



RESEARCH ARTICLE

SCENARIO OF ASPERGILLUS INDOOR CONTAMINATION IN PAKISTAN (2000-2020) – A REVIEW

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ABSTRACT

Bioaerosols in indoor environment include substantial portion of fungi which are considered as “hidden killers”. Pakistan like other countries, also bears the atrocities of fungi and their mycotoxins and suffers more due to its favourable climate, weak economy and unawareness. Genus *Aspergillus* of Fungi is quite important and is predominant in indoor environment, along with *Penicillium*. There are not adequate research studies on the indoor micro-floral composition, however, the available data shows that numerous *Aspergillus* species are found inside the buildings whether they be houses, hospitals, laboratories, cafeteria or slaughterhouses. The mycotoxins produced by *Aspergillus* species include aflatoxins, fumonisins, citrinin, ochratoxins and cyclopiazonic acid. They are mainly carcinogenic and cause various diseases like aflatoxicosis, pentaketide nephrotoxin, and necrosis. To avoid such issues, fungal growth should be avoided by controlling temperature and humidity. In addition, fungicides, ultraviolet radiation or essential oils can be used against fungi. The condition of the buildings can also be adjusted to minimize fungal growth like building material, ventilation system, wall paint and hygiene. The database of the country is not satisfactory with insignificant laws and regulation. To estimate the potential risks of *Aspergillus* species and their mycotoxins, regular monitoring is required at all levels. It will also help to devise solutions related to health and environment related problems.

KEYWORDS

Aspergillus, mycotoxin, health, indoor, Pakistan.

1. INTRODUCTION

The urbanization and advancement in technology have changed the human lifestyle from open air and ventilated environment to sealed and energy efficient environment of the building. Airborne contaminants, both biological as well as non-biological, pose a great threat to human health (Khan and Karuppaiyil, 2012). Fungi forms the significant portion of the bioaerosols. Fungi growing in houses are hazardous and regarded as “hidden killers” because their mycotoxins often cause allergic reactions. In addition, volatile organic compounds (VOCs) are also released during fungal growth and death. Pan American Health Organization (PAHO) has reported that the predominant form of pollution in developing countries is indoor air pollution (Alzahrani et al., 2020). Invasive Fungal Infections (IFIs) have been estimated equivalent to tuberculosis (TB) (Dylag, 2017; Jabeen et al., 2017).

Mycotoxins are secondary metabolites of fungi, produced chiefly by *Aspergillus* spp, *Fusarium* and *Penicillium* under specific conditions. They are not significant for the survival of fungi but provide them with an ecological advantage in competitive environments. Simultaneous and collective exposure could result in synergistic, antagonistic or additive effects in humans (Alassane-Kpembi et al., 2017). Inhalation of mycotoxins by living organisms requires direct inhalation of mycotoxin containing mould or dust particle, as they are non-volatile and cannot evaporate from

the substrate (mould) (Kelman et al; 2004).

Mycotoxins are available inside due to the presence of indoor fungi which is reported to be in paper products, fabric, insulation materials and jute (Li et al., 2016). Less ventilation and humid environment are favorable for fungal growth (Miller and McMullin, 2014). According to WHO guidelines on air quality (2009), there is 75% more risk of respiratory issues and asthma in moist and moldy buildings (Méheust et al., 2014). *Aspergillus* species can grow in very less moisture and invade less xerophilic molds (Chen et al., 2017). Mostly the countries, like those in South Asia, with humid climate face the contamination of *Aspergillus* in indoor environment due to the ability of fungi to grow over a broad temperature range with sufficient nutrients and dampness. The indoor fungal pollution has been associated with a variety of diseases including asthma, headache, allergy and irritant effects, respiratory problems, mycoses, and several other non-specific health problems (Er et al., 2016; Pitkaranta et al., 2011). The fungal genus *Aspergillus* is one of the most abundant and globally distributed with the 339 species reported till date (Perrone and Gallo, 2017). In addition to its biotechnological utility, many researchers observed that the *Aspergillus* species constitute a major portion of the indoor bioaerosols along with *Penicillium* (Sidra et al., 2015). However, the concentration varies based on the activities being carried out and the conditions established at site (Asif et al., 2018). A study reported six novel species in *Aspergillus* section, four homothallic and two anamorphic, in

