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REVIEW PAPER

# A meta-analysis of sensitization to the most common aeroallergens in a Middle Eastern region: an overview of the main molecular allergens

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**Abstract** The prevalence of sensitization to aeroallergens in communities is incomprehensible. We aimed to assess the prevalence of sensitization to common aeroallergens according to the reliable studies performed in different cities of Iran. Literature review was performed by the inclusion of data sources such as PubMed, Web of Science, Google Scholar, ProQuest, Scopus, Iran Medex, and Magiran. All studies determining the prevalence of indoor and outdoor common aeroallergens were included in this review. STATA 14 and metaprop command were used for meta-analysis of data. Random pooled estimate (ES) (pooled prevalence), 95% confidence interval (95% CI), and *p* value were calculated. Forty-two reliable studies were included in this study. The random pooled estimate (ES) (pooled prevalence) of positive family history of allergy and positive specific IgE (in vivo tests and/or in vitro) to at least one allergen was 69% (95% CI 64–74%) and 74% (95% CI 66–81%), respectively. The pooled prevalence for weeds, trees, and grasses as outdoor allergens was 57% (95% CI 46–68%), 43% (95% CI 33–52%), and 41% (95% CI 32–50%), respectively. *Salsola kali* (*S. kali*) and *Cynodon dactylon* were the most prevalent weeds and grass allergens being found in 56% (95% CI 45–66%) and 40% (95% CI 29–52%) of sensitized patients, respectively. Meta-analysis of indoor allergens revealed that 27% (95% CI 14–43%), 38% (95% CI 21–57%), 21% (95% CI 16–26%), and 16% (95% CI 10–24%) of allergic patients were sensitized to mold, house dust mite (HDM), cockroach, and cat allergens, respectively. The results of the current meta-analysis revealed that *S. kali* is the most common aeroallergens in southwestern and northeastern areas as well as the capital city (Tehran) of Iran, while allergic patients living in northern and southern coastal areas of Iran were more prone to suffer from HDM sensitization.

**Keywords** Allergen · Iran · Systematic review · Prevalence · IgE-mediated hypersensitivity

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## 1 Introduction

The term "allergy" was primarily applied by von Pirquet in 1906 for a description of harmful immune reactions for the host (Turk 1987). Allergenic sources that induce immunoglobulin E (IgE)-mediated diseases have been widely discovered through more than a century of experiments (Mari 2008). Allergic disorders have become a common health problem generating various socioeconomic problems (Pawankar 2014). There is a wide body of evidence to show the increase in the prevalence of allergic disorders especially in the young population of industrialized countries, representing a considerable burden to both healthcare systems and the society (Wang et al. 2016; Jousilahti et al. 2016; Anandan et al. 2009, 2010).

Global warming and changes in the level of precipitation and humidness as metrological changes could be stemmed from climate change which is developed as the result of raising the concentration of carbon dioxide (CO2) and other greenhouse gases such as ozone (Reid and Gamble 2009). These transformations can affect the plant's growth, production, distribution, the allergenicity of aeroallergens, and pollination time (Barnes 2018; Reid and Gamble 2009; Shahali et al. 2009c). A literature review revealed that increasing plants' growth is related to the rise in CO2 level as a nutrient for plants (Barnes 2018). Pollutants in ambient air independently or as adjuvant for inhalant allergens can also develop or worsen allergic diseases (D'Amato et al. 2016). For example, the entrance of pollen allergens to lower respiratory airway could be facilitated by air pollutants such as diesel exhaust particles (Reinmuth-Selzle et al. 2017).

Nasal and respiratory allergies could be developed as the result of sensitization to various outdoor and indoor aeroallergens such as pollens, molds, house dust mites, and animal dander (Mims and Biddy 2013; Bousquet et al. 2008). More than 20% of the world's population is affected by an IgE-mediated allergic disease (Prevention of Allergy and Allergic Asthma. Geneva: World Health Organization). It has been demonstrated that the prevalence of atopic diseases is increasing, predominantly in industrialized countries and among the pediatric population (von Ehrenstein et al. 2002). Recent investigations revealed that the prevalence of allergic diseases was found to be 36% in the capital of Iran (Tehran) (Shokouhi Shoormasti et al. 2018b), while the prevalence of asthma in Iranian adults was found to be 8.9% in a national survey (Fazlollahi et al. 2018). Regarding the gene–environment interplays for development of allergic diseases, environmental and lifestyle factors such as increased hygiene level and consequently lower exposure to pathogens, prenatal or early-life exposures, smoking status, traffic pollutants, living place, delivery type, food diet, vaccinations, the rate of acetaminophen and antibiotics consumption, immigration, and cultural factors are among the possible causes for the differences in the prevalence of allergic diseases among countries and even cities of a country (von Ehrenstein et al. 2002; Stenius et al. 2011; Garn and Renz 2007; Cabieses et al. 2014; Tham et al. 2019; Fazlollahi et al. 2017).

There are several allergy diagnostic tests that are usually applied as complementary modalities to the medical history and physical examination. IgE-mediated sensitization to aeroallergens is evaluated by prick/puncture skin testing and serum tests for specific IgE (sIgE) evaluation (Bernstein et al. 2008). Skin prick test (SPT) is used as an economical and minimally invasive modality the results of which are instantly accessible, especially when performed by trained specialists. This technique has been applied as a principal diagnostic approach by Helmtraud Ebruster since 1959 (Heinzerling et al. 2013). Radioallergosorbent test (RAST) was first introduced in 1967, resulting in a considerable development in sIgE assay technologies (Hamilton and Franklin Adkinson 2004). Other currently available commercial sIgE technologies include Hitachi VLA (multiple allergen solvent tests: MAST), CAP system, Hycor Turbo-MP, Ala Stat, HyTec E/A, ImmunoCAP systems, and Immulite 2000 (Kontis and Nayak 2008; Park et al. 2018). SPT and sIgE measurement are usually applied interchangeably in both clinical settings and research goals (Chauveau et al. 2017).

Beside conventional techniques, purification and production of natural and recombinant allergenic molecules have opened up a new way to detect major and cross-reactive allergens (Matricardi et al. 2016). ISAC ImmunoCAP and FABER test (Alessandri et al. 2017) (www.allergome.org) are multiplex methods for IgE detection playing an important role in identifying primary allergenic molecules, determining cross-reactivity phenomenon as well as immunotherapy purposes (Matricardi et al. 2016).

Allergen avoidance, pharmacotherapy, and immunotherapy in selected cases are the three general strategies for the management of allergic diseases (Holgate and Polosa 2008). Environmental control strategies may not be applicable if the prevalence of different allergens in different regions of a country is not determined.

In the current analysis, we present the estimates of the prevalence of the most common indoor and outdoor aeroallergens in Iranian adults and children by meta-analysis of reliable studies performed in different provinces and capital cities (including Tehran, Karaj, Ahvaz, Mashhad, Kerman, Sari, Tabriz, Sistan-Baluchestan, Isfahan, Shiraz, Zanjan, Ghazvin, Yazd, Yasooj, Semnan, Bushehr) of Iran. The most important molecular components of these aeroallergens were discussed in this review as well.

## 2 Methods

### 2.1 Geographical attributes

Iran is situated in an exclusive geographical location with four ecological regions and four discrete seasons, possessing a unique flora with approximately 8000 plant species that grow in mountains, temperate, semidry, and dry parts (Heshmati 2012; Environment; Ghahraman 1975). According to the Fourth National Report to the Convention on Biological Diversity, forests cover more than one-tenth of the country all over different geographical regions (Environment Department 2010). Outdoor and indoor aeroallergens and their sources used in this study are listed in "Appendix".

### 2.2 Protocol and registration

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were followed in this work (Liberati et al. 2009; Stroup et al. 2000). The protocol of this systematic review was approved by the Research committee and Ethics committee of Immunology, Asthma, and Allergy Research Institute and approved and registered by Tehran University of Medical Sciences (No: 31266).

### 2.3 Information sources and literature search

Relevant databases including PubMed, Web of Science, Google Scholar, ProQuest, Scopus, Iran Medex, and Magiran were searched up to August 2017. The searches were not limited by language, and both English and Persian sources were explored. The following keywords were identified in searching databases: allergen, common, aeroallergen, Iran, prevalence, sensitization, and sIgE. Two reviewers searched the databases and screened all the full-text articles (original articles, brief communications, and letter to the editor) and abstracts independently. The studies that determine the common aeroallergens were included in this systematic review. In order to increase the sensitivity, reference lists of relevant articles were also assessed to identify additional articles not recognized in the database searches. The participants included in the studies were both pediatrics and adults. The derived studies assessed the common allergens in subjects with allergic diseases including asthma, allergic rhinitis, and atopic dermatitis.

The evaluation form of articles was used to select the appropriate articles. Data extraction form was utilized to extract the data of articles. Finally, the articles were evaluated by the expert committee. Any controversy was discussed by the expert committee (Fig. 1).

