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ALLERGY AND ASTHMA: PREVALENCE AND FREQUENCY OF INHALANT ALLERGENS IN THE MIDDLE EAST

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between all authors. Author SMH as the first author (corresponding author) has had the main idea in the developing, analyzing as well as writing review. Author SH contributed in the discussion and review of the manuscript. Author AAF also contributed in the discussion and adding to the review. All authors read and approved the final manuscript.

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Review Article

ABSTRACT

The prevalence of asthma and allergic diseases are on the rise globally. Despite advances in the diagnostic tools and treatment modalities, control of such diseases has not been possible. The etiological or allergenic factors responsible for inducing asthma and allergy in genetically predisposed or susceptible individuals are present in outdoor and indoor environment. In this review, published data for aeroallergens from countries in the Middle East and some neighboring countries are presented. The data indicated their qualitative and quantitative variations in the region. Some plant species were found to be different from those prevalent in western part of the world. In Saudi Arabia, weed pollen, including *Amaranthus viridis, Chenopodium murale* and *Salsola imbricata*, were amongst the most common outdoor allergens. As regards to indoor allergens, House Dust Mites, cat, American cockroach, German cockroach and Oriental cockroach as well as fungal spores such as *Alternaria alternata, Ulocladium atrium* and *Cladosporium sphaerospermum* were found in the region. However, not all the countries in the region have reported detailed information on aeroallergens. Therefore, there is still a lack of information from most of the countries in the region.

Further studies are required from most countries in the region in order to ascertain etiological factors and their prevalence in the region. The data presented in this review can thus be improved by further investigations and evaluating the clinical impact of dominating factors in both outdoor and indoor environment. The information can also be utilized for the implementation of environmental control in the respective region.

Keywords: Aeroallergens; allergy; asthma; indoor allergens; Middle-east.

1. INTRODUCTION

Allergies are antigen-antibody reactions. Antigens are allergens, defined as agents, which induce IgE-mediated immediate hypersensitivity reactions following inhalation, ingestion or injection. It is well known that the environmental factors play an important role in the genetically predisposed

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individuals [1,2]. Such individuals inherit the tendency for allergies from their parents and become mono- or poly-sensitized by inhalant allergens. Aeroallergens are thus incriminated in sensitization and elicitation of asthma, allergic rhinitis, etc.

The most common symptoms of respiratory allergic reaction include: bronchial asthma, allergic rhinitis, rhino-conjunctivitis, sneezing, accompanied by runny or clogged nose, coughing, itchy eyes, nose and throat. One of the serious manifestations of allergic disorders is bronchial asthma [3]. Asthma is a heterogeneous lung disorder characterized by airway obstruction, inflammation and eosinophil infiltration into the lung [4]. Asthma, which typically begins in childhood and is the most common chronic disease of childhood, has reached epidemic proportions [5]. The symptoms of asthma include coughing, wheezing, shortness of breath, and even death.

The responsible causes for initiating asthma are specific factors referred as allergens, which are present in the patients' surroundings originating from outdoor and indoor environment. Hence, allergens are divided into two categories; the outdoor allergens such as pollen grains, fungal spores, dust particles and non-specific irritants, and the indoor allergens such as House Dust Mites (HDMs), animal allergens, fungal allergens, insects, and rodent allergens, etc.

In addition to sensitizing factors mentioned above and to be discussed in detail in this communication, there are other non-sensitizing or irritating factors such as air pollution (primarily chemicals), cigarette and tobacco smokes, etc. present in both outdoor and indoor environment. These irritating factors also play a role in the exacerbation of the allergic symptoms or may cause asthma and breathing problems temporarily. However, the present review discusses only the sensitizing factors in the Middle-East and neighboring countries.

