# Mycotoxins in Bangladesh from a Public Health Perspective

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# Declaration

It is hereby declared that

1. The thesis submitted is our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. We have acknowledged all main sources of help

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## Abstract

Mycotoxins are toxic secondary metabolites from various species of filamentous fungi. They thrive in conditions of high temperature and humidity akin to places like Bangladesh. Due to the damp and humid conditions of the long summers acclimatized by bouts of rain in Bangladesh, mycotoxins tend to contaminate a wide variety of crops and cereals, which include maize, wheat, rice, spices, and even animal feed. The contamination of these food and feed sources can then cause serious health effects ranging from maladies to long term health effects like cancer. Global mycotoxin exposure has been recorded to reach a staggering 4.5 billion people annually according to a study conducted in 2004 and it is subject to an increase in recent times and the near future. Some studies show that certain mycotoxins are produced indoors due to poor air ventilation and sanitation. This is particularly concerning in the times of COVID-19 as the majority of the population is advised to stay indoors to avoid the spreading of the virus. Exposure to mycotoxins is of great concern since it is directly linked to cancer, mainly due to its hepatocarcinogenic effects. It has also been associated with reproductive issues, malformations, immunosuppressive effects, neurotoxicity, and nephrotoxicity. Awareness of mycotoxins is often very minimal in lower-income countries like Bangladesh which puts these countries at a higher prevalence to these mycotoxins and their related health effects. While writing this review, we have noticed that only a limited number of researches on mycotoxin and its effect on health in Bangladesh have been done so far. As several Bangladeshi food items contain a high amount of mycotoxins and only a few research works have been done in this area, it should be a public health concern in Bangladesh, and further research is required for this topic

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### Keywords

Mycotoxin, Bangladesh, Public Health

## Introduction

Mycotoxins are toxic secondary metabolites produced by filamentous fungi and mold which can contaminate various agricultural products, either before harvest or under post-harvest conditions. These toxins tend to be produced in conditions with high humidity and temperature, therefore people in tropical countries like Bangladesh are more susceptible to suffer from mycotoxin infection via their staple food. Within the numerous species of fungi, only about 100 belonging to genera Aspergillus, Penicillium, and Fusarium are known to produce mycotoxins (Barrett,2000). There are different types of mycotoxins where Trichothecenes, aflatoxins (AFs), Alternaria toxins, fumonisins (FBs), ochratoxin A (OTA), and zearalenone (ZEN) are the most important classes of mycotoxins associated with health effects in human.

In a 2007 mycotoxin survey conducted by Biomin, it was found that North America and East Asia suffer from extreme, mycotoxin related, risks and threats as the contamination level are more than 75% above the risk threshold levels. However, in less industrialized and low-income countries, mycotoxins have not been taken seriously as a public health concern (Das et al., 2016), whereas it's these countries that have high risks of being exposed to this toxin (WILSON, 1978). Illnesses due to mycotoxins can be a larger public health problem than one may realize because a long period elapses before an illness is recognized unless large amounts of mycotoxins are consumed resulting in acute symptomatology (Hesseltine, 1985). The negative impacts of mycotoxin can be both acute and chronic on human health, which gives rise to problems such as liver cancer, reduction of immunity, alterations in the protein metabolism, gangrene, convulsions, and respiratory problems, among others.

Amongst all the mycotoxins, Aflatoxin is the most common one as it is associated with many health issues. According to a study by Williams et al (2004), 4.5 billion of the world's population has been estimated to be exposed to aflatoxins, and it would not be surprising if people in Bangladesh are unknowingly being exposed to it. A recent study in 2020 by Biomin shows that particularly Aflatoxin appears to be in 81% of samples of feed and raw commodities (average of positives at 50 ppb) in South Asia. Thus, putting public health at greater risk. Unfortunately, several staple foods that are consumed, by mostly people from south Asian countries daily have the chance of being contaminated by aflatoxins such as rice, lentils, wheat, nuts, dates, and spices. It has been studied that rice alone accounts for up to 60% of the energy intake in the typical Bangladeshi diet and has been shown to contain aflatoxin (Sudo et al. 2004; Reddy et al. 2009). In Bangladesh, other than just rice, wheat and lentils are most frequently consumed as well, which was found in a statistical analysis showing the daily dietary intake as 470g rice per day, 47.86g wheat per day, and 10.12g lentil per day (Nikita Saha Turna; Felicia Wu 2019). People are unaware of the fact that mycotoxins are stable for cooking and processing thus, it cannot be expected that food preparation procedures could safely get rid of mycotoxins (Rutledge, 1976; Rao et al., 1982; Bullerman, 2002). This puts the Bangladeshis, especially those in rural areas as they rely on such food sources, at a greater risk of suffering from mycotoxicity.

