Original Article :

Prevalence of Mycoses and investigation of Fungal Indoor Environment

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Abstract

Background and Aims:
The incidence of fungal infections in Saudi Arabia is increasing with an increase in the population of high-risk patients. Still, studies highlighting the impact of environmental fungal agents on infections in Saudi are limited, and none have examined the Medina region despite the city's stature, diversity, and travel flow. This study aims to determine the fungal distribution across the Medina region.

Methods:
A randomized 212 indoor samples were collected based on analyzed data from 1374 questionnaires. The prevalence of participants to fungal infection was 19.2% and 26.3% in the risk group. Fungal species were identified via macroscopic and microscopic examination..

Results:
Two hundred and three (96%) samples showed fungal growth. Yeast identified were 78 (34%) *Candida* species, 56 (25%) non-*Candida* species. The study identified 13 genera and 20 species for mould, including 38 (17%) *Aspergillus* spp., 20 (9%) *Rhizopus* spp. 9(4%) holoarthic/enteroatric conidiogenesis,7 (3%) *Mucor* spp. 4 (2%) of both *Penicillium* spp. and *Neurspora* spp. and only 2(1%) of *Madurella* spp., 3(1%) *Epidermophyton* spp., 2 (1%) *Lichtheimia* spp., and 1(1%) *Peacilomyces* spp.

Conclusions:
TThis study identified *Aspergillus* spp. as the most frequent fungi across the Medina region. The characterization of indoor fungal environment enables healthcare practitioners to anticipate fungal infection for individuals at risk. These findings can aid the prediction and prevention of fungal infections and fungal sensitization among the high-risk populations.

Keywords:
Environment, Saudi Arabia, Fungi, Indoor, *Aspergillus*.

Introduction

Fungal infections are the most common cause of morbidity and mortality in immunocompromised and chronic disease patients [1]. This is attributable to the steady

increase in opportunistic invasive fungal infections in risk groups [2]. It was estimated that a person inhales 5–5000 conidia of opportunistic pathological fungi daily. However, conidia are harmless cells in most individuals, except in immunocompromised patients who are at a higher risk of being affected by fungal infections [3]. Patients with impaired immune systems, such as diabetes, asthma, and transplant recipients, are the most susceptible to secondary infections due to prolonged treatment and general immunosuppression [4]. The prevalence of asthma varies worldwide, ranging from 1% –20% for both children and adults. The prevalence of asthma in Saudi Arabia, was estimated to be 11.3% [5]. The most common fungi found in these patients are *Candida* spp., *Aspergillus* spp., *Cryptococcus* neoformans, and *dermatophytes* [6]. This study focuses on establishing the distribution and characterization of the relationship between indoor environments and fungal abundance across Medina. The detection and characterization of Medina's environmental fungi in the area are inadequate. This study aims to determine the fungal distribution as well as identify the signature indoor fungi in Medina region and highlight the prevalence of environmental fungal infections in Saudi populations.

Materials and Methods

Study Design

This observational cross-section study assessed the indoor environmental fungi using a questionnaire for collecting demographic data and analysis of dust samples.

Inclusion and Exclusion Criteria

The inclusion criteria comprised individuals with or without fungal infections, immunocompromised illnesses, and healthy controls. Surveys and samples were excluded from individuals living outside the Medina districts.

Data and Sample Collection

The role of the questionnaire was to recruit the study subjects and to collect data of their homes. The questions focused on the resident's previous or current fungal infections, immunosuppression status, pets, and consent for participation. The questionnaire was distributed using snowball sampling to different regions in Medina, collected 1374 responses. Samples were collected from December 2019 to March 2020. The city's temperature (°C) and humidity (%) were moderate across the months (17.7°C -23.8 °C) and (38%- 28%), respectively. Questionnaires and samples were sorted before analysis to remove any inadequate information and sample. Data were then normalized by random selection to obtain an equal number of samples from each dis-

trict without bias. A final total of 212 samples were processed after removing insufficient samples and normalization between regions of Medina. The participant vacuum cleaners' content (suction power 250–320 watts) was collected into sterile, well-sealed, and labeled bags. Sample content description was recorded, which included dust, human hair, nails, and cat hair.