2. MATERIALS AND METHODS

2.1 Pollen Allergens in the Middle-East

The majority of the Middle East countries are generally known to be a desert region with low rainfall and very high temperatures [6,7]. As such, weeds are one of the common inhabitants of the plant kingdom as they require less water and can survive under harsh conditions [8]. Therefore, most of the countries in the region have weeds pollen prevalent in their environment (Table 1). Similar to the *Ambrosia artemisiifolia* (commonly known as ragweed), which is one of the primary causes of seasonal pollen allergy in the United States [9], *Amaranthus viridis* (commonly known as slender/green amaranth), a naturally growing widespread weed in the region, appears to be a major cause of allergy in the region. *Amaranthus* pollen is known to be highly allergenic and a potential cause of respiratory allergic diseases [10,11]. Of several species of *Amaranthus*, eight species are known to be foundin the Middle-East region. Amongst these, the most common species are *A. viridis, A. lividus, A. spinossus and A. graecizans. A. viridis* was found to be a major component of outdoor airspora, constituting a maximum of 96% of total pollen counts in Hail, followed by 89% in Al-Khobar, 87% in Jeddah, 85% in Qassim, 84% in Taif, 83% in Dammam and 61% in Jizan [12]. The data showed that *A. viridis* were present in the airspora throughout the year with distinct seasonal variations in their maximum appearance starting from August to November showing a peak in September and October.

Another study was performed in Saudi Arabia, where a Skin Prick Test (SPT) was conducted on 500 allergenic patients to examine their allergenic reaction toward a number of weed allergens [13]. Results revealed that the majority of patients reacted to weed pollen, which included *Atriplex polycarpa, Chenopodium album, Salsola tennifolia* and *Rumex crispus*. In fact, 21.8% of the patients reacted to weed pollen in Abha, while 75.5% in Gassim, 16.7% in Hofuf and 9% in Gizan. Individual pollen revealed *Chenopodium album* with maximum reactivity (81.8%) in agriculture setting (Gassim) followed by *Salsola tennifolia* (75.5%), (25% AI-Hofuf), *Rumex crispus* 27.3% (Gassim) and 18.1% (Gizan) [13]. Another study in the region also revealed that clinically, the common pollen allergens were: *Chenopodium album* 53%, *Prosopis juliflora* (mesquite) 46% and *Populus deltoides* (cottonwood) 38% [14]. *Prosopis juliflora* (a weed, but considered as a tree) is planted as ornamentals on the road side of some countries including Kuwait and Saudi Arabia. It is also found to be a common allergen in the UAE and Iran (Table 2). The *Populus deltoides* pollen was reported from UAE and KSA only.

Atriplex nummularia and Rumex vesicarius have been reported as allergenic weeds in Saudi Arabia and Kuwait. It is highly likely that these species will be present in other desert part of the region but until now no studies of their environmental concentration or clinical impact has been reported. Both *Chenopodium album* and *C. murale* have been found to be prevalent as outdoor allergen in Saudi Arabia. However, only *C. album* was reported to be allergenic in Kuwait, UAE, Jordan, Iran and Lebanon (Table 1).

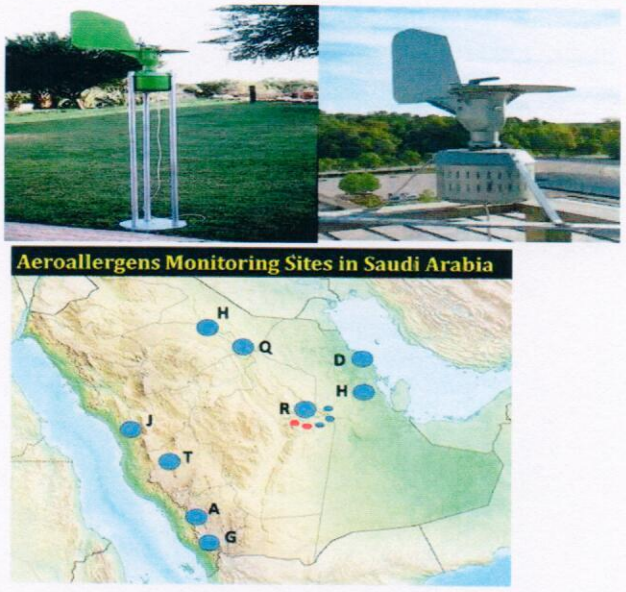

Fig. 1. Burkard 7-day recording volumetric spore trap and aeroallergens monitoring sites in Saudi Arabia

