb: r = –0.099	(1) 119/119 (100.0) (2) 48/99 (48.5) (3) 13/118 (11.0)
[35]	Tanzania	254	FB	Modelling maize consumption data (g/kg bw/day) with FB contamination patterns Participants were stratified according to 50th, 75th, 90th and 97th percentile of maize consumption	Infants (6 months)	2005: Contamination range, µg/kg: 50.0–11,048.0 Mean (95% CI): Total 26 (23–30) 50th 0.47 (0.41–0.54) 75th 2.14 (1.55–2.84) 90th 9.09 (6.56–14.20) 97th 36.99 (21.86–72.15) 2006: Contamination range, µg/kg: 19.0–1,758.0 Mean (95% CI): Total 3.0 (2.0–12.0) 50th 0.15 (0.14–0.19) 75th 0.24 (0.23–0.66) 90th 0.39 (0.35–2.25) 97th 2.06 (1.03–8.31)	
[21]	Tanzania	131/191[a]	FB	$FB_1 + FB_2 + FB_3$ levels in cooked maize and habitual maize consumption	Infants (6–8 months)	Median (range), µg/kg bw/day: 0.48 (0.003–28.838)	131/191 (68.9)

pg/mg = pg 2 AF-lysine equivalents per mg of albumin; pg/ml = pg AFM_1 equivalents per ml of breast milk; IQR = interquartile range. * $p < 0.05$; ** $p < 0.001$. [a] A total of 191 infants were included in the study, while 131 consumed FB-contaminated maize (statistics were included on the 131 FB-exposed infants).

Table 4. Mycotoxin studies conducted during the last decade on growth faltering

Reference	Country	Sample size, n	Mycotoxin tested	Method	Results
11	Benin and Togo	480	AF	Children (9–60 months) from 16 villages in 4 geographic zones were included Anthropometric measures were taken, z-scores calculated and AF-alb adducts tested	Association: AF-alb adduct and HAZ** AF-alb adduct and WAZ** AF-alb adduct and WHZ*
12	Benin	200	AF	Fifty children from 4 villages (2 high-contamination risk areas and 2 low-contamination risk areas) Measurements were conducted in February and October	Mean AF-alb and height increase after 8 months: Exposure[a] — Mean height (SD), cm Lower quartile — 5.9 (5.2–6.6) Mid-lower quartile — 5.3 (4.8–5.9) Mid-upper quartile — 4.8 (4.4–5.2) Upper quartile — 4.2 (3.9–4.6)
16	Benin and Togo	479	AF	A cross-sectional study that included children of weaning age. Anthropometric measures were taken, z-scores calculated and AF-alb adducts tested	Association: AF-alb adduct and HAZ** AF-alb adduct and WAZ** AF-alb adduct and WHZ
15	The Gambia	138	AF	Infants were included at birth and followed up monthly for 12 months Serum AF-alb adduct levels were measured in maternal blood during pregnancy, in cord blood and in infants at 16 weeks of age	Maternal AF-alb levels and infant weight, multiple regression coefficient: Maternal AF-alb and infant WAZ: –0.249* Maternal AF-alb and infant WAZ profile over time: –0.004** Cord AF-alb and infant WAZ: –0.024 Maternal AF-alb and infant WAZ at week 16: –0.355 Maternal AF-alb levels and infant height: Maternal AF-alb and HAZ: –0.207* Maternal AF-alb and HAZ profile over time: –0.008** Cord AF-alb and infant HAZ: –0.049 Maternal AF-alb and HAZ at week 16: –0.558*
17	Kenya	242	AF	Maize was collected from households with children aged 3–36 months and analysed Anthropometric measures of the children were taken	Intake from malnourished[b] children: Wasted children: 53.8% AF consumers vs. 27.7% non-AF consumers* Stunted children: 32.4% AF consumers vs. 28.9% non-AF consumers Underweight children: 41.4% AF consumers vs. 27.3% non-AF consumers
21	Tanzania	131	FB	$FB_1 + FB_2 + FB_3$ levels in cooked maize and habitual maize consumption	LE Mean (SD) — HE Mean (SD) WAZ: –0.32 (1.00) — –1.77 (1.17)* LAZ: –0.97 (1.05) — –1.60 (1.13)* WLZ: 0.46 (1.01) — 0.44 (1.27)

LAZ = Length-for-age z-score; WLZ = weight-for-length z-score; LE = low-exposure group; HE = high-exposure group. * $p < 0.05$; ** $p < 0.01$. [a] Lower quartile: <23.3; mid-lower quartile: 23.3–53.0; mid-upper quartile: 53.0–101.5; upper quartile >101.5 pg/mg. [b] According to the Welcome classification.