Sample Processing

All sample processing was performed in a class II cabinet for safety reasons and to avoid any contamination. Fungal identification was made using macroscopic and microscopic fungal morphological classification using standard mycological methods (Lactophenol cotton blue staining by the scotch tape and Gram stain method) [7]. The sample content was transferred to 10 mL falcon tubes and weighted for normalization (0.7 g). Samples were eluted using 2 mL sterile physiological saline and vortexed for 30 seconds to be cultured on the agar. Agar plates were inoculated in the centre (10 µL) using a platinum loop (Superior Marienfeld Company - Germany) then the inoculation was spread using a glass spreader (Superior Marienfeld Company - Germany) in a circular motion. After incubation at 37 °C for 48 h, all yeasts and moulds colony were counted manually then colony-forming-unit (CFU) was calculated, and two dominant well isolated colonies were selected for purity culture and further investigation.

Ethical Considerations

This project was approved by the Ethical Committee of Scientific Research at the College of Applied Medical Sciences, Taibah University. Ethical training was organized by the King Abdulaziz City National Committee of Bioethics.

Statistical Calculation

All epidemiological, statistical, and laboratory data were calculated using Microsoft Excel 2016. CFU\ml was calculated using (number of colonies × dilution factor) \ volume of sample, prevalence was calculated using (number of people with disease / total number of people), frequency (number of n isolates / total number of isolates) and risk ratio (RR) (Risk of disease in a group of primary interest / Risk of disease in the comparison group).

Results

The Prevalence of Fungal Infections in Madina

Based on the analysis of the questionnaire from 1374 participants among different regions from Medina, the prevalence and risk of fungal disease who were calculated. The prevalence of fungal infections among the participants was 19.2%. The responses included 133 individuals were identified

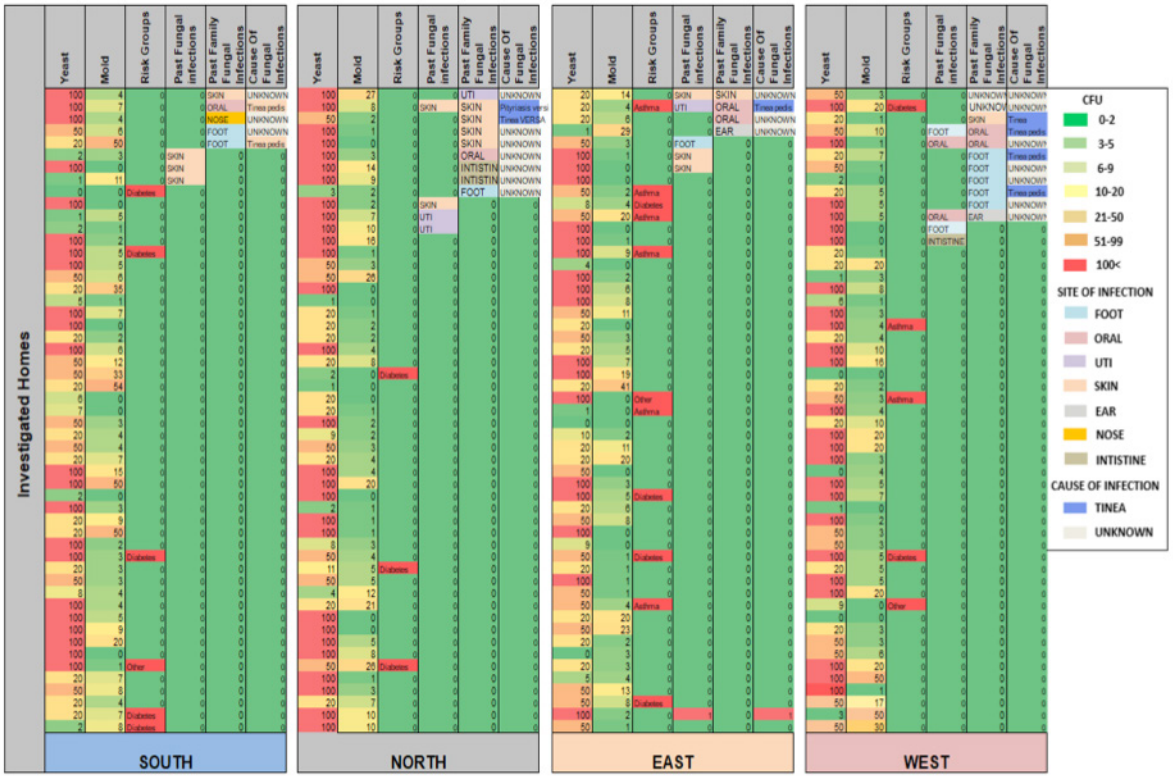
as risk groups (diabetes, asthma, organ transplant, thyroid disease, irritable bowel syndrome). The prevalence of fungal infections in risk disease was 26.3%.