Fig. 2. Photographs of three common weeds in Saudi Arabia (a) and the photomicrographs of their pollen grains (b)

Salsola imbricata was found to be prevalent in Saudi Arabia but *S. kali* is also known to be prevalent in other part of the regions. A study in Kuwait revealed 76.7% of the allergic patients had a positive reaction to *Salsola* pollen [15]. *Phoenix dactylifera* is a very abundant crop in the UAE and KSA and its pollen grains are not wind pollinated and therefore have a low allergenic influence on people other than individuals working in date plant industry.

Amongst the grasses, *Cynodon dactylon* (commonly known as Bermuda grass), *Perrennial rye, Lolium perenne,* Timothy grass and *Phleum pretense* can be found in the region. Grass pollen grains appear to be least prevalent as outdoor allergens in the Middle East region. Some particular regions with agricultural activities such as Al-Ain in UAE, Gassim and Hail in Saudi Arabia have a number of grasses growing in the city [16]. However, skin test reactivity is common with grasses in KSA, Bahrain, UAE, Jordan, Iran and high reactivity in Turkey (Table 2).

2.2 Fungal Allergens in the Middle-East

Fungal spores belonging to deuteromycotina (conidia / spores), basidiomycotina (basidiospores), and ascomycotina (ascospores) have emerged to be prevalent amongst airborne spores in the Middle-East

[17,46,47]. However, the majority of known fungal allergens belong to the conidia or dry spores which are prevalent all over the world. This includes *Alternaria, Cladosporium, Aspergillus, Penicillum, Ulocladium* and to a lesser extent *Stemphylium, Helminthosporium* etc. (Table 3 lists the references that have been published in the region). However, basidiospores or ascospores allergen are rarely included in the Diagnostic (SPT) Profiles. This is possibly because none or limited companies dealing in allergen manufacturing are producing basidiospores or ascospores as diagnostic antigens unless requested.

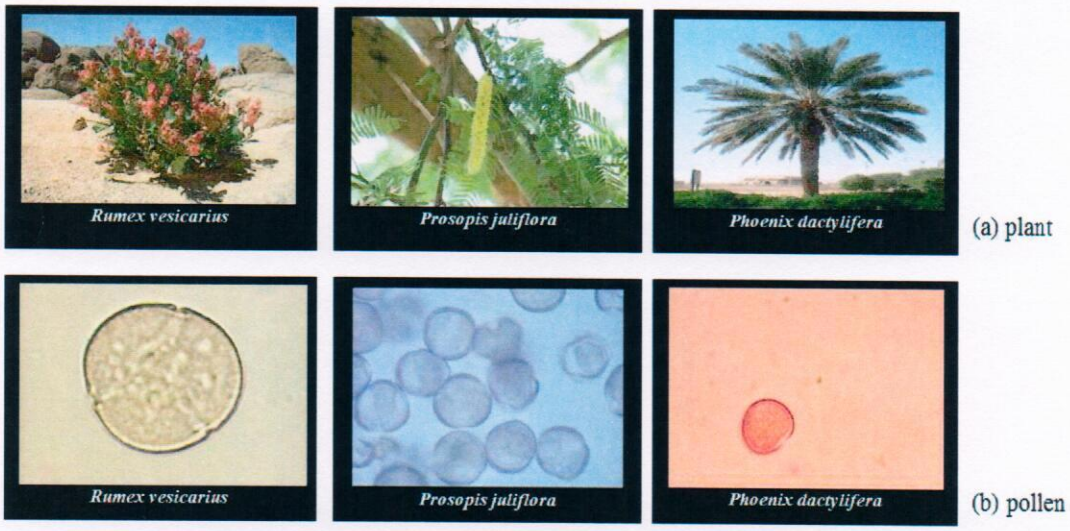

Fig. 3. The photographs are two common trees (*P. juliflora* and *P. dactyliflera*) and another weed (*R. vesicarius*) (a) and their pollen (b)