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indoor environment in USA (Sklenar et al., 2020). A group researchers isolated *Aspergillus flavus* from farmhouses in Odisha, India (Nayak et al., 2018). *Aspergillus sp.* (mainly *Aspergillus niger*) are highly detected in household's unfiltered air, ventilation systems, contaminated dust, water, and can even contribute to food (fruits, vegetables, cereals, meat etc.) degeneration and contamination causing some serious respiratory problems related to emitted allergens (Costa et al., 2016; Kalalian et al., 2020). *Aspergillus fumigatus* was isolated from a wide range of environmental conditions at an optimal temperature of 37°C (range: 12–65°C) and pH of growth sites between 2.1 and 8.8 (Kwon-Chung et al., 2013).

Common mycotoxins of *Aspergillus* are aflatoxins and ochratoxin A. Inhaling its mycotoxins can cause several diseases, depending upon the host immunity. They primarily affect mucous membranes and epithelia of respiratory tract. Most prevalent diseases include aspergilloma, pulmonary aspergillosis, various antipathy diseases like Allergic Bronchopulmonary Aspergillosis (ABPA), hypersensitivity, pneumonitis and allergic asthma. Ochratoxin A exposure causes renal failure and respiratory problems while *fumigatus* exposure is cilio-inhibitory, causing fatigue, nausea and fever (Table 2) (Mousavi et al., 2016; Reijula and Tuomi, 2003). There are many different manifestations of aspergillosis including allergic aspergillosis both rhinosinusitis and bronchopulmonary, chronic pulmonary and rhinosinus aspergillosis, invasive aspergillosis and superficial disease (Richardson et al., 2019).

Pakistan is bearing a substantial burden of fungal infections and diseases, mainly due to the absence of well-structured healthcare system. The condition is worse in areas having poor sanitation, lack of awareness, unavailability of antifungal agents and insufficient diagnostic facilities (Jabeen et al., 2017). Remediation of fungal pollution requires removal of the fungi present and modifying the indoor environment to become less favorable to growth. These steps may include treatment of indoor environments with an antifungal agent to prevent future growth (Alzahrani et al., 2020; So et al., 2016).

Aspergillus was found consistent among the top four major mycotoxins and spore producing fungi genus in indoor environment, in most of the consulted studies throughout the world. Indoor fungal concentration is also found to be linked with that of outdoor air quality. Health implication due to poor indoor air quality and *aspergillus* contamination has caused exacerbated symptoms (36 to 48%) and random episodes of asthma in children and elder population in Pakistan and in other parts of the world (Dannemiller et al., 2015; Sharpe et al., 2015; Sheehan and Phipatanakul, 2016). Such problems are poorly understood and have gained little attention in the past, so more studies are needed in the future to increase awareness and research to increase the quality of indoor air and minimize

the risk of fungal contamination.

This article is a meta-analysis of indoor environments of Pakistan, contaminated with *Aspergillus* species and their mycotoxins. The major challenge when reviewing the literature on the *Aspergillus* in indoor environment of Pakistan is deficiency of published literature. Most of the techniques being used across the world are not in use in Pakistan. Moreover, limited recent literature is available for review. Various studies show that indoor air quality of houses is poor due to the presence of particulate matter and bioaerosols from bacteria and fungi. There are only few studies on micro-floral composition of indoor environment in contrast to extensive studies on particulate matter pollution. The main aim of this study was to collect the available information on *aspergillus* contamination of indoor environment, focusing on Pakistan only and to highlight its significance for human health.

2. METHODOLOGY

The study focused on the *Aspergillus* contamination of the indoor environment. The study area was the whole country of Pakistan. Electronic searches through databases, including and not restricted to Google Scholar, Science Direct and Science Hub were used for restricted studies published during 2000 and 2020. The latest books were also consulted for supporting the information. The articles included in the study consisted of the association between the *Aspergillus* species, indoor environment, and the respective health impacts. Furthermore, health effects due to various types of mycotoxins, released by *Aspergillus* species, were also linked to identify the factors which allow the growth of *Aspergillus* species, in closed environments.