The Relationship Between Participants and Fungal Agents

The randomly selected 212 representative samples from each home were analysed considering different variables (Figure 1). The population risk group analysis showed; 25 individuals (12%) risk group which 14 (7%) had diabetes, 8 (4%) had asthma, and 3 (1%) had an organ transplant, thyroid disease, irritable bowel syndrome, and 187 (88 %) healthy individuals. The fungal load among these risk groups was analysed and showed that six of asthmatic patients have *Candida* spp and one *Rhizopus* spp. Among diabetic patients, five *Candida* spp, three non-*Candida* spp, and one of each *Aspergillus* spp., *Rhizopus* spp., and Madurella spp. in their samples. Other risk groups had only two of *Candida* spp.

Among 212 participants, 18 cases reported to have a past fungal infection, which represented (9%) of the study's population. The data revealed that the percentage of yeast and mould in which they were 134 isolates (60%) and 90 isolates (40%), respectively.

The data include the counts for yeast, mould, risk groups, previous fungal infec-



.Figure 1: Overview of the randomly selected 212 representative samples and their questionnaire data

tion, previous fungal infection for more than one family member, causative agent if known. The data was randomized and normalized to investigate the same number of homes based on geographical distribution of Medina regions.

The association between fungal infections and risk group was measured based on the risk group ratio. Therefore, the risk ratio for the risk group was 0.4, indicating that there is no significant association between risk group and fungal infections as the RR is less than 1 (Table1 - A).

The association was carried out between the isolates found during our study from risk groups with past infection and isolates from risk groups with no past infection.

Table 1: Association between the fungal load in risk groups with past fungal infections and risk group with no past fungal infections in addition to the number members living in a household.

A	Past fungal infection	No infection	Total
Number of			
Risk groups	2	23	25
Healthy people	37	150	187
Total	39	173	212
B	Yeast	Mold	Total
Risk groups			
With past fungal infection	120	24	144
With no past fungal infection	1203	120	1323
Total	1323	144	1467

The isolates were classified into yeast and mould. The RR then was set to be 0.8, indicating no significant difference between the number of isolates in risk groups with past fungal infections and the isolates from risk groups with no past fungal infections (Table 1 - B).

Fungal Variability in Medina Indoor Environment

Fungal diversity and distribution across four regions of Medina were identified. Of the 212 homes, 203 (96%) homes showed fungal growth, among them the frequency of each was found to be as shown in (Table 2), whereas 9 (4%) showed no growth.