Infant Growth

Five studies [11, 12, 15–17] (conducted in Benin, Togo, the Gambia and Kenya) investigated the role of AF in infant growth (table 4).

Gong et al. [11] reported a strong inverse association between serum AF and IYC growth [weight-for-age z-scores (WAZ scores), height-for-age z-scores (HAZ scores) and weight-for-height z-scores (WHZ scores)]. The study revealed that stunted and/or underweight children were exposed to 30–40% higher mean serum AF levels. Subsequently, the authors conducted an 8-month longitudinal study and reported strong negative associations between serum AF and height and weight increase of children [16]. The following year, Gong et al. [12] reported that the highest quartile of AF-alb adducts was associated with a 1.7-cm reduction in height compared to the lowest quartile.

Okoth and Ohingo [17] analysed weaning flours from 242 households (Kenya) with children aged 3–36 months for AF. Anthropometric measures of the children were also taken and compared to maize AF consumption levels. Although only 28% (n = 68) of non-wasted children were from households with AF-contaminated flour, approximately 54% (n = 131) of the wasted children were from households with detectable AF in the flour. There was a significant association between AF exposure and wasting (WAZ score), but not between AF exposure and stunting (HAZ score) and between AF exposure and underweight (WHZ score) (table 4). AF were also more frequently detected in the flour of stunted and underweight children compared with normal children, even if values were not significantly different [17].

In 2007, Turner et al. [15] conducted a study in the Gambia that included in utero exposure levels and reported a significant association between maternal exposure and impaired infant growth (especially during the first year of life) (table 3). They further reported that growth faltering in these children occurred during the weaning process and compared maternal AF levels with infant growth rates (table 4). After adjusting for covariates, significantly higher mean maternal serum AF levels were associated with lower WAZ scores (table 4). When comparing data from maternal AF and infant age (in weeks), it was found that infants with higher levels of maternal exposure had a significant WAZ score decrease over age (table 4). Cord AF levels, however, had no effect on infant WAZ scores (table 4).

In terms of the HAZ score, a significantly higher level of mean maternal AF levels was related to lower HAZ scores (table 4), with no significant association between cord AF and infant HAZ scores [15].

Fumonisin

FB were first identified by Gelderblom et al. [19] in 1988 and include three major FB, of which FB_1 is the most abundant (table 2) [9]. Maize is infected in the field, and the majority of toxin is present at the time of harvest, making the control of FB more focused on pre-harvest practices and on the subsequent effects of processing and preparation of foodstuffs [20].

Exposure

Very little is known about maternal and infant FB exposure, mostly due to the lack of validated biomarkers. Two studies, both conducted in Tanzania, were included in the review (table 3).

Kimanya et al. [21] reported that 12% (n = 26) of infants exceeded the provisional maximum tolerable daily intake (PMTDI) of 2 $mg \cdot kg^{-1}$ body weight [21]. Maize consumption and FB contamination patterns in rural South Africa and Tanzania are similar [22]. The average per capita maize consumption can be as high as 397 g/day in South Africa [23] and as high as 356 g/day in Tanzania [24]. FB contamination concentrations in home-grown maize are up to 10,140 mg/kg in South Africa [23] and up to 11,048 mg/kg in Tanzania [25].

IYC Growth

Only 1 study investigated the relationship between IYC growth and FB exposure (table 4). It was found that children with FB intakes greater than the PMTDI were significantly shorter (1.3 cm) and lighter (328 g) than children with FB intakes less than the PMTDI [25].

Very little is known about maternal and infant FB exposure, mostly due to the lack of validated biomarkers.

Deoxynivalenol

DON is the most frequently encountered mycotoxin in regions of the world with a mild climate (table 2). It contaminates wheat, maize and barley, and due to its stability during processing, exposure is predicted to be frequent [26].

This review found that, to date, there have been no epidemiological studies in humans conducted in Africa looking at maternal and infant DON exposure. DON has, however, been associated with diarrhoea and vomiting [6], impaired gastric emptying and gut mobility [6], reduced weight gain [27] and impaired immune function in

humans [28]. However, because of the lack of valid biomarkers, the effects of DON exposure on growth in children have not yet been studied [28]. Nevertheless, it is expected that (based on animal studies) DON has a negative effect on growth because of decreased food intake and reduced weight gain.