### 2.4 Data collection

To extract the related data from the derived studies, an Excel data sheet was utilized. The collected variables were as follows: study design, sample size, date of the study, the age range of participants, sex of participants, diagnostic method (in vivo or in vitro), region of study, family history of allergic diseases, type of allergic diseases, the percent of sensitization to at least one positive allergen, and common allergens.

To evaluate the quality of the included studies, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) was used (von Elm et al. 2007). This quality assessment checklist includes 22 items.

### 2.5 Statistical analysis

STATA 14 (StataCorp, College Station, TX) and metaprop command were used for meta-analysis of

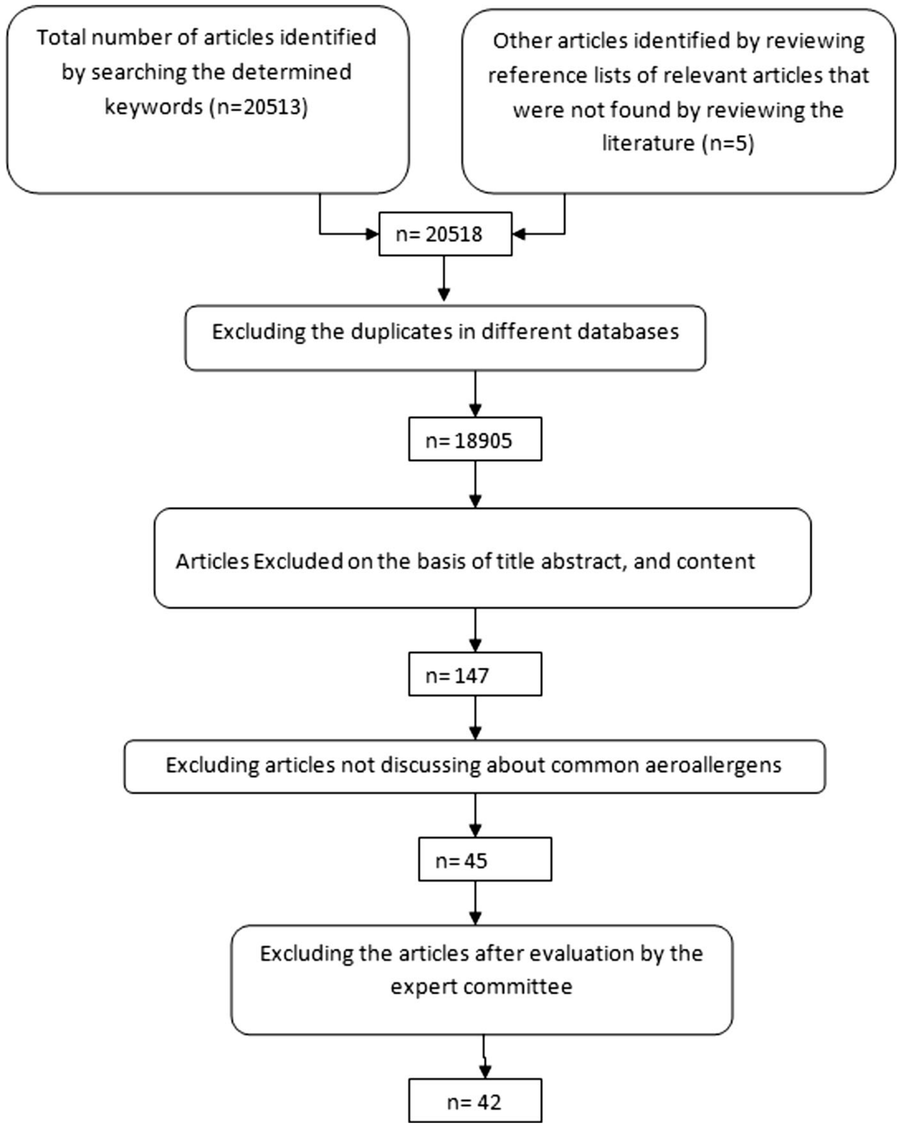


**Fig. 1** Flow diagram of literature review and selecting studies for systematic review and meta-analysis

data. To combine the results of various studies as well as consider the heterogeneity, the logistic-normal random-effects model with Freeman–Tukey double arcsine transformation was used. In case of detecting more than 75% heterogeneity, a random-effects model was used. Random pooled estimate (ES) (pooled prevalence), 95% confidence interval (95% CI), and p-value were calculated. For evaluating the effect of covariates (sex and age group), meta-regression method was used. Additionally, the forest plot was drawn for each variable.

## 3 Results and discussion

Forty-two reliable studies were included in this study (Table 1). In the studies performed in different cities of Iran, sensitization to approximately 58 plant species including 15 weeds species from eight families, 14 grass species from one family, and 28 trees species from 16 families was evaluated ("Appendix"). The prevalence of the most common aeroallergens in different cities of each province is depicted in Fig. 2. The result of our meta-analysis revealed that 69% (95% CI 64–74%) of allergic individuals had a positive family history of allergy (Fig. 3). Besides

**Table 1** List of included studies in different cities and their applied tests

| Column | Study (references) | Year | City | Type of allergic tests | No. of subjects |
|---|---|---|---|---|---|
| 1 | Movahedi et al. (2000) | 2000 | Tehran and Karaj | SPT | 400 |
| 2 | Hedayat and Rezaei (2000) | 2000 | Isfahan | SPT | 1077 |
| 3 | Farhoudi et al. (2003) | 2003 | Tehran and Karaj | SPT | 100 |
| 4 | Khazaei et al. (2003) | 2003 | Sistan and Balouchestan | SPT | 1286 |
| 5 | Kashef et al. (2003) | 2003 | Shiraz | SPT | 212 |
| 6 | Mesdaghi et al. (2005) | 2005 | Tehran | SPT | 116 |
| 7 | Farhoudi et al. (2005) | 2005 | Karaj | SPT | 226 |
| 8 | Hedayati et al. (2006) | 2006 | Sari | SPT | 84 |
| 9 | Fazlollahi et al. (2007) | 2007 | Tehran | SPT | 250 |
| 10 | Ahmadiafshar et al. (2008) | 2008 | Zanjan | SPT | 200 |
| 11 | Mohammadi et al. (2008) | 2008 | Tehran | SPT | 206 |
| 12 | Fereidouni et al. (2009) | 2009 | Mashhad | SPT | 306 |
| 13 | Nabavi et al. (2009) | 2009 | Semnan | SPT | 300 |
| 14 | Arshi et al. (2010) | 2010 | Tehran | SPT | 245 |
| 15 | Ghaffari et al. (2010) | 2010 | Sari | SPT | 375 |
| 16 | Behmanesh et al. (2010) | 2010 | Mashhad | SPT | 133 |
| 17 | Moghtaderi et al. (2010) | 2010 | Shiraz | SPT | 230 |
| 18 | Hodjati et al. (2010) | 2010 | Tabriz | RAST | 101 |
| 19 | Amirmajdi et al. (2011) | 2011 | Mashhad | SPT | 58 |
| 20 | Nabavi et al. (2011) | 2011 | Semnan | SPT | 220 |
| 21 | Bemanian et al. (2012) | 2012 | Yazd | SPT | 95 |
| 22 | Shakurnia et al. (2013) | 2013 | Ahvaz | SPT | 407 |
| 23 | Assarehzadegan et al. (2013b) | 2013 | Ahvaz | SPT | 299 |
| 24 | Mahram et al. (2013) | 2013 | Ghazvin | SPT | 163 |
| 25 | Assarehzadegan et al. (2013a) | 2013 | Ahvaz | SPT | 111 |
| 26 | Ahanchian et al. (2013) | 2013 | Mashhad | SPT | 207 |
| 27 | Nabavizadeh et al. (2013) | 2013 | Yasooj | SPT | 184 |
| 28 | Teifoori et al. (2013) | 2013 | Tehran | ImmunoCAP | 202 |
| 29 | Bonyadi et al. (2014) | 2013 | Tabriz | SPT | 90 |
| 30 | Shakurnia et al. (2014) | 2014 | Ahvaz | SPT | 111 |
| 31 | Farrokhi et al. (2014) | 2014 | Bushehr | SPT | 91 |
| 32 | Bakhshaee et al. (2014) | 2014 | Mashhad | SPT | 100 |
| 33 | Fouladseresht et al. (2014) | 2014 | Kerman | SPT | 157 |
| 34 | Hosseini et al. (2014) | 2014 | Tehran | SPT | 313 |
| 35 | Teifoori et al. (2014) | 2014 | Tehran | ImmunoCAP | 202 |
| 36 | Moghtaderi et al. (2015) | 2015 | Shiraz | SPT | 656 |
| 37 | Farrokhi et al. (2015) | 2015 | Bushehr | SPT | 567 |
| 38 | Pazoki et al. (2015) | 2015 | Tehran | SPT | 165 |
| 39 | Zare Marzooni et al. (2016) | 2016 | Khuzestan | SPT | 150 |
| 40 | Mahboubi Oskouei et al. (2017) | 2017 | Mashhad | SPT | 1006 |
| 41 | Shokouhi Shoormasti et al. (2017) | 2017 | Tehran | RIDA | 602 |
| 42 | Shokouhi Shoormasti et al. (2018a) | 2018 | Tehran | RIDA qline | 604 |