Table 2: The frequency of signature species in Medina

	Frequency	Relative Frequency %
Fungal isolate		
Candida Yeast	78	34 %
Non-*Candida* Yeast	56	25 %
Aspergillus spp.	38	17 %
Rhizopus spp.	20	9 %
Mucor spp.	7	3 %
Holoarthic\Enteroatric	9	4 %
Madurella spp.	2	1 %
Neurspora spp.	4	2 %
Penicillium spp.	4	2 %
Epidermophyton spp.	3	1 %
Lichtheimia spp.	2	1 %
Paecilomyces spp.	1	1 %

The analysis of dominant fungal strains showed; *Candida* spp, were more frequent than non-*Candida* spp. The highest number

of *Candida* spp isolate was 20 (36%) that was found in the Eastern regions of Medina, whereas the lowest number 9 (16%) was obtained from the Northern region. The highest number of *Candida* spp was 22 (28%), obtained from the Eastern region, whereas the lowest number 15 (19%) was obtained from the Western region. Based on macroscopic and microscopic examination, each region showed the presence of distinct types of fungi. As for the moulds, 13 genera and 20 species were identified. *Aspergillus* spp. accounted for the highest count, which was 38 homes (15%); they were found mainly in the Northern region in 13 homes (34%) and least in the Southern region in 7 homes (19%). The second most counted type of moulds was *Rhizopus* spp., which was found in 20 homes (9%); as they were found mainly in the Western region in 9 homes (45%) and less common in the Eastern region in 3 homes (15%) (Figure 2). Other moulds were also detected, such as *Mucor* spp. In 7 homes (3%), *Neurospora* spp. In 4 homes (2%), *Penicillium* spp. 4 in homes (2%), *Epidermophyton* spp. In 3 homes (1%), *Madurella* spp. In 2 homes (1%), *Lichtheimia* spp in 2 homes (1%), Paecilomyces spp. In 1 home (1%) and unknown fungi with holoarthic/enteroatric conidiogenesis in 9 homes (4%). A total of 134 (60%) yeasts