3. RESULTS AND DISCUSSION

The indoor contamination by any biological agent is of significant interest due to potential health adversities. Humans spend 70 to 80% of their day indoor exposing them directly to the contaminants. The indoor concentrations are usually found to be higher than the outdoor (Yang et al., 2015). The concentration of bioaerosols and period of exposure determine the intensity of effect on human population (Salthammer et al., 2016). The subject of indoor aerial microflora is usually neglected and therefore there are few researches on the matter. *Aspergillus* is highlighted in this study as it is regarded as the most abundant fungal genus with some of the most toxic mycotoxins. *Aspergillus* is an opportunistic and versatile organism that has potential to survive and grow in number of environmental conditions, and variety of host organisms including human beings (Kwon-Chung and Sugui, 2013). The table 1 shows the occurrence of *Aspergillus* species in various indoor environments and their reported health impacts.

Table 1. Indoor *Aspergillus* Contamination in cities of Pakistan

Location	Environment	Fungal Species	Health Effects	References
Islamabad	Cafeteria, Semi-government university	<i>Aspergillus spp.</i> (2.4%)	-	(Asif et al., 2019)
Islamabad	Operation theaters, surgical wards, general medicine wards, emergency ward and OPD.	<i>A. fumigatus</i> , <i>A. niger</i> , <i>A. flavus</i> (17.1%)	Human opportunistic infections, nosocomial infections and allergies, invasive aspergillosis	(Asif et al., 2018)
Lahore	Kitchens and living room	<i>A. fumigatus</i> , <i>A. nidulans</i> , <i>A. flavus</i> , <i>A. niger</i> , <i>A. terreus</i>	Asthma, hypersensitivity reactions, allergic fungal sinusitis	(Safdar, 2016)
Azad Jammu and Kashmir	Household, hospital, school and industry	<i>Aspergillus spp.</i>	allergic alveolitis, allergic rhinitis, asthma, cancer.	(Nasir et al., 2015)
Lahore	Kitchen and living room (growth on paint, filters, dust, cooling coils)	<i>A. fumigatus</i>	Asthma, sinusitis, rhinitis, sick building syndrome, aspergillosis	(Sidra et al., 2015)
Karachi	Indoor Residential	<i>A. flavus</i> , <i>A. niger</i> , <i>A. fumigatus</i> , <i>A. terreus</i> , <i>A. glaucus</i> , <i>A. nidulans</i>	Acute exacerbation of asthma (dominantly female – average age 46)	(Zubairi et al., 2014)
Karachi	Cafeteria and microbiology lab	<i>A. niger</i> , <i>A. flavus</i>	-	(Mursaleen et al., 2014)
Islamabad	Hospital labs and wards	<i>A. fumigatus</i> , <i>A. niger</i> , <i>A. flavus</i>	Dizziness, headache, nausea, irritation of eyes, nose, and throat	(Hussain et al., 2012)
Railway Colony, Lahore	Kitchen indoor environment	<i>Aspergillus</i> (61% - 17 unidentified species)	Allergies, chronic fatigue, effect on lung immunological response, aspergillosis	(Mushtaq et al., 2011)
Civil Hospital Karachi, Liaquat University of Medical and Health Sciences, Jamshoro	-	<i>A. fumigatus</i> , <i>A. flavus</i> , <i>A. niger</i>	Otomycosis (Ears and Lungs), Aspergillosis (Lungs)	(Thebo et al., 2006)
Lahore	Slaughterhouses	<i>Aspergillus spp.</i> (18.0 %)	Respiratory infections	(Adeeb and Shooter, 2003)

The big cities of Pakistan namely Islamabad, Karachi and Lahore were only studied in past twenty years for indoor aerosol content. The indoor environment of kitchen, living room, institutional cafeteria and hospital wards are analyzed. The presence of *A. niger*, *A. fumigatus*, *A. flavus* and *A. terreus* was observed in all environmental conditions. The mycotoxins associated with each type of *Aspergillus spp.* (Table 2) could be expected to transmit to humans via inhalation, ingestion, and dermal contact and cause various diseases. The four species stated above were reported to be responsible for most of the cases of invasive Aspergillosis in human beings, *A. fumigatus* contributing to the 90% of case adversities (Iqbal et al., 2016).