Table 1. Air-borne and allergenic weed pollen grains

Pollen / Country	*Amaranthus*	*Atriplex*	*Chenopodium*	*Salsola*	*Plantago* spp	*Kochia* spp	*Rumex* spp
K.S.A	+++ [11,12, 13, 17] [$]	+ [13]	+++ [13,14, 17,18]	+++ [13,18]	+ [13,17]	++ [14]	++ [13,17]
Kuwait	NA	NA	++ [15,19, 20,21]	+++ [15]	+ [21]	NA	NA
Qatar	NA	NA	NA	NA	NA	NA	NA
Bahrain	NA	NA	NA	NA	NA	NA	NA
Oman	NA	NA	NA	+ [22]	NA	NA	NA
U.A.E	NA	NA	++ [23]	NA	NA	+ [23]	NA
Jordan	+ [24]	NA	+ [24]	NA	+ [24]	NA	+ [24]
Turkey	+ [25,26]	NA	+ [25,26]	NA	+ [25,26,27,28]	NA	+ [25]
Egypt	NA	NA	NA	NA	NA	NA	NA
Iran	+ [29]	NA	++ [29,30]	+ [29]	NA	+ [29]	NA
Lebanon	NA	NA	+ [31]	NA	NA	NA	NA
Morocco	NA	NA	NA	NA	NA	NA	NA

 # NA: No available data
[$] Amaranthus viridis

Alternaria spores are considered as one of the most common fungal allergens in KSA, Kuwait, Qatar, Jordan, Turkey, Egypt and Iran. In addition, *Aspergillus* spores are also very common airborne allergens in KSA, Kuwait, Qatar, UAE, Jordan, Turkey, Egypt and Iran (Table 3).

Cladosporium emerged to be the most prevalent genus in the outdoor environment in KSA, Qatar and Iran. In Saudi Arabia, *Cladosporium* spp. was found to constitute up to 25% of all fungal spores in the dry region and 37.1%, 41.2% in two coastal cities. The SPT results revealed positive reactions with majority showing mild reactions [48]. Moreover, the spores of *Cladosporium* spp. are commonly described as the most allergenic spores in Turkey and Jordan.

In Kuwait, *Aspergillus* spp. were the predominant component of the outdoor airspora while *Cladosporium* spp. formed the major component of the indoor airspora followed by *Aspergillus* spp., *Penicillium* spp. and *Bipolaris* spp [49].

On the other hand, *Penicillium* spp. is the most common indoor allergen in Turkey followed by *Cladosporium* spp. *Aspergillus* spp. and *Alternaria* spp. [50] In Egypt, the most frequent indoor and outdoor fungi were *Aspergillus* spp. and *Cladosporium cladosporioides* followed by *Alternaria alternata* and *Penicillium chrysogenum* [51]. In Iran, the most common fungal allergen was *Aspergillus* followed by *Alternaria, Cladosporium* and *Penicillium* [41]. In a recent study in Iran, using Skin Prick Test on both Male (n=36) and Female (n=34), various fungal allergens (*Alternaria alternata, Aspergillus fumigatus, Cephalosporium acremonium* and *Penicillium* spp) showed between 5.1% - 11.5% positive reactivity. Important among these allergens is *Cephalosporium acremonium* with higher reactivity (11.5%) [52]. However, the genus *Cephalosporium* is not a common fungal allergen nor is commonly isolated from the air. The allergenicity to this genus is therefore not well defined.