Animal studies found that DON crosses the placenta [29]; it is therefore likely that in utero exposure to DON will occur in humans as well. This is mostly because the detoxification capacity of the foetus has not been fully developed at a time of rapid growth and cell turnover; thus, pregnancy may represent a critical window for DON exposure [26]. Seen in this light, it is vital that more epidemiological studies are conducted in terms of maternal and infant DON exposure as well as its effect on IYC growth.

Zearalenone

ZEA originates from *Fusarium graminearum* and infects maize, wheat, barley and sorghum. Very little is known concerning ZEA and infant and maternal exposure levels in Africa, once again mostly due to the lack of valid biomarkers. However, the primary symptoms of ZEA toxicosis include nausea, vomiting and diarrhoea [29]. All three of these symptoms could influence IYC growth negatively (especially in terms of food refusal and weight loss), and therefore it is assumed that there might be associations between ZEA exposure and IYC growth impairment. Furthermore, ZEA exposure in animal studies has been associated with reduced body weight and histopathological changes in the liver and the kidneys [30]. For these reasons, it is imperative that more research is conducted on infant and maternal ZEA exposure and also its effect on IYC growth.

Discussion

Various studies have been conducted looking at different AF exposure measures (infant serum levels, infant consumption, in utero exposure and cord AF levels) and infant growth (WAZ, HAZ and WHZ scores). Exposure levels in the different studies ranged from 36 to 100% and increased during May to November. There were strong inverse associations between all AF exposure measures and IYC WAZ, HAZ and WHZ scores.

Only 1 study looked at infant FB consumption and also reported that significant IYC exposure is connected with lower WAZ and HAZ scores. However, infant consumption is always difficult to accurately measure (in terms of portion sizes and frequency of consumption); therefore, more studies using biomarkers (newly validated and thus available) should be conducted on the abovementioned exposure measures. Since FB has been associated with neural tube defects and growth impairment (animal studies), determining its impact in epidemiological studies is vital. Extremely high levels of FB in maize have been documented in rural areas in South Africa, Kenya and Tanzania, where residents are predominantly subsistence farmers.

Furthermore, no epidemiological studies have been conducted looking at DON or ZEA and maternal and IYC exposure or growth impairment. This is due to a lack of valid biomarkers and, thus, research should focus on the development and validity of biomarkers to accurately measure DON and ZEA. However, DON and ZEA levels in maize samples can be determined and, therefore, exposure levels and the impact on growth should be measured in terms of maternal and IYC consumption exposure as has been done on FB in Tanzania.

Based on the current limited information that is available on mycotoxin risk assessment, it is clear that epidemiological as well as additional basic research is urgently needed to further understand the role of mycotoxins in IYC exposure and growth. The high prevalence and exposure levels that have been reported by various studies conducted in Africa as well as the persistent growth faltering found in Africa suggest that child growth and development could be critically affected by mycotoxin exposure. However, to date very little attention has been given to this problem and, hence, very little is known about the mechanism(s) involved and the size of the problem.

Since FB has been associated with neural tube defects and growth impairment, determining its impact in epidemiological studies is vital.

Regardless of high exposure levels in various African countries and regardless of the fact that the effects of mycotoxins have a large burden on low-income countries' health economy, mycotoxins have mostly not been prioritised from a public health perspective [3]. There are various reasons for this, including the lack of knowledge, poor communication between researchers, health professionals and policy makers and perceived low value of mycotoxin reduction interventions [3].

Based on the results found in this study, the following research is thus suggested:

- basic research in understanding the mechanisms and their individual downstream pathways involved [6];
- basic research in developing and validating biomarkers for measuring mycotoxin exposure;
- because mycotoxin exposure may be an indication of poor diet quality, research must address this as a potential confounder [12];
- effect of mycotoxin exposure on the development and severity of other undernutrition-related diseases such as kwashiorkor and marasmus;
- effect of mycotoxin exposure on the development and severity of diseases related to physical and cognitive development such as neural tube defects, and
- economically feasible and sustainable intervention strategies to reduce exposure.

Conclusion

A limited number of epidemiological studies have been conducted on two mycotoxins (AF and FB) with no epidemiological studies investigating DON and ZEA in terms of maternal and IYC exposure and its effect on growth. Strong inverse associations have been found between AF exposure and WAZ, HAZ and WHZ scores and between FB and WAZ and HAZ scores. However, seen in the light of (1) the severe and persistent growth impairment in African countries, (2) the known high levels of these mycotoxins in African staple food, and (3) the strong inverse associations with growth impairment found in animal studies, more epidemiological research is urgently needed to better understand the effect of mycotoxins on growth impairment.

Disclosure Statement

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