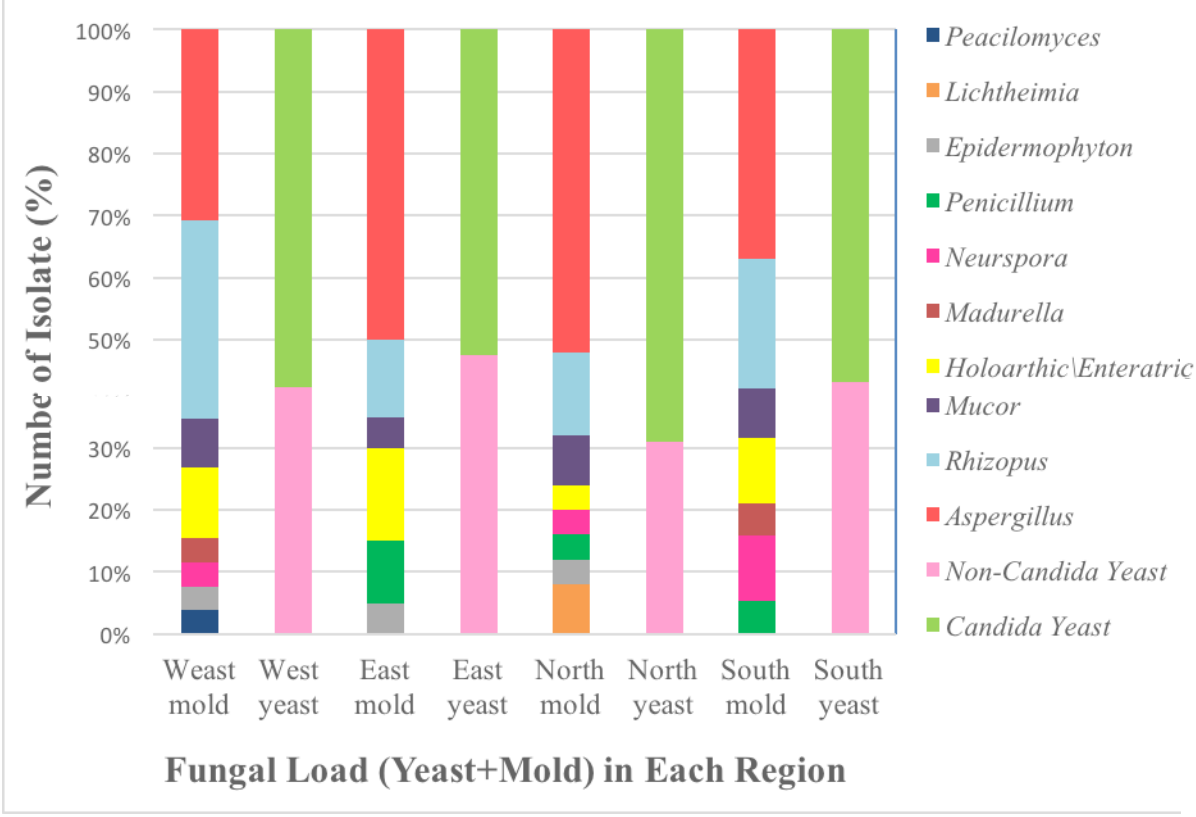


Figure 2: Distribution of fungi in different regions of Medina

and 90 (40%) moulds were isolated and analyzed. *Candida* yeasts were the most dominant yeast compared to non-Candida yeast. *Aspergillus* spp. were the most dominant followed by *Rhizopus* spp. in the Northern region and least prevalent in the Southern region.

Aspergillus Species in Medina Indoor Environment

Among *Aspergillus* spp., *A. candidus* 9 houses (24%) were the most dominant species, followed by *A. niger* and *A. terreus* complex in 6 homes (16%), *A. flavus* complex in 5 homes (13%), while *A. fumigatus* complex, *A. ustus* complex, and *A. versicolor* complex showed a low presence in 2 homes (5%) each; however, *A. oryzae* and *A. glaucus* complex in one home (3%) were the lowest to be detected. *A. niger* was only found in the Northern and Southern regions. Likewise, *A. oryzae*, *A. ustus* complex, and *A. versicolor* complex were only exclusively found in the Eastern and Western regions (Figure 3).

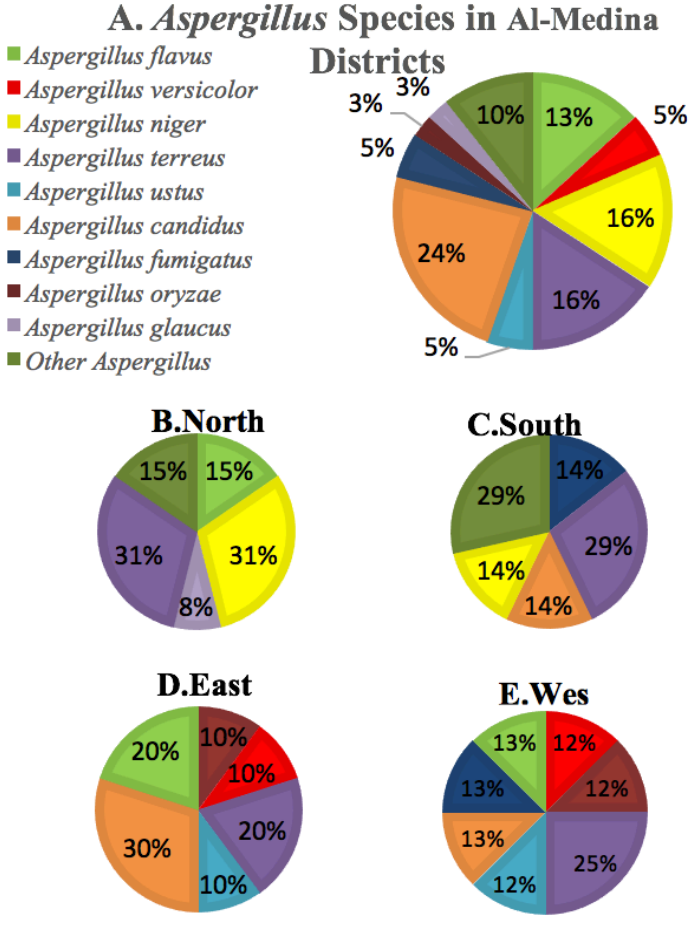


Figure 3: Distribution of *Aspergillus* spp. across all the regions of Al-Medina Al-Monawwarah.