Table 2. Mycotoxins associated with Aspergillus and their health impacts

Mycotoxins	Subtype	Toxin producing species	Health Impacts	References
Aflatoxins (AFBs)	AFB ₁	<i>A. niger</i> , <i>A. flavus</i> , <i>A. fumigatus</i> , <i>A. parasiticus</i>	Most toxic, carcinogenic	(Perrone and Gallo, 2017; Varga et al., 2015)
	B ₁		Hepatocarcinogenic, immunosuppressive, aflatoxicosis (weight loss, suppressed immunity, hemorrhage)	
Ochratoxin	OTA	<i>A. niger</i> , <i>A. ochraceus</i>	Pentaketide nephrotoxin, carcinogenic, neurotoxic,	(Perrone and Gallo, 2017; Tola and Kebede, 2016)
Fumonisin	FB ₂ , FB ₄ , B ₁	<i>A. niger</i> , <i>A. welwitschiae</i>	Carcinogenic (human esophageal cancer), disrupt sphingolipids biosynthesis	(Perrone and Gallo, 2017; Varga et al., 2015)
Cyclopiazonic acid	-	<i>A. flavus</i>	Degeneration and necrosis in body organs	(Varga et al., 2015)
Citrinin	-	<i>A. terreus</i> , <i>A. niveus</i>	Nephrotoxin	(Varga et al., 2015; da Rocha et al., 2014)
Patulin	-	<i>A. terreus</i> , <i>A. clavatus</i> , <i>A. giganteus</i>	Not conclusive	(da Rocha et al., 2014)

Several studies have confirmed the association between indoor humidity, fungal growth and allergic symptoms in the residents. *A. niger*, *A. flavus*, and *A. fumigatus* are the most potent allergens (Mousavi et al., 2016; Singh et al., 2014). The indoor and outdoor temperature, relative humidity, condition of building and ventilating systems, kitchen substrates, cleanliness practices and occupant density are some other factors regarded as the determinants of type and growth of fungi (Crawford et al., 2015; Mushtaq et al., 2011).

In living rooms where A/C units, carpets and plant plots are present, the probability of occurrence of fungi increases. The pathogen growth can be attributed to the moisture generated by A/C and soil as ideal growth media. It is very common practice to switch off the Air Conditioning (A/C) units, after intervals. It gives water a chance to condense, rising the relative humidity favouring the growth of fungi. (Khan and Karuppaiyil, 2012). However, the fungal growth can be mitigated by controlling the indoor moisture and humidity. Programming of A/C functional periods, regular cleaning of A/C filters and installation of HEPA (High efficiency particulate air) filters can serve the purpose (Hussain et al., 2012). The plant pots should be regularly monitored for any fungal infestation. Living rooms should be regularly cleaned through washing and using vacuum cleaner (Khan and Karuppaiyil, 2012).

Cafeteria of the institutes are the sites with considerable occupant density, that could be potential vector for fungal spores. Moreover, food stuff and

food handling impact the quality and hygiene of indoor air. Indoor environment where food material is handled and served is more critical as it may potentially transmit fungal products and mycotoxin through ingestion. The quality of food ingredients, preservation and processing techniques are the determinants of the safety of food on table and human thereof (Asif et al., 2019). In hospitals, patients with fungal infections are the prime distributors of fungal spores. The presence of bioaerosols in hospital environment is critical for the immune-deficient patients (Napoli et al., 2012). In slaughterhouses, the animal feed, excreta and bedding material serve as the source of fungal spores and other bioaerosols (Adeeb and Shooter, 2003; Saleemi et al., 2010).