Ulocladium spores are dominant species in the air of KSA, Kuwait, Qatar, Jordan and Egypt. In fact, *Ulocladium* emerged to be one of the five most prevalent fungi in the outdoor environment of Saudi Arabia [53]. *Helminthosporium* spp. and *Candida* spp. are also found in the Middle East and neighboring countries. A study in the region revealed high concentrations of *Ganoderma* basidiospores. High concentration levels were detected in a Saudi town called Jizan, close to the Red Sea with required humidity. The town appears to be in close proximity to the source areas (near Yemen border). Interestingly, Jizan has the highest level of asthma prevalence in children and it is possible that *Ganoderma* may be a causative factor. In addition, up to 17% of all basidiospores counted were identified as *Ganoderma* spp. while less than 1% *Ganoderma* spp. were identified at two non-coastal sites in Jizan [46].

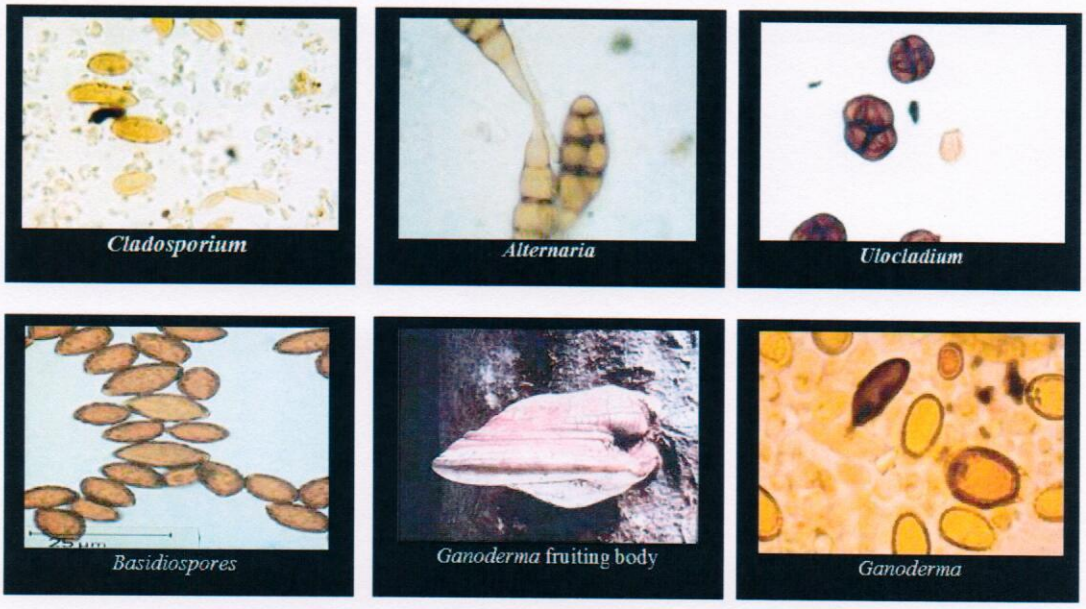

Fig. 4. Pictures showing different types of fungal spores

Table 2. Air-borne and allergenic trees and grass pollen grains

Pollen / Country	*Prosopis juliflora* (Mesquite)	*Populus deltoides* (Cotton wood)	*Phoenix dactylifera* (Date palm)	*Cynodon dactylon* (Bermuda grass)	Other trees	Other grasses	Misc. pollen
K.S.A	++ [13,14,17,18,32]	++ [14]	+ [17]	+ [13,14]	NA	++ [14]	+ [14,17]
Kuwait	++ [19,20,21,32]	NA	NA	++ [15,19,20,33]	NA	NA	+ [19,20,21]
Qatar	NA	NA	NA	NA	NA	NA	NA
Bahrain	NA	NA	NA	NA	+ [34]	+ [34]	NA
Oman	NA	NA	NA	+ [22]	NA	NA	NA
U.A.E	++ [23,32]	++ [23]	+ [23,35]	++ [23]	NA	++ [23]	++ [23]
Jordan	NA	NA	NA	NA	++ [24]	+ [24]	+ [24]
Turkey	++ [33]	NA	NA	NA	++ [25,28,36,37,38]	++++ [28,36,37]	++ [25,26,27,36,37,38]
Egypt	+ [39]	NA	NA	NA	NA	NA	NA
Iran	+ [29]	NA	NA	NA	++ [29,30,41,41]	++ [30,40,41]	++ [30,42]
Lebanon	NA	NA	NA	+ [43]	NA	NA	+ [31,43]
Morocco	NA	NA	NA	NA	NA	+ [44]	+ [44,45]