A. *Aspergillus* spp. across all the regions of Medina *A. candidus* was the highest followed by A. *niger* and A. *terreus* complex.

B. *Aspergillus* spp. in the Northern region of Medina. *A. niger* and *A. terreus* complex had the highest numbers.

C. *Aspergillus* spp. in the Southern region of Medina *A. terreus* complex was the highest to be detected.

D. *Aspergillus* spp. in the Eastern region of Medina *A. candidus* was the highest followed by *A. flavus* complex and *A. terreus* complex

E. *Aspergillus* spp. in the Western region of Medina *A. terreus* complex was the highest.

Discussion

This study aimed to calculate the prevalence of fungal infections, identifying the signature indoor fungi and determine their distribution in Medina. We hypothesized that this region has signature fungal species that may have further contributed to the public health. As seen in modern societies, people spend 90% of their time indoors, and it is not surprising that factors contributing to poor indoor quality are receiving significant attention from researchers as well as the government [8]. Vacuum cleaner dust samples were selected as representative indoor environmental samples, with a heterogeneous mixture of emanation from human subjects, pets, plants, and air. It also contained viable and non-viable fungi, fungal proteins, mycotoxins, and endotoxins [9]. The vacuum cleaner was used as sampler for simplicity compared to the air sampling method in regards to, homes privacy, time, and accessibility to a larger sample size. Environmental fungi may be inhaled or ingested due to their adherence, invasion, and colonisation properties [10]. We identified *Candida* and *Aspergillus* spp as opportunistic fungi, which ranks as top pathogenic fungi for immunocompromised patients [11,12]. The dominance of these species in the indoor samples may serve a high risk of infection. Many factors facilitate the occurrence of these fungal infections such as contamination of surfaces, poor hand hygiene, and indoor air pollution. Patients administered immunosuppressive drugs for prolonged periods are at a higher risk for infection [6,13]. A recent study highlights an increased incidence of superficial fungal infections in diabetes patients [14]. This study included many individuals at risk of fungal infections (patients with diabetes, asthma, organ transplant, chronic diseases, thyroid disease, irritable bowel syndrome, and allergy). In this study, only a few participants had fungal infections; two of them were in the class of risk group. However,

population size was not enough to evaluate their exposure risk to fungal disease. The prevalence of fungal infections among all participants in this study showed a result of 19.2%. Participants with risk disease showed a prevalence of 26.3% for fungal infections. However, the study investigation and results were all based on the data obtained from the 212 samples collected from participants and the questionnaire data so we were able to identify only superficial fungal infection without systemic fungal infection; based on this, clinical specimens analysis are recommended in order to identify systemic fungal infection or conduct data collection analysis study from hospitals to obtain patient history whether a previous systemic or superficial fungal infection were acquired or not.

Nine culture plates out of 212 were negative using Sabouraoud Dextrose Agar, which further confirmed the limitation of routine culture not supporting the growth of all types of fungi. Other methods such as Polymerase Chain Reaction (PCR) or sequencing are best to enhance the detection and allow comprehensive analysis. Many studies highlighted the superiority of PCR over culture in patient samples and environmental studies. Ross et al, found that 25% of negative cultures were found to be positive for dermatophytes using PCR [15]. Another study showed, indoor dust samples were examined using mould-specific quantitative PCR (MSQPCR) [16]. This study focused on fungal presence in an indoor environment during wintertime when allergic symptoms are higher. Yet, other seasons may show slight variations. Geographical location and climate are important determinants that affect the biodiversity of yeasts and moulds. In this study, the total number of yeast isolates was higher than that of mould isolates. These findings could be explained considering humidity as a factor, as moulds prefer to grow under high humidity. It has been shown that several moulds begin to grow when humidity exceeds 55% [17], while the highest growth was recorded when humidity ranged below 70% [18]. During the study conduction, indoor humidity was not recorded in each home. However, the city's highest humidity recorded between December 2019 and March 2020 was 38%. Although the temperature range during the study was suitable for the growth of both moulds and yeasts, temperature alone as a factor was insufficient to promote higher growth of moulds [19].