According to several studies, there has been alarming information that needs to be taken as serious consideration in the public health of Bangladesh. One of them is aflatoxins being hepatocarcinogenic (National Liver Foundation of Bangladesh, 2013). The inducer to liver cancer involves the synergy of Aflatoxin with Hepatitis B Virus (HBV). But aside from liver cancer, if there are more health risks associated such as infertility, growth impairment, nephrotoxicity, immunosuppression, and other illnesses. The aim of this review is to give an overview of the presence of mycotoxin in Bangladeshi food and its associated risks

## Sources of Mycotoxins in Bangladesh

Mycotoxins appear globally from fungi and are responsible for the contamination of agricultural crops and related food products. The major types of mycotoxins that contaminate food commodities and pose a public health concern are aflatoxins (AF), zearalenone (ZEN), and ochratoxins (OTA). They impose adverse health effects on the global population. The global contamination of mycotoxins is depicted in (Figure 1). This shows that mycotoxins are more prevalent in Asia and South Asia among other continents where the climate tends to be on the tropical side with hot, humid temperatures. Food commodities exclusive to Bangladesh include betelnut, red chili, sorghum, and lentils, all of which show levels that ominously exceed US regulatory limits and need attention from the public health perspective as these are consumed popularly. Dates are heavily consumed during the month of Ramadan; here, human exposure to mycotoxins occur ubiquitously and unknowingly. Moreover, exposure to mycotoxins in food sources tends to be more prevalent in warmer, more humid environmental conditions, particularly in places where farmers have minimum income (Kyei et al., 2020). This factor must be thoroughly considered as per the environment of Bangladesh which has fluctuating rainfall throughout the year and a long summer where the temperature is relatively high, and the conditions are humid. Food sources recurrently found to be contaminated with mycotoxins is an issue of public health concern.