 # NA: No available data, Miscellaneous pollen: Acacia, Olea europea, Pinus strobus, Platanus occidentalis, Cupressus arizonica, Lolium multiflorum

Table 3. Air-borne and allergenic fungal allergens

Fungi / Country	*Alternaria*	*Aspergillus*	*Cladosporium*	*Penicillium*	*Ulocladium*	Misc. fungi
K.S.A	++ [14,17,18,54,55]	+ [55]	+ [17,18,48,55]	+ [55]	+ [17,18,55]	+ [17,46,47,53,55]$^{\eta}$
Kuwait	+ [33,49,56]	+ [33,49]	+ [33,49,56]	+ [33,49]	+ [56]	+ [19,20,33,49,56]
Qatar	+ [57$^{\$}$]	+ [57]	++ [57^^]	+ [57$^{\xi}$]	+ [57]	NA
Bahrain	NA	NA	NA	NA	NA	+ [34]
Oman	+ [22]	+ [22]	NA	+ [22]	NA	NA
U.A.E	NA	+ [58]	NA	NA	NA	NA
Jordan	+ [59]	+ [59]	+ [59]	+ [59]	+ [59]	+ [59]
Turkey	+ [50,60]	+ [50]	++ [50,60]	+ [50]	NA	+ [60]
Egypt	+ [51$^{\$}$,61$^{\$}$,62]	++ [51,62,63]	+ [51,61^,62,63]	+ [61$^{\xi}$,62]	+ [51˜,61˜]	+ [62,63]
Iran	++ [41,64]	++ [41,64,65]	++ [41,64,65]	++ [41,64,65]	NA	+ [40]
Lebanon	NA	NA	NA	NA	NA	NA
Morocco	NA	NA	NA	+ [66]	NA	NA

 # NA: No available data

Miscellaneous fungi: Candida spp. [33], Helminthosporium spp. [33], molds [19,20,34,36]

$^{\$}$Alternaria alternata
$^{\eta}$Basidiospores
$^{\xi}$Penicillium chrysogenum
^Cladosporium cladosporoides
^^Cladosporium sphaerospermum
˜Ulocladium tuberculatum

2.3 Indoor Allergens in the Middle-East

Table 4 list the indoor allergens published in the region. As it is known House Dust Mites (HDM) are a common cause of asthma and allergic symptoms. Two species of House Dust Mites; *Dermatophagoides pteronyssinus* (*Der p*1) and *Dermatophagoides farinae* (*Der f*1), are prevalent in the region. In addition, *Periplaneta Americana* (American cockroach, per a 1), *Blattella germanica* (German cockroach, *Bla g* 1) as well as Felis domesticus (Cat salivary allergens, *Fel d* 1) are also present in some of the countries in the region. However, the prevalence of *Blomia tropicalis* and *Blattella orientalis,* which are known to be prevalent in the temperate region, has not been investigated at all (Table 4).