*SPT* skin prick test, *RAST* radioallergosorbent test, *RIDA* or *RIDA qline* immunoblotting test


**Fig. 2** Distribution of the most common aeroallergens in different cities of each province in Iran. Iran map of Köppen climate classification was applied and merged with the classic map of Iran. *Dermatophagoides Pteronyssinus* (D.P), *Dermatophagoides Farinae* (D.F), *Alternaria Alternata* (*A. Alternata*), House dust mite (HDM), *Salsola Kali* (*S. Kali*), *Amaranthus palmeri* (*A. Palmeri*), *Amaranthus Retroflexus* (*A. Retroflexus*), *Chenopodium album* (*C. album*)

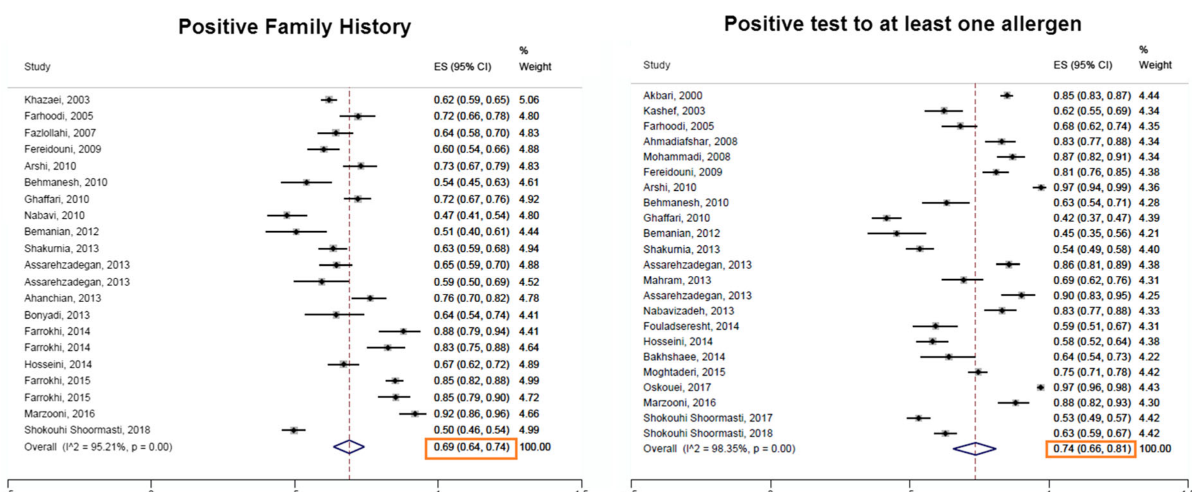


**Fig. 3** The pooled prevalence of positive family history of allergy and sensitization to at least one allergen among studies performed in different cities of Iran (forest plot)

environmental factors, other criteria such as genetic predisposition may affect the susceptibility of individuals in acquiring allergic symptoms (Ober and Yao 2011). Previous studies have shown a significant relationship between a positive family history of allergy and development of asthma in both childhood and older individuals (Vazquez Nava et al. 2006; Paaso et al. 2014), while such association was not found in the study of Rhodes et al. (2001). The results indicated that the pooled prevalence of sensitization to at least one allergen was 74% (95% CI 66–81%) (Fig. 3). This prevalence is higher than the findings of other studies (Newson et al. 2014; Salo et al. 2014). According to some studies, allergic sensitization could be considered as a predictor factor for some allergic diseases, especially allergic rhinitis and allergic conjunctivitis (Shokouhi Shoormasti et al. 2018a; Warm et al. 2015). Heterogeneity between different studies regarding common aeroallergens in each region could originate from variations in geographical condition, plant coverage, climate change, exposure rate to allergens, ethnicity, different methodology, study population, applied techniques (in vivo or in vitro tests), and lifestyle in each area (Anastassakis et al. 2010; Arbes et al. 2005; Assarehzadegan et al. 2013b; Kang et al. 2017). Nevertheless, assessing allergic sensitization in different communities in defined intervals and discovering the respective panel of inhalant allergens could be practical. The results of the current meta-analysis revealed that *S. kali* was found to be the most common aeroallergens in southwestern and northeastern areas and the capital of Iran. Individuals living in northern and southern coastal areas were more prone to be affected by mite sensitization (Fig. 2).

The meta-analysis results of most common indoor and outdoor aeroallergens of Iran and their allergenic molecules are reported and discussed in the below-mentioned sections.

## 3.1 Outdoor allergens

### *3.1.1 Weeds*

The ability of weeds to thrive in regions with low precipitation and high temperature has made it as one of the most common plants and accordingly aeroallergens in the Middle East (Hasnain et al. 2016). The results of this meta-analysis revealed that the pooled prevalence of sensitization to weeds was 57% (95% CI 46–68%) among different cities of Iran (Fig. 4). As reported by Hasnain et al. (2016), weeds such as *Amaranthus*, *Chenopodium*, and *Salsola* are considered among the common allergenic pollens in the Middle East. In some countries from other continents such as the USA, other types of weeds may cause allergic reactions in susceptible individuals, especially species of *Ambrosia* or Ragweed (Arbes et al. 2005; Salo et al. 2014). According to the study of Heinzerling et al. (2009), *Artemisia* (16.8%) and *Ambrosia* (14.1%) were the most prevalent allergenic weeds in Europe. The respective sex-based pooled prevalence of weeds sensitivity was 40% (95% CI 22–60%) and 37% (95% CI 20–55%) in males and females, respectively, with no significant difference among genders. Salo et al. (2014) revealed higher IgE sensitization to inhalant allergens in males. Additionally, age-related pooled prevalence revealed higher prevalence of weeds sensitization for adults [65% (95% CI = 48–80%) rather than for children [46%, 95% CI (32–59%)] ($p = 0.07$). Similar to this meta-analysis, Larenas-Linnemann et al. (2014) showed higher IgE reactivity to weeds in adults compared with children.

### *3.1.2 Salsola kali (Russian thistle, saltwort)*

*S. kali* is a tumbleweed plant of salty soils in low-rainfall areas. It also grows in arid and semiarid areas as well as grasslands and pollinates in summer and fall and is one of the most representative pollens from the Amaranthaceae family regarding the allergenic characteristics (Gadermaier et al. 2014; FEIS). As the results of this meta-analysis depicted, the total prevalence of sensitization to *S. Kali* was 56% (95% CI 45–66%) and was the most common aeroallergen (Fig. 5). As the results of the sex-related meta-analysis showed, a similar prevalence of *S. kali* was observed in men and women (59% vs. 55%). Regarding the findings of previous studies, sensitization to this pollen has the first rank among patients with pollen allergy in Iran (Assarehzadegan et al. 2009). *S. Kali* pollen has been known as one of the main inhalant allergens in Northern Hemisphere, Australia (Pablos et al. 2016), western US (Salo et al. 2014), and Middle Eastern semiarid countries such as Iran (Assarehzadegan et al. 2009; Villalba et al. 2014). Regarding the fact that *Salsola Kali* mainly grows in salty soils, arid and semiarid areas as well as grasslands, and having in mind that a considerable region of Iran is located in

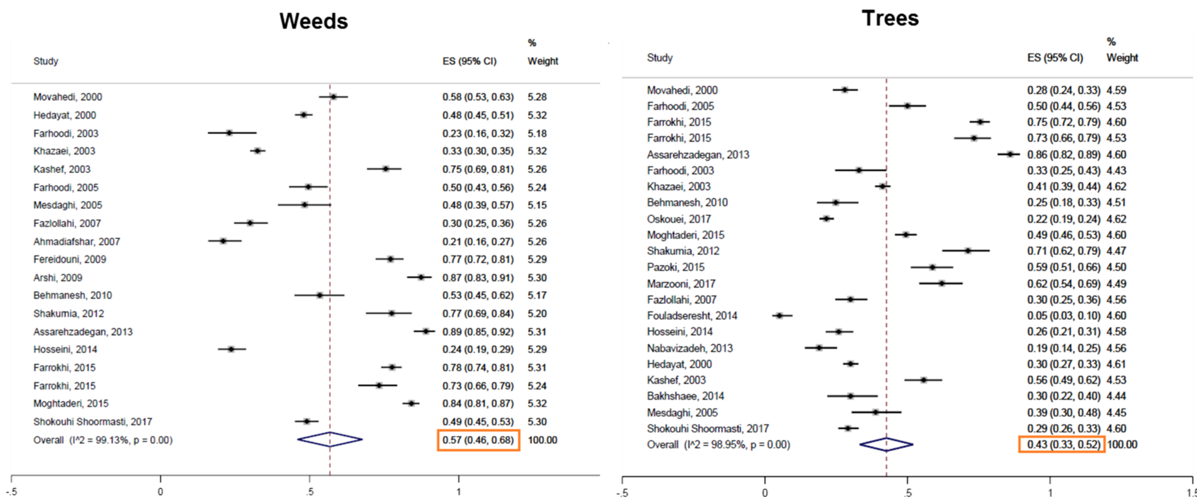


**Fig. 4** The pooled prevalence of weeds and trees sensitization among studies performed in different cities of Iran (forest plot)