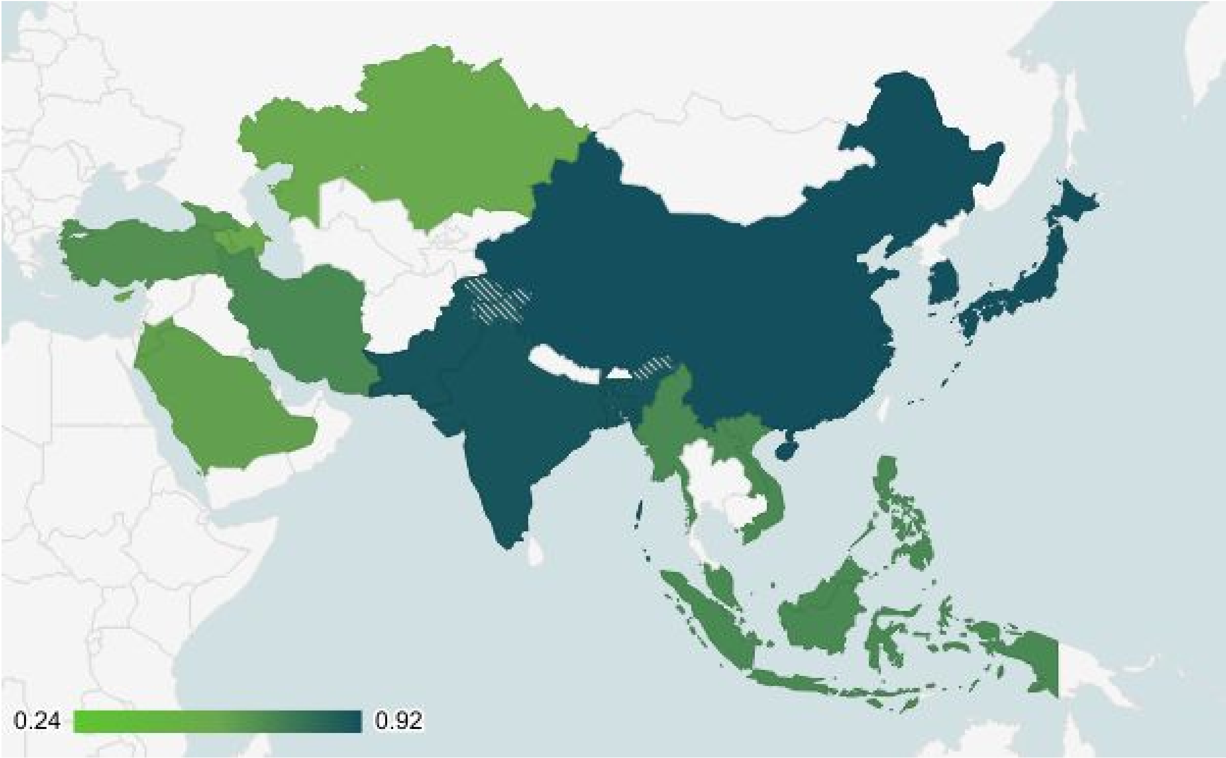


Figure 1: According to the Biomin survey (BIOMIN, 2019), this is a map of the South Asian region showing the prevalence of Mycotoxin. Here, the measurement is done in percentage and it is scaled in the diagram with color (0.24-0.92). The lighter color shows a lower percentage of mycotoxin found in samples of feed and raw commodities, and the darker it gets the higher the concentration. As it can be seen from Figure 1, Bangladesh, India, Pakistan, and China are showing a higher prevalence of Mycotoxin. The Indian subcontinent (which includes Bangladesh) had around 90% of samples with mycotoxins. A major contributor to this result is the climate in those tropical regions, hot and humid.

In the following sections, the major types of mycotoxins and their common sources are thoroughly outlined:

**Aflatoxins:**

Aflatoxins are a global concern from a public health standpoint. The most lethal form of aflatoxin is aflatoxin B1 (AFB1) and it has been found in commodities such as cereals (rice, wheat, sorghum, and corn), oilseeds (groundnuts), spices (red chili, ginger), and tree nuts (pistachio, almond, and walnut) and it most often occurs in the highest concentrations (Lee & Ryu, 2015). The maximum regulatory limit of aflatoxin is 20µg/kg according to the US regulatory limit. Bangladeshi food sources have aflatoxin contents that exceed European regulations (EC 2006) and US regulatory limits (Saha Turna & Wu, 2019) (Figure 2). Included in these food sources are red chili (Ali et al., 2016), maize, groundnuts, cereals, pulses, tree nuts, spices, dried fruits, meat and dairy products (Roy et al., 2013), dates (Saha Turna & Wu, 2019) and betel nuts (Roy et al., 2013). Some other sources of mycotoxins include cereals such as rice and wheat which are the staple foods of Bangladesh but the levels are below US regulations (Saha Turna & Wu, 2019). AFB1 levels infrequently occurring Bangladeshi food commodities and also including poultry feed, betelnut and ginger are depicted in the form of a bar chart (Figure 3). This is of particular concern since, according to FAO, the regulatory limit imposed by Bangladesh [BD], 2003, is 100µg/kg for poultry feed. However, it is still a concern as the total aflatoxin in poultry feed should not exceed 20µg/kg (Fareed et al., 2014). The presence of AFB1 in poultry feed may pass on aflatoxins to poultry meat which can then prove to be harmful when poultry meat is subsequently consumed by humans (HOSSEIN & GÜRBÜZ, 2016). The metabolite of AFB1 is aflatoxin M1 (AFM1) which can be found in the milk and urine of mammals prior to consumption of food sources containing AFB1. Exposure to AFB1 can therefore be detected by the presence of AFM1 in urine and milk (Ali et al., 2016). AFM1 can also be present in infant milk and infant milk formula and dairy milk in general(Lee & Ryu, 2015). Aflatoxin-producing Aspergillus fumigatus has been extracted from multiple rice straw samples from various locations in Bangladesh and India (Phillips et al., 1996).