This study reported *Aspergillus* spp. and *Rhizopus* spp. being the most common mould found in Medina. Several characteristic features enabled *Aspergillus* spp. to be the most dominant, such as tolerance to high temperatures, pH and other stress

conditions [20]. *Rhizopus* spp. is known as spoilage microorganism and is commonly found in agricultural products and food fermentation process [21]. Another finding was reported by Aquino *et al*, in which that the most frequent fungi present in the air filter of vacuum cleaners were environmental contaminants such as *Rhizopus* spp. and *Aspergillus* spp. [8].

Among *Aspergillus* spp., Each district showed varied distribution. *A. niger* and *A. terreus* complex were the highest in the North region, *A. terreus* complex was the highest in the South and West regions, and *A. candidus* was the highest in the East region. These variations may be due to different factors and influences such as indoor sources (ventilation, building statue like wall cracks, exposed places, and dampness) besides participants' occupation and pet's reservoirs. In this study, we found that the North region ranked with the highest number of household pets. *Aspergillus* spp. Wide range of thermotolerance increases its dominance among other mould species. For example, temperatures (20-25°C) allowed *A. versicolor* to grow. As for the other species of *Aspergillus*, preferred to grow at (37°C). A. niger is known as an outdoor fungus that prefers warm soil, this may indicate their increased transfer from outdoor sources. *A. niger* was only detected in the Northern and Southern regions which was probably due to the increase of outdoor playgrounds and parks in the Medina region. The abundance of these species in the Northern and Southern regions may also be due to the presence of farms and suitable groundwater providing an optimal growth environment [20]. In contrast, A. oryzae, A. ustus complex, and A. versicolor complex are known as indoor fungi that are usually found in damp environments (xerophilic area) and food products. Since Eastern and Western regions have limited farms and plants (outdoor sources), the predominant fungi in these regions were indoor fungi, such as A. oryzae, A. ustus complex, and A. versicolor complex [22,23].

The most common yeast species observed was Candida spp. However, further testing to differentiation between Candida albicans and other Candida spp. could not be completed due to the COVID-19 pandemic and quarantine. Nowadays, environmental isolates and non-pathogenic fungi are becoming a threat. Both aspergillosis and mucormycosis are ranked the highest reported fungal infection in immunocompromised patients [24]. Coronavirus disease 2019 (COVID-19) has been associated with a wide range of opportunistic fungal infections. More importantly, aspergillosis has been reported as the main fungal pathogen for co-infection in COVID-19

patients [25].

Conclusion

This study evaluated the diversity of the environmental fungal isolates across Medina. We showed that household dust was an important source of exposure to environmental fungi. The results of this study indicate that *Aspergillus* spp. and *Candida* spp. were the most dominant species in Medina. However, further efforts are needed to examine the dust samples using other diagnostic methods such as PCR, sequencing to ensure that all fungal strains, even rare and unculturable ones are detectable. Although this study focused on investigating environmental samples, further studies on establishing a correlation between household environments of patients, exposure to fungal strains and health are necessary. This study will increase awareness about the spectrum of fungal species across the Medina region and promote better hygiene practices and periodic decontamination of the households. The findings of this study have several important implications for future practice which help the development of appropriate control strategies to eliminate fungal exposure for immunocompromised, COVID-19 and other patients at risk, further improving public behaviour and health.

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Conflict of Interest

The authors declare no potential conflicts of interest.

Author Contributions

Project conceptualisation, methodology, resources, validation, project administration, and supervision: Aiah Khateb

Formal analysis, investigation, and data curation: Aiah Khateb, Fadwa Mohammed, Fai Alsubhi, Razan Abdullah and Saniyya Alkatib

Writing—original draft preparation

Fadwa Mohammed, Fai Alsubhi, Razan Abdullah and Saniyya Alkatib

Rewriting—review and editing

Aiah Khateb

Visualisation

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