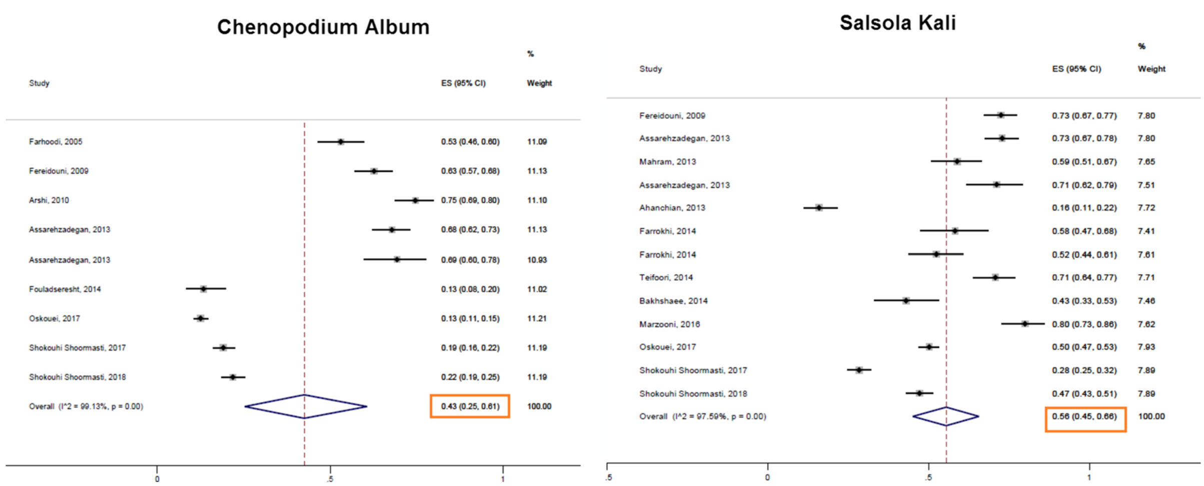


**Fig. 5** The pooled prevalence of *Chenopodium album* and *Salsola kali* sensitization among studies performed in different cities of Iran (forest plot)

arid and semiarid areas, the high prevalence of *Salsola kali* may be logical (FEIS; Gadermaier et al. 2014; Heshmati 2012).

Sal k 1, Sal k 2, and Sal k 3 are the three main described allergens of *S. Kali* (Villalba et al. 2014) (www.allergome.org). Two allergenic molecules (42.0 and 39.0 kDa) were first described by Shafiee et al. (1981) that were subsequently named Sal k 1 and Sal k2 as major allergens of the *S. kali* pollen. Sal k1 is a pectin methylesterase with a high polymorphism which is believed to be an allergenic marker to differentiate allergenicity to Chenopodiaceae pollen (Barderas et al. 2007). Sal k 3 was first identified by Assarehzadegan et al. (2011) as an important allergenic component in *S. kali* pollen with a noticeable sIgE level in approximately 67% of patients with positive allergy to *S. Kali*. *S. kali* has several IgE-binding components, resulting in a high cross-reactivity (Sal k 4) with other pollen-derived profilins (Assarehzadegan et al. 2010). Lombardero et al. (1985) evaluated the cross-reactivity between Chenopodiaceae and Amaranthaceae family. Close cross-allergenicity was also detected between *S. kali* and *S. incanescens* (Assarehzadegan et al. 2009). In a recent study, a high cross-reactivity was presented between *S. kali* and *S. imbricata* in ELISA inhibition (Al-Ahmad et al. 2017). Similar isoelectric points were described in proteins with molecular weight of 40, 60, and 75 kDa that may be the possible cause of cross-reactivity between *S. kali* and *S. imbricate* (Al-Ahmad et al. 2017). The results of another study performed in allergic patients from Saudi Arabia, the United Arab Emirates, and Sudan revealed that *S. imbricate* had the second-rank sensitization among local allergens (Hasnain et al. 2012). Similarly, *S. imbricate* from the Amaranthaceae family has been introduced as one of the *salsola* species in Pakistan with a high rate of sensitization for the Amaranthaceae family (Perveen et al. 2015). Reports from neighboring countries with a high rate of sensitization to *C. imbricate* suggest that high prevalence of allergenicity to *S. kali*, especially in a southern area that is abutting with previously mentioned countries, may be due to cross-reactivity of these pollens (Hasnain et al. 2012; Al-Ahmad et al. 2017).

#### *3.1.3 Amaranthus retroflexus (Rough/Redroot Pigweed)*

*Amaranthus retroflexus* (*A. retroflexus*) is a flowering and annual weed from the Amaranthaceae/Chenopodiaceae family and mainly grows in desert and semidesert areas, all over the world (Tehrani et al. 2010). The main blossoming period is from August to October that may cause severe allergic conditions in a considerable number of Iranian allergic patients (Assarehzadegan et al. 2013b; Tehrani et al. 2010; Fereidouni et al. 2009). Six components ranging from 10 to 85 kDa have been presented by immunochemical evaluations of the pollen extract *obtained from A. retroflexus* pollen (Tehrani et al. 2010). Ama r 2 was the first allergen from *A. retroflexus* which was introduced as a member of the profiling family (Tehrani et al. 2011). Ama r 1, which belongs to the Ole e 1-like protein family, was then established as the second allergen from *A. retroflexus* pollen (Morakabati et al. 2016).

#### *3.1.4 Chenopodium album (White Goosefoot, Fat hen, Lamb's quarter)*

The *Chenopodium* genus is cultivated worldwide either as pseudocereals or leafy vegetables, consisting of an approximate number of 150 species (Hong et al. 2017). *Chenopodium album (C. album)* is one of the important crops mostly planted in India with high nutritional characteristics as a rich source of vitamins and micronutrients (Bhargava et al. 2007). The pollination time of this pollen is from June to October (Villalba et al. 2014). According to our findings, the random pooled prevalence of this allergen sensitization was 43% (95% CI 25–61%) in Iran (Fig. 5). The minimum sensitization (13%) was found in the study of Fouladseresht et al. (2014) and Oskouei et al. (12.5%) (Mahboubi Oskouei et al. 2017), while the maximum sensitization (75%) belongs to the study of Arshi et al. (2010). This type of weeds showed somewhat high prevalence among weeds pollens. Similar to Iran, other countries such as Spain, western USA, Kuwait, and Saudi Arabia reported a high prevalence (Villalba et al. 2014). Che a 1 (17 kDa) which has a similar structure to the Ole e 1-like protein family is found as a major allergenic protein in sera of patients who are allergic to *C. album* pollen (Barderas et al. 2002). Barderas et al. introduced purified Che a 2 (profilin, 14 kDa) and Che a 3 (polcalcin, 10 kDa) with the respective prevalence of 55% and 46% in patients with *C. album* allergy. Moreover, a high cross-reactivity was found between these two allergens with olive pollen profilin (Ole e 2) and polcalcin (Ole e 3) (Barderas et al. 2004). Furthermore, *Salsola kali* and *C. album* showed a strong cross-reactivity that may be caused by Ole e 1-like molecules (Matricardi et al. 2016).