On another occasion, higher consumption of rice among people living in rural conditions resulted in higher amounts of AFM1 in urine samples when compared to people living in urban conditions (Ali et al., 2016). This is of great concern from a public health perspective as further research is required for biomonitoring of aflatoxins from rice samples as awareness of this toxin is vital. In addition, chili samples (Ali et al., 2016), dates (Saha Turna & Wu, 2019), and betel nuts (Roy et al., 2013) have been found to exceed EU (EC 2006) and US regulatory limits (Saha Turna & Wu, 2019)

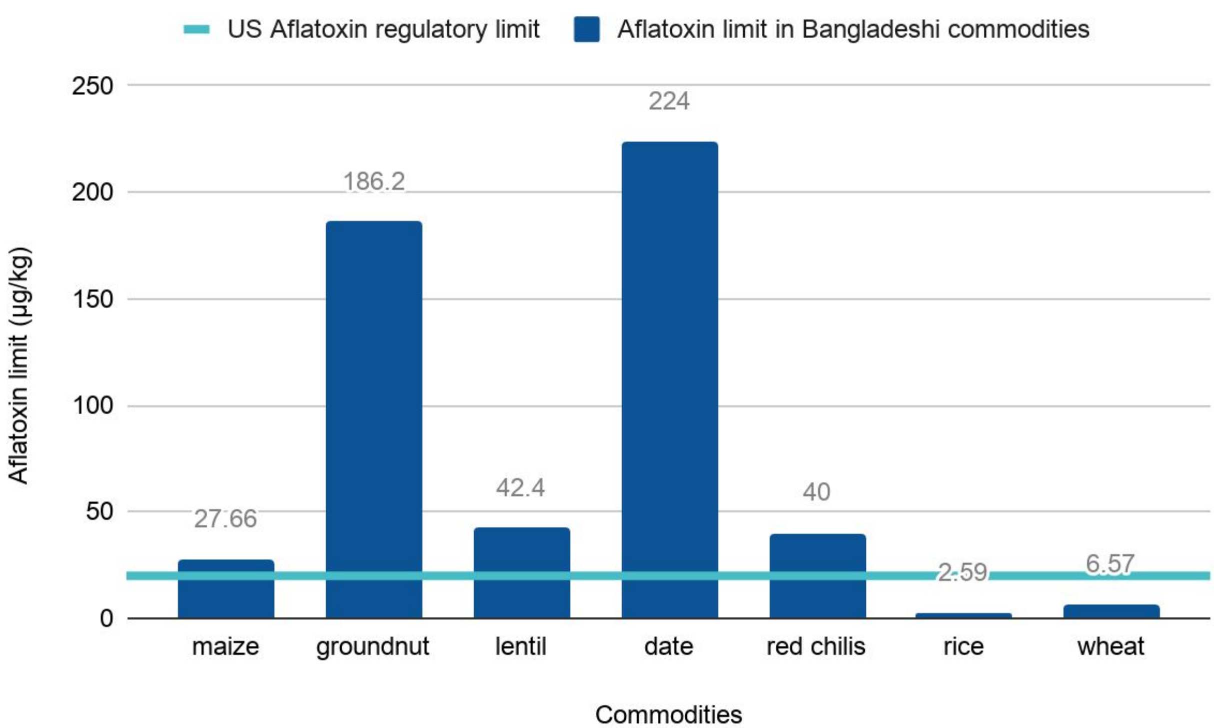


Figure 2: Comparison of Aflatoxin level in Bangladeshi commodities compared to the US regulatory limit.

## Ochratoxin

Ochratoxin A (OTA), which is a great variant of Ochratoxin has been widespread in food sources such as baby foods, breakfast cereals, coffee and beer (Araguás et al., 2005). There were other sources of OTA that have been discovered, which includes fruits (grapes) and fruit juices (grape juice and wine), spices, dried fruits, nuts, cocoa and meats (Lee & Ryu, 2015). From a public health standpoint, it should be taken into account that oats and oat-based products can be highly contaminated with OTA and this requires further review (Lee & Ryu, 2015).

## Zearalenone:

Food sources that are mainly associated with zearalenone (ZEN) are wheat, rye and oats (Lee & Ryu, 2015). However, ZEN is mostly prevalent in European and American countries where regulations and research are more rigorous. ZEN is a toxin of public health concern due to resultant estrogenic effects and reproductive health concerns. Thus, it requires acknowledgement from the public health sector of Bangladesh in order to mitigate its effects on the population