In buildings, the fungal growth was observed in deteriorated painted wall surfaces, ceiling tiles, broken insulations and any moisture retaining structures (Elumalai et al., 2014; Mihinova and Pieckova, 2012). To control fungal growth on damp walls, use of fungicides is recommended. Fungicide is an antifungal compound that destroys and eradicate the fungal spores and reduces the survival probability of fungi. Chlorinated fungicide or chlorine bleach is effective to kill spores. Common bleach is useful for treating *Aspergillus* species (Schroder et al., 2017). However, it is crucial to confirm the fungi killing potential of fungicide for different types of fungal spores (Shafa et al., 2014). Elimination of mycotoxin producing fungi can also be done by irradiation of the indoor environment with ultraviolet lamps, as UV light has germicidal effects on myriad of fungal species (Alangade, 2011). However, a few species are resistant to UV rays by virtue of melanin cell wall like the conidia of *Aspergillus fumigatus*, which makes them more virulent (Kwon-Chung and Sugui, 2013).

However, there are number of side effects associated with the use of anti-fungal agents if exposure persist for long time or antifungal agent has a bad odor. It indicates that the application of fungicide should comply with the health safety or should be substituted with the non-toxic alternatives. To substitute the toxic chemical treatment, numerous studies on antifungal attributes of biological extracts have been carried out on essential oils, including that of clove, eucalyptus and lavender. Essential oils are aromatic substances and are considered safe for consumption in any form in daily life. They have also been used since ages as medicines for their anti-microbial characteristics (Table 3). Eucalyptus oil is mildly effective for *Aspergillus sp.* (Schroder et al., 2017). Lemon oils were found to be potent biological fungicide for ochratoxin producing *Aspergillus niger* (Verma et al., 2011a).

Table 3. Experimental results manifesting the efficacy of anti-fungal biological extracts

Biological Treatment	Fungal Species	References
Extract from thyme (<i>Thymus vulgaris</i>) and ginkgo (<i>Ginkgo biloba</i>) leaves	<i>A. niger</i>	(So et al., 2016)
Tea tree oil (<i>Melaleuca alternifolia</i>)	<i>A. fumigatus</i>	(Rogawansamy et al., 2015)
Cinnamon oil (<i>Cinnamomum verum</i>) and clove oil (<i>Saromaticum</i>)	<i>Aspergillus spp.</i>	(Yingprasert et al., 2015)
Oregano (<i>Origanum vulgare</i>) essential oil	<i>A. fumigatus</i> , <i>A. nidulans</i>	(Stupar et al., 2014)
Coriander (<i>Coriandrum sativum</i> L.), and Lavender essential oils	<i>A. alternate</i> , <i>A. niger</i>	(Zabka et al., 2014)
Essential oils from black pepper (<i>Piper nigrum</i> Linn.), castor oil (<i>Ricinus communis</i>), lemon (<i>Citrus limon</i>), olive (<i>Olea europea</i>)	<i>A. niger</i>	(Verma et al., 2011b)
VOCs produced from evaporation of essential oils of lavender, eucalyptus and tea tree	Air-borne fungi samples	(Su et al., 2007)

4. RECOMMENDATIONS

There is not significant set of standards and regulation for indoor microbiological contaminants. The scientific research base is also weak in Pakistan and demands attention of academia and scientific community. Quantitative evaluation of indoor airborne microflora is imperative to determine the exposure and relation between enhanced concentration and health issues. The monitoring of air quality must also incorporate the evaluation of bioaerosols, so the potential health hazards could be avoided.

5. CONCLUSION

The article is a review on indoor contamination of *Aspergillus* in past twenty years, in different areas of Pakistan. Most common indoor species include *A. niger*, *A. flavus* and *A. fumigatus*. Aflatoxins and ochratoxins are their main mycotoxins among others. Unhygienic and moist conditions prove to be most favorable for the proliferation of the fungi. First, moisture should be removed through ventilation to control fungal growth. Second, the buildings should be maintained with suitable construction material. Furthermore, different chemical, physical and biological methods can also be used to reduce fungal growth namely fungicides, UV-lamps and essential oils respectively.

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