#### *3.1.5 Grasses*

Grass pollens are highly associated with different types of seasonal allergies and asthma (Jung et al. 2018). As depicted in Fig. 6, the respective random pooled ES of sensitization to grasses and Bermuda grass was 41% (95% CI 32–50%) and 40% (95% CI 29–52%), showing significant differences for all both variables ($p < 0.001$). Moreover, similar pooled prevalence of grass sensitization was found for males (32%) and females (30%). According to our results, adults [53%, 95% CI (36–70%)] showed higher prevalence of grass sensitization in comparison with children [33%, 95% CI (22–44%)] ($p = 0.06$). The higher prevalence of grass sensitization in adults was compatible with the study of Larenas-Linnemann et al. (2014). In the study of Salo et al. (2014), a higher prevalence of Bermuda grass sensitization was reported in the second to fourth decades of life. Patients with grass pollen allergy had IgE antibodies to carbohydrate determinants with an extensive cross-reactivity with vegetable, foods, animal, and insect venom (Aalberse et al. 1981; Popescu 2015). The

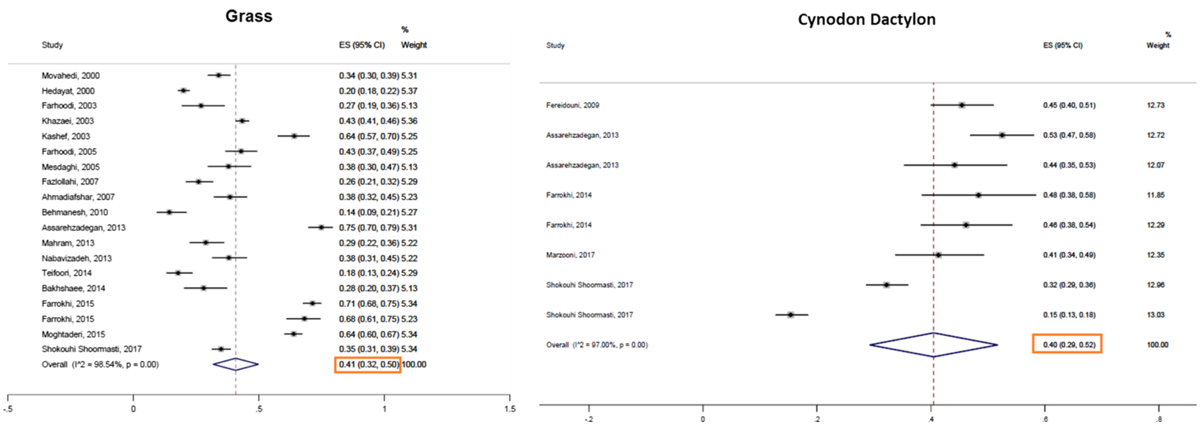


**Fig. 6** The pooled prevalence of sensitization to grasses and Bermuda grass (*Cynodon dactylon*) among studies performed in different cities of Iran (forest plot)

results of a multicenter study in Europe showed a high prevalence of grasses sensitization ranging from 19.5 to 69.9% (Heinzerling et al. 2009). According to the results of the National Health and Nutrition Examination Survey (NHANES) 2005–2006, grasses are the most common airborne sensitizers, especially in the western USA (Salo et al. 2014).

### 3.1.6 *Lolium perenne (Ryegrass)*

*Lolium perenne* is a cool-season perennial grass in the Pooideae subfamily with bunch-like growth habits the performance of which is limited in warmer and transition regions (Wang et al. 2017). A limited number of studies regarding sensitization to ryegrass make the meta-analysis impossible for this type of grass. However, *Lolium perenne* sensitization was reported in 22.2% to 41% of patients with allergic diseases (Shokouhi Shoormasti et al. 2017; Ahmadiafshar et al. 2008). Allergenic specificities of *Lolium perenne* were first described by Ekramoddoullah et al. (1982). Lol p 1(27 kDa), also known as a beta-expansion protein (www. allergen.org), is recognized by sIgE antibodies in more than 50% of patients sensitized for *Lolium perenne* (Griffith et al. 1991). However, Lol p 2 (11 kDa) is less common and its sIgE is found in approximately 50% of sensitized individuals (Freidhoff et al. 1987), while IgE antibodies against Lol p 3 (11 kDa) was detected in 26.2% of patients (Ansari et al. 1989). Lol p 4 (57 kDa) is a high molecular weight basic allergen (HMBA) causing immediate skin reactions in subjects with grass allergy the sIgE of which was found in all patients sera (Ekramoddoullah et al. 1983). Pooled sera of patients with grass pollen allergy were applied for recognition of Lol p 5 (31 kDa) (Singh et al. 1991). sIgE against Lol p 11 (16 kDa) was detected in sera of more than 65% of grass pollen-allergic patients (van Ree et al. 1995).

### 3.1.7 *Cynodon dactylon (Bermuda grass)*

*Cynodon dactylon* is one of the most widely planted grasses that belong to the Poaceae family in Chloridoideae subfamily (Huang et al. 2017), causing a number of respiratory allergies in warm weather (Orren and Dowdle 1977). The pooled prevalence of 40% (95% CI 29–52%) was estimated for Bermuda grass sensitization according to the results of the current analysis (Fig. 6). *Cynodon dactylon* has a multifaceted mixture of allergens; a few of them have been recognized. Cyn d 1 (32 kDa) is considered as the major allergen of *Cynodon dactylon* the sIgE of which was found in more than 96% of individuals allergic to *Cynodon dactylon* (Su et al. 2003; Chow et al. 2005). The sequential epitopes for human IgE and IgG4 isotypes of Cyn d 1 were recently mapped that may be worthwhile for further diagnostic and immunotherapy purposes (Yuan et al. 2012). The first crystal construction of this pollen allergen which was naturally extracted belongs to Cyn d 4 (Huang et al. 2012). IgE reactivity to Cyn d 7 (12 kDa) that is a calcium-binding protein was detected in 10% of allergic individuals (Smith et al. 1997). Cyn d 12 (14.5 kDa) which has profilin structure could be considered as the reason for 20% of the cross-reactivities among pollen and food allergens (Asturias et al. 1997). Cyn d 24 (21 kDa) was first identified by Chow et al. (2005) as a pathogenesis-related protein. Cyn d 15, Cyn d 22w, and Cyn d 23 are other recognized allergens of Cynodon dactylon (www.allergen.org).

#### 3.1.8 Phleum pratense (Timothy grass)

*Phleum pratense* as a wide climate range grass is naturally grown in Europe, Asia, and North Africa (Matricardi et al. 2016). Phl p 1 (27 kDa) is one of the major allergens of *Phleum pretense* that is recognized by about 95% of patients who are grass pollen allergic (Valenta et al. 1992). Recombinant Phl p 2 (10–12 kDa), Phl p 4 (55 kDa), Phl p 5 (32 kDa), and Phl p 6 (11 kDa) have also high allergenicity characteristics and are recognized by 65% to 95% of pollen-allergic patients (www.allergen.org) (Valenta et al. 1992; Vrtala et al. 1999). Other allergens with less allergenic features include Phl p 7 (6 kDa) and Phl p 11 (20 kDa) that are distinguished by 10% and 32% of pollen-allergic patients, respectively (Niederberger et al. 1999; Marknell DeWitt et al. 2002). Phl p 12 (14 kDa) is an actin-binding protein (profilin) that could be the cause of developing cross-reactive reactions in about 20% of patients with pollen and food allergy (Sanchez-Salguero 2014; Matricardi et al. 2016). Phl p 13 (55 kDa) is a high molecular allergen with different mass components compared to Phl p 4 (Suck et al. 2000).

#### 3.1.9 Fescuta Pratensis (Meadow fescue)

*Festuca* genus includes about 450 species. Annuals (Vulpia) and perennials (Eufestuca) are two important subgroups of Fescue grasses (Weber 2014). This pollen consists of different molecules such as Fes p1, 4, 5, and 13 (www.allergome.org).

#### 3.1.10 Trees

Inhaling of fine and powdery tree pollens could induce allergic reactions, especially allergic rhinitis and asthma (Asam et al. 2015; Mansouritorghabeh et al. 2017). Random pooled ES for sensitization to tree allergens was 43% (95% CI 33–52%) with a significant difference between studies ($p < 0.001$) (Fig. 4). A literature review by Mansouritorghabeh et al. (2017) revealed that sycamore (plane tree) was the most common tree pollens in Iran, while palm, mesquite, and olive tree were reported as the most common allergenic trees in other Middle Eastern countries. Evaluation of 371 allergic patients in the surrounding New York between 1993 and 2000 revealed that oak, birch, and maple pollens were the most prevalent tree allergens, while beech, hickory, ash, elm, and poplar pollens were the least allergenic tree pollens (Lin et al. 2002). According to Heizerling et al. (2009), the most common tree sensitizers in Europe were, in turn, birch (24.2%), hazelnut (22.8%), and alder (21.2%). The results of our age-related meta-analysis indicated a lower prevalence of tree sensitization in children [44%, (95% CI 32–58%)] compared with adults [61%, (95% CI 38–82%)] that was found to be insignificant. According to the study of Larenas-Linnemann et al. (2014), a significantly high frequency of tree sensitization was observed in subjects aged more than 18 years.

#### 3.1.11 Platanus spp. (Plane tree, Sycamore)

*Platanus spp.* is one of the common species of Platanaceae family which is considered as one of the main reasons for pollinosis. Because of its high abundance, especially in big cities, allergic reactions to this type of pollen are increasing (Alcazar et al. 2015). In spite of a lot of complaints regarding allergy to plane tree, especially in Tehran, there are very few publications regarding the prevalence of its sensitization in Iran, reporting a prevalence of 26–57% (Farhoudi et al. 2005; Shokouhi Shoormasti et al. 2018a). Two important genera of this tree are *Platanus acerifolia* and *Platanus orientalis* with more studies being conducted on *Platanus acerifolia* (Pazouki et al. 2008). The pollination duration of this tree is usually between March and April. One of the main factors in the pollination season and pollen count of this plant is temperature (Matricardi et al. 2016). Having air pollution tolerance, these trees are frequently cultivated as street trees, especially in big cities such as Tehran (Rashidi and Jalili 2018) and Shanghai (Chen et al. 2015).