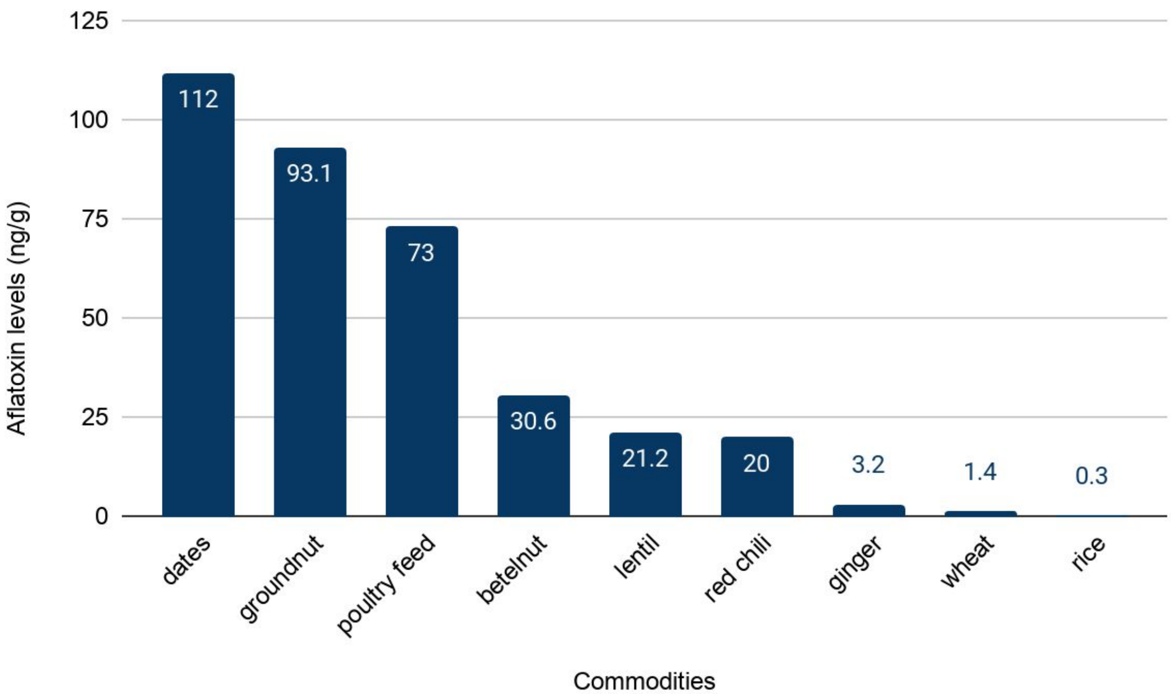


Figure 3. Bangladesh's aflatoxin level in human food and poultry feed

## Health effects of Mycotoxins

Mycotoxins can cause a wide range of debilitating effects to both human and animal health. These effects have a wide range, starting from acute poisoning (which occurs quickly after consumption of food products) to conditions that will emerge in the long run such as immune deficiency and cancer. There are several hundred mycotoxins that have been discovered till date but only a few dozen of them are known to cause adverse effects on human and animal health such as aflatoxins, ochratoxin A, patulin, fumonisins, zearalenone and nivalenol/deoxynivalenol.

There are some important mycotoxin-associated health matters which have been sketched as follows:

**Aflatoxins, the most concerning mycotoxin:**

The number of studies conducted related to mycotoxin-associated disease in Bangladesh are limited. From the finite number of reports, aflatoxins have been mostly found to cause certain disorders in both animal and human health. Aflatoxins have been examined to have carcinogenic, teratogenic and mutagenic properties (Begum and Samajpati, 2000). This mycotoxin, among all mycotoxins, arguably poses the greatest threat to both human and animal health. It was reported in a study (Williams et al., 2004) that approximately 4.5 billion people of the world's population are exposed to aflatoxins. That study was conducted 16 years ago and due to climate change, the exposure should have significantly risen in 2020 (Battilani et al., 2016). Some notable health issues caused by aflatoxins are stated below:
Increased doses of aflatoxins can result in the following diseases: acute aflatoxicosis acute liver damage and in certain cases even death. Impediment in the functionality of the immune system and impairment of growth have also been connected with exposure to aflatoxins (Khlangwiset et al., 2011; Wu et al., 2014; Mitchell et al., 2017). Aflatoxins may potentially cause neonatal health issues. This is because during seasonal changes in African countries, aflatoxins have been detected in the blood of pregnant women, neonatal umbilical cord blood and in the breast milk (Lamplugh et al., 1988).

Aspergillus flavus is an important ubiquitous fungal species which is linked with many human diseases, particularly the severe case of invasive aspergillosis (Powell et al., 1994). This mould is also known to cause diseases in insects (Campbell, 1994) and crops (wheat, maize, rice etc.). Aspergillus flavus is one of two major Aspergillus species which are known to produce aflatoxins and ochratoxins as their secondary metabolites, the other species being Aspergillus parasiticus (Kuiper-Goodman, 1998).