It is evident from our data that the two clinically important HDM species, *Dermatophagoides pteronyssinus* (*Der p* 1) and *Dermatophagoides farinae* (*Der f* 1) are present with regional diversity in Saudi homes in levels exceeding threshold values for sensitization and for acute attacks of bronchial asthma. SPT results of 462 patients tested with *D. pteronyssinus* and *D. farinae* show that up to 25.1% and 19.1% positive reactions were obtained by *D. pteronyssinus* and *D. farinae* respectively in asthmatic children in the mountainous region, while 56.3% positive reactions were obtained by *D. farinae* in coastal areas. In agricultural and dry regions, the figures were 7.6% and 12.6% respectively for *D. pteronyssinus* and *D. farinae*. However, 31% positive reactions to HDM reveal sensitization of individuals (or those already sensitized) in the dry region (Riyadh) as well [67].

The *Dermatophagoides* (*Der p* 1 & *Der f* 1) are the most common HDM in Iran as shown in Table 4, followed by Saudi Arabia, Kuwait, Qatar, Morocco, Bahrain, Turkey and UAE. Besides that, *Periplaneta americana* (*Per a* 1) and *Blattella germanica* (*Bla g* 1) are also amongst the common allergens in Kuwait with low rate in Saudi Arabia and Iran. *Felis domesticus* (*Fel d* 1) was also reported to be allergic in Saudi Arabia followed by Kuwait, Bahrain and UAE. On the other hand, *Blomia tropicalis* (*Blo t*) and *Blattella orientalis* (*Bla o*) were not reported in any of these countries or no studies have been carried out yet.

Fig. 5. Picture displaying the three types of cockroaches: *Periplaneta americana, Blattella germanica, Blattella orientalis*

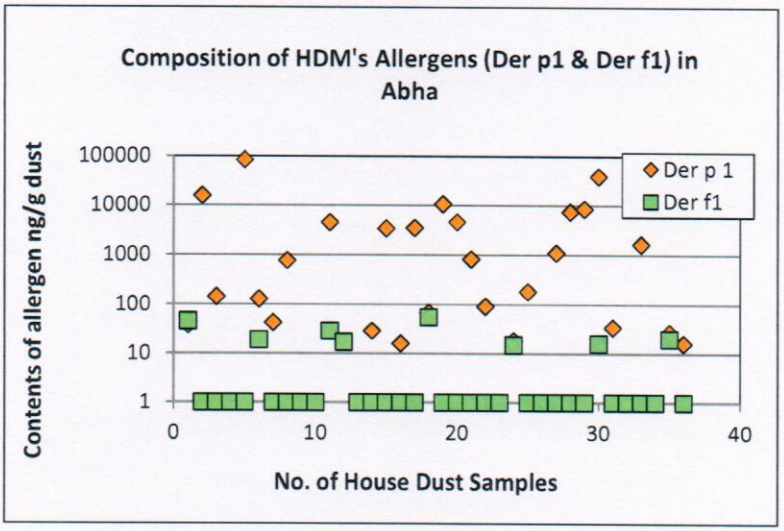

Fig. 6. A graph showing distribution of HDMs (*Der p*1 & *Der f*1) in Abha (Mountainous region), Saudi Arabia

(Adapted from AlFrayh et al. [67])

Most of the information available in the publications of the region regarding the prevalence description or pattern of indoor and outdoor allergens are based on *in vivo* or *in vitro* diagnostic studies and none of these have conducted studies involving visual or immunochemical characterization of either the House Dust Mites, *Bla g* (1,2), *Per a* 1, *Fel d*, etc. Therefore, the graph in Fig. 6 is one of the rarest examples of data generated in this part of the world. It shows that there is a variation even in the levels of *Der p*1 & *Der f*1 in the region of Abha in Saudi Arabia.

3. DISCUSSION AND CONCLUSION

The current review presents data from published work including authors own work from the Middle-East region. The data presents inhalant allergens particularly outdoor allergens including pollen and fungal spores as well as indoor allergens including HDMs, cockroach and cat allergens. However, there are many other fragments and irritating factors present in both indoor and outdoor environment which were not taken into consideration in this communication. The presented data are the ones or likely to be the ones that most physicians and allergist include in the diagnostic skin test panel and advices patient to take, if possible, preventive or precautionary measures.