There is a high degree of cross-reactivity between allergenic molecules of a different species of Platanus (Pazouki et al. 2008). Pla a1, Pla a2, and Pla a3 are the major allergens of *Platanus acerifolia* (Chen et al. 2015). The prevalence of sensitization to these allergenic molecules is between 87.5 and 45% with the highest allergenicity reported for Pla a1 (Matricardi et al. 2016). *Platanus Orientalis* as one of the common inhalant allergens in southwest Asia such as Iran (Pazouki et al. 2008) is highly known for its major allergenic components including Pla or1, Pla or2, and Pla or3 (Matricardi et al. 2016). Pazouki et al. reported a new allergenic molecule of *Platanus orientalis* with molecular weights of 18KDa which is a cyclophilin (Pazouki et al. 2009).

#### *3.1.12 Cupressus arizonica (Cypress)*

*Cupressus arizonica* (*C. arizonica*) as a member of the Cupressaceae family is one of the main triggers of pollinosis in the world. The low protein and high carbohydrate content of this pollen is attributed to its particular characteristics (Shahali et al. 2007). The allergic reactions to *Cupressaceae* pollen which usually occur in winter could have overlapping symptoms with common cold or influenza (Gomes et al. 2019) This genus is able to adapt to different environmental and climate conditions (Shahali et al. 2009b), and various reports have presented the prevalence of cypress allergenicity in different countries (Charpin et al. 2017). Meta-analysis was not possible due to a limited number of studies regarding the prevalence of sensitization to *C. arizonica* in Iran. Nevertheless, Shahali et al. have performed numerous studies regarding the structure, characteristics, and protein contents of this pollen in Iran (Shahali et al. 2007, 2009a, 2010). According to their findings, some intraspecies characteristics have been recognized in *C. arizonica* pollens, indicating that environmental conditions could change the protein content of *C. arizonica* pollen (Shahali et al. 2010). The pollination time of (*C. arizonica*) is from January to February. Additionally, there is somewhat cross-pollination between *C. arizonica* and *C. sempervirens* (February to March). This issue resulted in prolonged pollination season for allergic patients to these trees (Aceituno et al. 2000). These two pollens are responsible for 2.4% to 35.4% of allergic sensitizations in the general population (Asam et al. 2015).

Cup a 1 and Cup s 1 are the major allergens of *C. arizonica* and *C. sempervirens*, respectively. These two components showed more than 90% similarity in their protein type (pectate lyases) as a CCD-bearing protein (Asam et al. 2015). Cup a 1 (45 kDa) has been detected as the most prominent allergenic molecule in pollen extracts of Mediterranean region, while a 35-kDa protein was more representative in extracts obtained from both varieties in Iran (Shahali et al. 2007). In addition to Cup a1, other allergenic molecules have been characterized in *C. arizonica* including Cup a 2, Cup a3, and Cup a 4 (www.allergome.org). Shahali et al. (2009a) determined IgE reactivity to a 35-kDa molecule in Iranian allergic patients.

#### *3.1.13 Fraxinus spp. (Ash)*

*Fraxinus spp*. belongs to the Oleaceae family. This tree is widely distributed throughout Europe (Thomas 2016) also in southwestern Asia to the Caucasus and Alborz mountains (Petrova et al. 2017). The allergy to Ash should not be neglected as a prevalence of 18–34% has been reported in France and Italy (Imhof et al. 2014). The prevalence of Ash sensitization ranges from 11.40 to 53.5% as determined in some studies in Iran (Fereidouni et al. 2009; Shokouhi Shoormasti et al. 2018a). Despite low frequency of Ash tree in some cities such as Bushehr (South of Iran), a high level of sensitization was detected in this region that may be stemmed from cross-reactivity of ash with other pollens (Farrokhi et al. 2014, 2015). According to a recent study, the *Fraxinus* genus is considered as one of the most common allergenic tree pollens in the Middle East (Mansouritorghabeh et al. 2017). Ash and olive trees are in the same family and show the high cross-reactivity together (Weber 2007). Additionally, Ash tree shows significant cross-reactivity to the *Betulaceae* family (Imhof et al. 2014). Fra e 1 as the major allergen of F. excelsior is detected in more than 70% of patients with ash allergy (Barderas et al. 2005). This glycoprotein shows high cross-reactivity with Ole e 1 (major allergen of olive tree) (Palomares et al. 2006). Besides Fra e 1, there are other minor allergens including Fra e 2 and Fra e 3 that develop cross-reactivity to proteins with profilins and calmodulin in their structure (Imhof et al. 2014).

### 3.2 Outdoor/indoor allergens

#### *3.2.1 Molds*

Environmental and ecological features such as temperature, humidity, and direction and speed of winds are considered as effective factors in the concentration of outdoor fungi species in each region. Accordingly, the level of both indoor and outdoor fungal levels is highly linked to dust storms (Shabankarehfard et al. 2017). There are a lot of studies regarding sensitization to molds allergens in Iran (Hedayati et al. 2006; Nabavi et al. 2009). The results of the present meta-analysis revealed that 27% (14–43%) of allergic patients showed sensitization to molds (Fig. 7). Furthermore, the age-dependent meta-analysis revealed a pooled prevalence of 23% (95%CI 15–32%) and 18% (95% CI 7–33%) for children and adults, respectively. Similar to this study, Larenas-Linnemann et al. found no significant difference in mold sensitization between children and adults (Larenas-Linnemann et al. 2014). Considering the fact that people living in modern countries are spending long periods indoors, improving the quality of the indoor environment has become an imperative health concern (Žuškin et al. 2009). In this regard, atopic individuals are of high risk of health problems created by indoor molds (Ahluwalia and Matsui 2018). It has been estimated that from a total of 1.5 million species of mold, more than 225 species are found in indoor environments (McGinnis 2007). According to the results of a meta-analysis from eight studies of European countries, there is a significant association between exposure to mold in the first 2 years of life and increased risk of asthma (Tischer et al. 2011).

### 3.2.2 *Aspergillus spp.*

Some species of *Aspergillus* genus such as *A. fumigatus*, *A. niger*, A. *flavus*, and *A. oryzae* have revealed allergenic features (Hedayati et al. 2007). According to the findings of the current study, the prevalence of allergenicity to this type of mold was 11% (95% CI 5–17%) (Fig. 8). The results of another study in European countries showed that the prevalence of sensitization to *Aspergillus* ranged from 0.4% in Italy to 10.3% in Greece with a total prevalence of 4.4% (3.7–5.2) in Europe (GA2LEN) (Heinzerling et al. 2009). A significant relationship was found between the onset of adult asthma and sIgE to *A. fumigates* (Jaakkola et al. 2006). The results of a meta-analysis revealed that problems related to respiratory and asthma were significantly associated with building humidity and mold existence (Fisk et al. 2007).

Over 20 allergens have been distinguished in *A. fumigatus*, while a number of allergens have been characterized in *A. flavus* (Asp fl 13 as the major allergenic molecule) and *A. oryzae* (such as Asp o 13, Asp o 21, Asp o lactase, and Asp o lipase (www.allergome.org and www.allergen.org).

### 3.2.3 *Alternaria alternata*

*Alternaria alternata* (*A. alternata*) is one of the most frequent fungal spores in the atmosphere as declared by epidemiological studies (Woudenberg et al. 2015). A wide variety of toxic metabolites such as dibenzopyrone, perylene, and tetramic acid derivatives are produced *by A. alternata* (Pose et al. 2010). A large panel of allergenic proteins is also produced by this fungal species, resulting in severe respiratory manifestations particularly in atopic individuals (Gabriel et al. 2016b). According to the current report, a

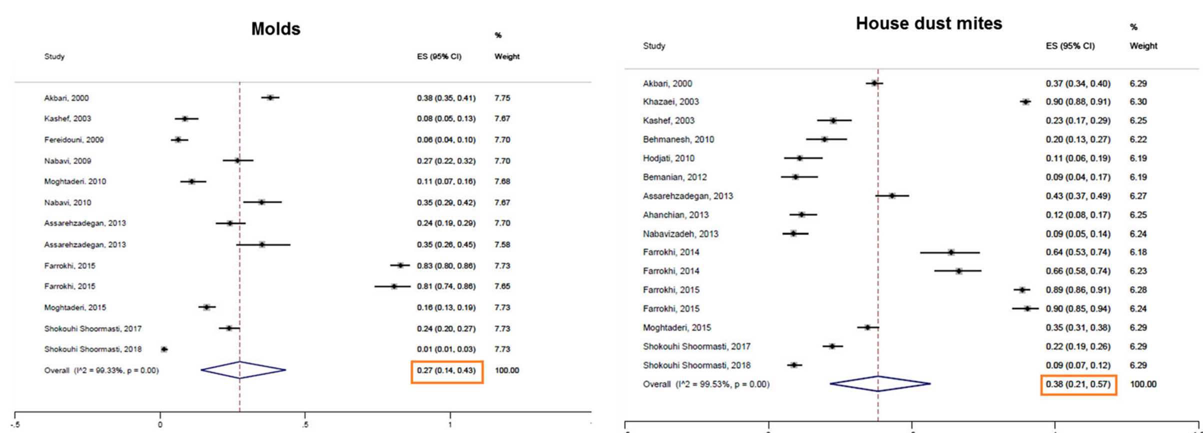


**Fig. 7** The pooled prevalence of sensitization to molds and HDM among studies performed in different cities of Iran (forest plot)