Poultry feed has been found to be contaminated with Ochratoxin A and four different structural types of aflatoxins, labeled as AFB1, AFB2, AFG1 and AFG2 (Gentles et al., 1999). Aspergillus flavus solely produces B aflatoxins, whereas Aspergillus parasiticus produces both B and G aflatoxins (Peraica, M et al., 1999). Aflatoxins have been studied extensively and are known to produce clinical toxicosis, reduce the resistance to diseases and disrupt the vaccine-induced immunity in poultry birds (Sharma, 1999). In the types of aflatoxins that have been mentioned previously, AFB1 has the most frequent presence in food and has been identified to be the most toxic and potentially hepatocarcinogenic (Bennett and Klich, 2003). If livestock and poultry are fed with aflatoxin-contaminated feeds, it can cause immune suppression, growth reduction and even death.

**Aflatoxins and liver cancer: an alarming connection:**

AFB1, if exposed to humans and animals for an extended period of time, has been found to increase the risk of liver cancer (hepatocellular carcinoma [HCC]) (Kew, 2014). Hepatitis B virus (HBV) affects almost 9 million people in Bangladesh and is the primary reason behind the emergence of liver cancer in this country, accounting for 47-61% cases (Al-Mahtab, 2015). Synergistic effects of aflatoxin along with chronic hepatitis B viral infection have been found to increase the likelihood of liver cancer by 30-fold when compared to patients who are HBV-negative (JECFA, 1998).

Exposure to aflatoxins single-handedly causes 291-6100 liver cancers annually with an average of 1311 cases per year (Saha Tundra and Wu, 2019). This has been estimated via counting both HBV-positive and HBV-negative patients based on the average dietary intakes of aflatoxin-contaminated food commodities. Thus, dietary aflatoxin exposure accounts for approximately 43.9% of the total estimated liver cancer cases (3022) in Bangladesh per year (GLOBOCAN, 2012). The estimated global average of aflatoxin-related liver cancer cases is 5-28% (Liu and Wu, 2010; Liu et al., 2012). Henceforth, it is clearly indicated that the average aflatoxin-related liver cancer cases in Bangladesh is noticeably higher than the global average.

**Zearalenone's effects on reproductive health:**

Zearalenone is a non-steroid estrogenic mycotoxin that is produced primarily by Fusarium graminearum and its related species. Zearalenone has been found to produce potential estrogenic effects on numerous animal species. Some of the health hazards found in females are infertility, vulval oedema, vaginal prolapse and mammary hypertrophy (Peraica, M et al., 1999). The amount of zearalenone uptaken was important as well. This is because at low doses, the female estrogen hormone was affected which caused a longer time for the mammary gland to mature. At high doses, interference was seen in the conception procedure and the mycotoxin was secreted in the milk, negatively impacting the viability of newborn animals. In males, feminization has been observed such as atrophy of testes and mammary gland enlargement (Jones, FT et al., 1994). In humans, there was once a report of an outbreak of precocious pubertal changes in thousands of young children in Puerto Rico. The symptoms observed were premature thelarche, premature pubarche, prepubertal gynecomastia and precocious pseudopuberty (Sáenz de Rodríguez, 1984, 1985). There have not been any extensive studies carried out on the impact of zearalenone in the population of Bangladesh. However, research is required on the matter as zearalenone can cause major reproductive health problems.

**Ochratoxin A's effect on health:**

Among the species of ochratoxins, ochratoxin A has been found to be the most toxicogenic. This mycotoxin has exhibited nephrotoxic, immunosuppressive, carcinogenic and teratogenic capabilities in all animals that have been tested upon (Geneva, World Health Organization,1990). The most notable effect this toxin has is the damaging of the kidney (Fuchs, R et al., 2005) but it may also negatively impact the development of the fetus and the immune system. Furthermore, at high doses, it reportedly causes nephrotoxicity, damage to the gut and lymphoid tissue (Harwig J., 1974).