It can clearly be seen that there is a lack of data in many countries of the region and those countries are using some of the allergens for both diagnosis and treatment on the pretext of the allergens availability in the other part of the world. This situation needs to be changed and data needs to be obtained by investigation and research for the benefit of the patients.

Table 4. Air-borne and allergenic indoor allergens

	Der p* 1 & *Der f* 1** ***Dermatophagoides **(House dust mite)**	***Per a* 1** ***Periplaneta americana*** **(American cockroach)**	***Bla g* 1** ***Blattella germanica*** **(German cockroach)**	***Fel d* 1** ***Felis domesticus*** **(Cat)**	***Blo t*** ***Blomia tropicalis*** **(House dust mite)**	***Bla o*** ***Blattella orientalis*** **(Oriental cockroach)**
K.S.A	++ [14*^,18,67*^,]	+ [14]	+ [14]	++ [14]	NA	NA
Kuwait	++ [15*,19,33,68*]	++ [15]	++ [15,19,68]	+ [68,69]	NA	NA
Qatar	++ [70*^]	NA	+ [70]	NA	NA	NA
Bahrain	+ [34]	NA	NA	+ [34]	NA	NA
Oman	+ [22]	NA	NA	NA	NA	NA
U.A.E	+ [23,71]	+ [23]	+ [23]	NA	NA	NA
Jordan	NA	NA	NA	NA	NA	NA
Turkey	+ [36]	+ [36]	+ [36]	NA	NA	NA
Egypt	+ [71]	NA	NA	NA	NA	NA
Iran	+++ [29*^,30,40,41,42*^,72]	+ [29,30]	+ [29,30]	NA	NA	NA
Lebanon	+++ [43*^]	NA	NA	NA	NA	NA
Morocco	++ [44]	NA	NA	NA	NA	NA

*# NA: No available data, *Dermatophagoides pteronyssinus (Der p 1), ^Dermatophagoides farinae (Der f 1)*

One of the important points to be noted is that most countries used different allergenic extracts to test their patients without background knowledge of prevalent inhalants and/or aeroallergens in respective countries. One of the reasons, probably, is the lack of information of allergenic profiles which is evident from the tables presented in this review. e.g. most of the countries have information on the prevalence but there is no allergen ever reported or published.

Our survey showed that the most common allergens were outdoor allergens: pollen grains (e.g. *Amaranthus, Chenopodium, Salsola*, etc) and indoor allergens: House Dust Mites and fungal spores (e.g. *Alternaria, Aspergillus, Cladosporium, Penicillium*, etc). The distribution of these aeroallergens is also different among the different countries depending on the climate and environment factors as well. An additional importance of Aspergillus is their role in allergic fungal sinusitis among patients with nasal polyps [73].

The diagnosis or cross-reactivities are not always obtained, therefore, local species has to be included but most of the studies do not specify the species that they obtained and this can cause a problem in choice and selection of allergenic extract which may be different in the country.

Allergens are highly heterogeneous in nature and different species are more prominent in one region than the others. Knowledge of indigenous allergens should be provided to the patient by advertising in radios and televisions. It is very important to create awareness in general public on various allergens that are prevalent in their region and the season for the pollination so as to be able to take preventive measures like avoiding contact with the outdoor allergens by staying indoors at peak pollination season and trying to eliminate all indoor allergens.

Therefore, it necessitates further studies on the subject in the region using a standardized protocol and physician diagnosis with standard diagnostic criteria for a better understanding of the disease. This will not only help health care providers to provide appropriate care and treatment but will also help the ministries and government department to plan and execute their health strategies to minimize, reduce and/or educate their suffering population, reducing billions of dollars currently provided by the government.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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