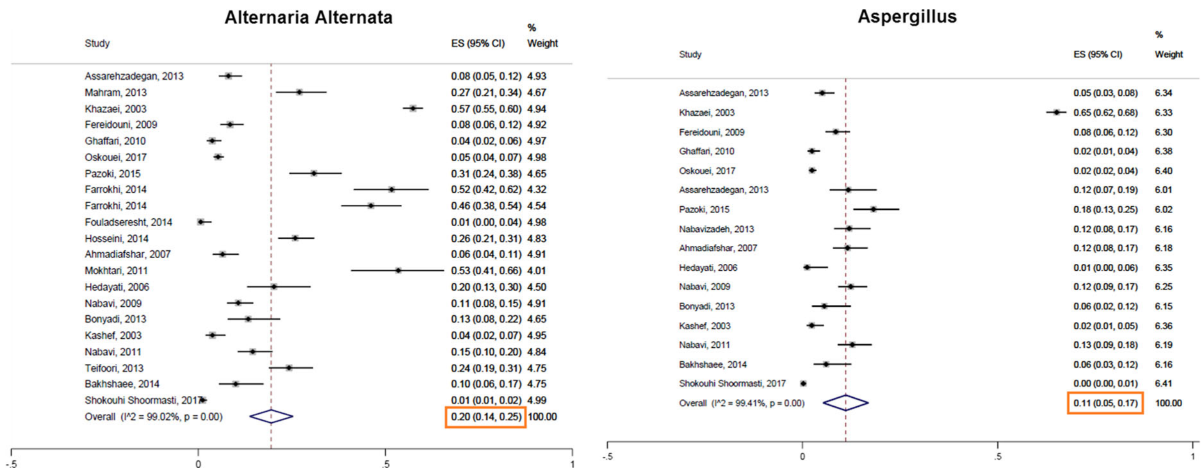


**Fig. 8** The pooled prevalence of sensitization to *Alternaria alternata* and *Aspergillus* allergen among studies performed in different cities of Iran (forest plot)

prevalence of 20% (95%CI 14–25%) was detected for allergenicity to *A. alternata* that was noticeably higher than the statistics reported from a multicenter study in Europe [8.9% (95%CI 7.9–9.9%)] (Fig. 8) (Heinzerling et al. 2009). Accordingly, the highest prevalence of *A. alternata* sensitivity (23.8%) was reported in Greece (Heinzerling et al. 2009).

Alt a 1 which is mainly found in the cell wall of spores can induce allergic reactions by the respiratory tract (Twaroch et al. 2012). Alt a 1 is the major allergen described in *Alternaria* which is commonly applied as a diagnostic marker (Postigo et al. 2011). Alta 3, Alta 5, Alta 7, and Alta 10 are known as minor allergens of *A. alternata*, while Alt a 4 (57 kDa) bounds IgE in 42% of the sensitized population (De Vouge et al. 1998; Achatz et al. 1996). The most recent official allergen of A. *alternata* is Alt a 15 (Gabriel et al. 2016a). IgE-mediated sensitization to Alt a 15 was shown to be more prevalent in those who are poly-sensitized to molds, especially to Curvularia lunata (Gabriel et al. 2016a). The sensitization to A. *alternata* allergens was introduced as strong markers for asthma severity that are usually ignored compared to other widespread aeroallergens sources (Gabriel et al. 2016b).

## 3.3 Indoor allergens

House dust mite (HDM): HDM allergens are one of the important indoor allergens the role of which in sensitization and development of allergic symptoms is well documented (Sanchez et al. 2017; Zeytun et al. 2017). As the current results depict, the prevalence of mites sensitization is 38% (95%CI 21–57%)(Fig. 7) with respective prevalence of 21% (95%CI 16–26%) and 20% (95%CI 15–25%) for *Dermatophagoides Pteronyssinus* (*D. Pteronyssinus*) and *Dermatophagoides farinae (D. Farina)* (Fig. 9). Moreover, both sex-related and age-related meta-analysis showed similar prevalence for males/females and adults/children. However, according to the study of Larenas-Linnemann et al. (2014), adults showed a lower prevalence of HDM compared to children that were statistically significant. Mites' growth and prevalence are highly attributed to temperature, humidity, and altitude (Kalpaklioglu et al. 2004). Accordingly, sensitization to HDM allergens has been considered to be between 60% and 100% in asthmatic individuals (Roche et al. 1997). The count of mites which is about 300 per 1 g of house dust is an important factor in the severity of allergic reactions (Lassiter and Fashing 1990). HDM has been reported as the most common aeroallergens in Asia, especially Asian Pacific countries (Tham et al. 2016). Heinzerling et al. presented a prevalence of 31.3% (95%CI 29.7%–33.0%) and 28.9% (95%CI 27.3–30.5%) for *D. pteronyssinus* and D. farinae, respectively (Heinzerling et al. 2009). These statistics are higher than the prevalence *D. pteronyssinus and D. farina* sensitization obtained from the current study. Mites belong to the spider family which 50 species of them have been found in the dust (Fereidouni et al. 2013).

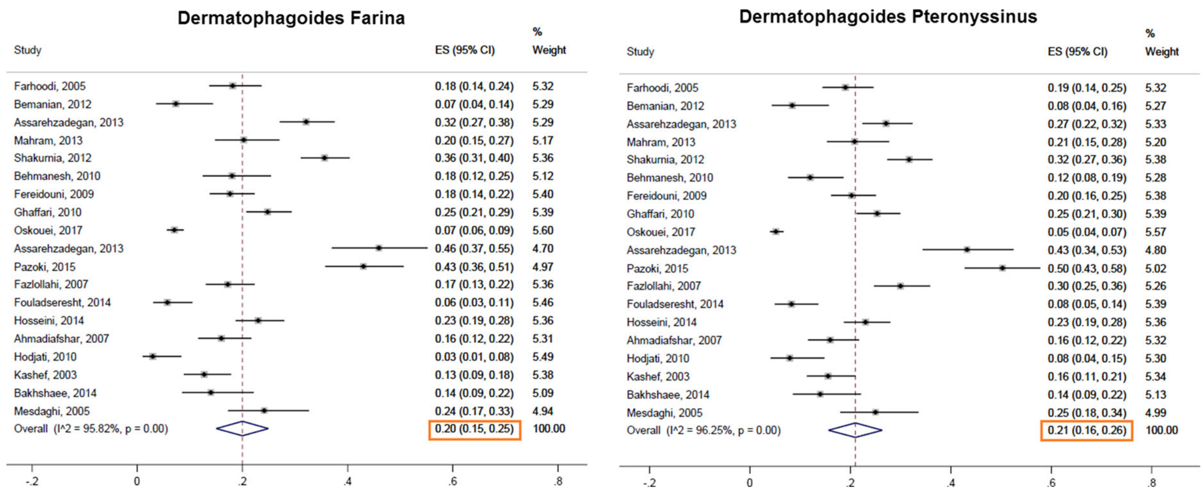


**Fig. 9** The proportion of sensitization to *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* among studies performed in different cities of Iran (forest plot)

*D. pteronyssinus* and *D. farina* are the most important members *of* Pyroglyphidae family in terms of allergenicity and clinical importance (Solarz 2009). Der p 1 and Der f 1 are two major allergens initiating IgE-related responses in patients being sensitive to pyroglyphid mites (Arlian 1991). Having in mind the huge number of studies on HDMs in Iran, the results of previous investigations have shown that *D. pteronyssinus* is more prevalent (Ziyaei et al. 2017; Soleimani-Ahmadi et al. 2017).