**Trichothecenes, a neuromycotoxin:**

Trichothecenes are neuromycotoxins produced mainly by the genus Fusarium. There are studies that have reported the primary target of this toxin is the brain. Clinical symptoms which are most commonly observed are eye pain, nausea, muscle tremor, vomiting, dyspnea, weakness, etc. In farms, during the drying and milking process, trichothecenes have been discovered in the air samples (Lappalainen S. et al., 1996). They have also been found in the ventilation systems of private houses and office buildings and on the walls of houses (Croft WA. et al., 1986) when there is high humidity (Nikulin M. et al., 1994). The fact that trichothecene is a neuromycotoxin and it can have adverse effects on the brain, there have been reports in the development of ``sick building syndrome", which have been linked to Trichothecenes as a causative agent. The symptoms of airborne toxicosis absolutely vanished when the buildings and ventilation systems were properly cleaned. This is a major concern in Bangladesh right now, since people are advised to stay indoors as much as possible due to the COVID19 pandemic. During the full lockdown that was imposed by the government (to counteract the effects of the coronavirus in Bangladesh), which lasted from 23 March to 30 May, people may have suffered from airborne toxicosis due to the presence of trichothecenes in the air. Poor sanitation in the ventilation systems of buildings is a common scenario in Bangladesh and the likelihood of people developing "sick building syndrome" is very high. However, no studies have been carried out in this regard to establish a proper verdict.

| | Aflatoxin | Ochratoxin | Fumonisin | Trichothecene | Zearalenone | Reference |
|---|---|---|---|---|---|---|
| Cancerous | ✔ | ✔ | ✔ | | | (Claeys et al., 2020) |
| Liver | ✔ | ✔ | ✔ | | | (Mekuria et al., 2020) |
| Immune system | ✔ | ✔ | ✔ | ✔ | ✔ | (Berek et al., 2001; Pierron et al., 2016) |
| Kidney | | ✔ | ✔ | | | (Berndt et al., 1980) |
| Brain | | | ✔ | ✔ | | (*Mycotoxins & the Brain – Naturopathic Doctor News and Review*, n.d.; Ratnaseelan et al., 2018) |
| Reproduction | | | | | ✔ | (Santos et al., 2013) |
| Malformations | ✔ | ✔ | | | ✔ | (R. Schoental., 2007) |

Table: Types of Mycotoxins and the effects on organs/systems.

## Conclusion

Mycotoxins are considered to be 'silent killers' present in our food commodities. Especially in tropical countries that have suitable conditions for its production. It is still not taken seriously as a public health issue in such countries, which leads to lack of awareness and risk assessments of such dangerous toxins. Bangladesh falls at a greater risk as these occur more post harvest in paddy fields, and the high temperature and humidity promote such crops to be sources of mycotoxins. From what we have found, Aflatoxin is more common and it is responsible for more severe illnesses and diseases than rest of the mycotoxins. However, there isn't much research or surveys done regarding mycotoxins. But we have focused on a general view of other toxins that need to be further investigated in Bangladesh. The ones that were available are specifically on Aflatoxins, but they still do not give us an overview of  Bangladesh as a whole, only a few regions were covered. Staple foods of Bangladesh such as rice, wheat, maize and lentils are sources of Aflatoxin. Dates also contain huge amounts of it as found in a study where dates are highly consumed during the islamic month of Ramadan (Saha Turna & Wu, 2019) and other than that  most bengalis consume betel nuts for recreation,  which are also found to be a great source of Aflatoxin.(Roy, et al., 2013). It can be a threat to the population of Bangladesh as it can be passed on to chickens via poultry feed, that can eventually be passed on to people. We would consider it as a matter of concern as aflatoxins are hepatocarcinogenic. Another source of mycotoxin that can be concerning, according to our research, is trichothecenes that can be found indoors. Due to the current situation of the pandemic caused by COVID-19, many are staying indoors. Bangladesh is known to have congested buildings in cities which leads to poor ventilation. As stated previously, lack of air ventilation and sanitation can cause the production of this mycotoxin with toxicodynamic properties that can inhibit protein synthesis and have immunomodulatory effects (Sudakin, D.; 2003). This is something we need to look out for, as the lockdown may increase the chances. A daily exposure of such mycotoxins may gradually accumulate and cause a greater effect on health that many are unaware of. As the Public Health sectors of Bangladesh prioritise maternal health, we should pay heed to zearalenone as well.  All these toxins can give rise to several immunosuppressive, carcinogenic effects alongside reproductive health issues and other health risks as unknowingly, the majority of Bangladesh's population are exposed to them. Therefore, we believe that this mycotoxin is taken as a serious public health concern before it is too late. More investigation and research needs to be carried out to deduce the main sources, causes, effects, and various correlations that the mycotoxin may have, in advance to the damage that might be done as it is currently being brushed aside.

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