### *3.3.1 Cockroaches*

As a potent source of allergen, cockroaches are known to induce sensitization and result in allergic symptoms (Do et al. 2016). The sensitization to cockroach has been evaluated in a number of studies in Iran with a random pooled ES of 21% (95%CI 16–26%) obtained from meta-analysis of these studies (Fig. 10). Moreover, males [22% (95% CI 8–40%)] showed similar prevalence of cockroaches sensitization to females [23% (95% CI 11–38%)]. In addition, the age-related pooled prevalence revealed a higher prevalence of cockroaches' sensitization for adults compared with children (26% vs. 18%). A prevalence of 17% to 41% has been reported for cockroach allergy in the USA (Sanchez et al. 2017). The most common worldwide cockroaches include Periplaneta americana (American cockroach), Blatta Orientalis (oriental cockroach), *Blattella germanica* (German cockroach), and *Supella longipalpa* (Brown-banded cockroach) (Lihoreau et al. 2012; World Health Organization). The results of a recent systematic review revealed that bathrooms, toilets, and kitchens are highly infested with cockroach dried droppings in household environments (Nasirian 2017). In the same way, cockroach allergen was frequently detected in children's bedrooms compared to the kitchen area with a direct relationship between allergen concentration and duration of residence (Moghtaderi et al. 2016). The prevalence of cockroach allergy in Iranian asthmatic children was similar to other common inhalant allergens (Farhoudi et al. 2003). In another study performed in a south-western city of Iran, asthma severity was considerably associated with sensitivity to aeroallergens such as cockroach (Farrokhi et al. 2015). The majority of studies in Iran have evaluated Periplaneta Americana and *Blattella germanica*. According to the study of Heinzerling et al. (2009), sensitization to *Blattella germanica* was detected in 8.9% (95%CI 7.9%–9.9%) of sensitized individuals living in Europe while clinical relevance was found in 5.7% (95% CI 4.9%–6.6%) of these cases (Burbach et al. 2009). Additionally, a relationship was found between cockroach sensitization and low socioeconomic status (Salo et al. 2014).

Regarding a large number of studies, some major immunogenic components of these allergens have identified. The primary cloned cockroach allergen was Bla g 2 in 1995 (Arruda et al. 1995). Bla g 1-9 and Bla g 11 are the most commonly known allergens from *Blattella germanica*, while Per a 1, Per a 2, Per a 3, Per

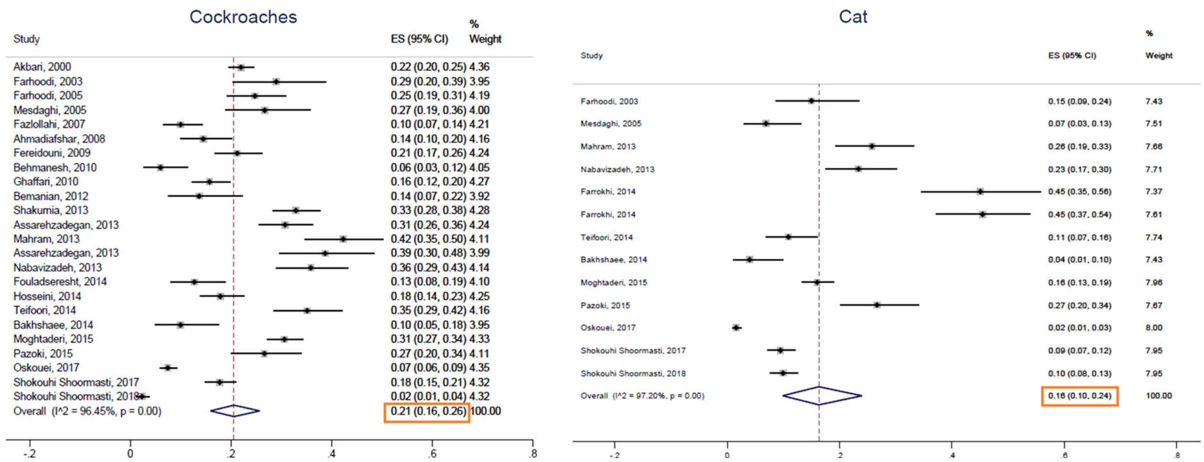


**Fig. 10** The proportion of sensitization to cockroach and cat among studies performed in different cities of Iran (forest plot)

a 6, Per a 7, Per a 9, Per a 10, Per a 11, and Per a 12 have been introduced for Periplaneta Americana (www.allergen.org). In addition, genetically predisposed patients are more prone to show an allergic reaction to dried secretions and remained parts of cockroach body (Arruda et al. 2014).

### *3.3.2 Cat*

Cats (*Felis domesticus*) are considered as spreaders of critical allergens for atopic individuals that have the potential to commence the occurrence of symptoms ranging from rhinitis and conjunctivitis as common and mild discomfort to the severe asthmatic crisis, while a recent study has reported that 30.3% of the US population with asthma were cat-sensitized (Gergen et al. 2018). According to our analysis, 16% (95% CI 10–24%) of allergic patients showed cat sensitization (Fig. 10). According to our most recent evaluations, cat sensitization was the most frequent sensitizations comparing indoor allergens (Shokouhi Shoormasti et al. 2018a). In a recent study performed in a southwestern city of Iran, cat allergen (Fel d1) was one of the allergenic triggers that were detected in children's bedrooms and a direct association was found between this allergen and the average size of home (Moghtaderi et al. 2016). In another study performed in patients with asthma and allergic rhinitis, there was a significant relationship between sensitization to animal dander such as cat and the severity of asthma and allergic rhinitis (Farrokhi et al. 2015). In Heinzerling et al. study, IgE-mediated sensitization to the cat was detected in 26.3% (95% CI 24.8–27.9%) of individuals living in European countries (Heinzerling et al. 2009) which is higher than the statistics obtained in the present study. Furthermore, a significant association was observed between sensitization to cat and higher socioeconomic status (Salo et al. 2014).

Fel d 1 as the most prominent allergen is a secretoglobin that is found in cats' sebaceous, anal, and salivary glands (Charpin et al. 1991; Bonnet et al. 2018) and is a tetrameric protein (35–40 kDa) that is consisted of two heterodimer weighting about 18–20 kDa (Chapman et al. 1988). Accordingly, a significant decrease was found in skin test reactivity and RAST in cat-allergic patients after removing Fel d 1 from cat dander extract (Ohman et al. 1976). A recent study revealed a substantial number of mutations in sequences of Siberian cats (low-level allergenic cats) that may be attributed to decreased synthesis of allergen in these cats (Sartore et al. 2017). Other in vitro investigations revealed 14–23% and 60–90% allergenicity to Fel d 2 (serum albumin, 69 kDa) and Fel d 3 (cystatin, 11 kDa), respectively (Hilger et al. 1997; Ichikawa et al. 2001). Other allergens include Fel d 4, Fel d 5w, Fel d 6w, Fel d 7, and Fel d 8 (www.allergen.org).

## 4 Conclusion

The results of the current meta-analysis revealed that *S. kali* is the most common aeroallergens in capital, southwestern, north-eastern areas of Iran, while allergic patients living in northern and southern coastal areas of Iran were more prone to suffer from HDM sensitization. However, adequate reliable studies were not performed in all provinces and determining the particularity of allergy in those regions was not feasible. Considering the fact that Iran is a country with diverse geo-climatic conditions with different temperature, altitude, and humidity, public health professionals may benefit from the results of this systematic review for appropriate health endorsement programs including selection of the most suitable diagnostic panel containing the most common allergens and choosing the finest allergens for immunotherapy in each area. In addition, allergenic plants of each distinct province may be replaced with hypoallergenic species in order to reduce the prevalence of allergic diseases in the long term.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** The protocol of this systematic review was approved by the Research committee and Ethics Committee of Immunology, Asthma, and Allergy Research Institute and approved and registered by Tehran University of Medical Sciences (No: 31266).

## Appendix

| Aeroallergens | Kingdom | Order | Family | Genus | Species | Common name |
|---|---|---|---|---|---|---|
| *Outdoor* | | | | | | |
| Weeds | Plantae | Caryophyllales | Amaranthaceae | *Salsola* | *kali* | Russian Thistle/Saltwort |
| | Plantae | Caryophyllales | Amaranthaceae | *Chenopodium* | *album* | Lamb's quarter/White goosefoot |
| | Plantae | Caryophyllales | Amaranthaceae | *Amaranthus* | *retroflexus* | Pigweed |
| | Plantae | Caryophyllales | Amaranthaceae | *Amaranthus* | *palmeri* | Careless weed |
| | Plantae | Caryophyllales | Chenopodiaceae | *Kochia* | *scoparia* | Burning Bush |
| | Plantae | Asterales | Asteraceae | *Artemisia* | *vulgaris or douglasiana* | Mugwort |
| | Plantae | Lamiales | Plantaginaceae | *Plantago* | *lanceolata* | Plantain |
| | Plantae | Asterales | Asteraceae | Leucanthemum | vulgare | Oxeye daisy |
| | Plantae | Rosales | Urticaceae | Urtica | dioica | Nettle |
| | Plantae | Asterales | Asteraceae | *Taraxacum* | *Officinale* | Dandelion |
| | Plantae | Caryophyllales | Polygonaceae | *Rumex* | *acetosella* | Sheep's Sorrel |
| | Plantae | Asterales | Asteraceae | *Xanthium* | *strumarium* | Cocklebur |
| | Plantae | Fabales | Fabaceae | Medicago | sativa | Alfalfa |
| | Plantae | Asterales | Asteraceae | *Solidago* | spp. | Goldenrod |
| | Plantae | Rosales | Rhamnaceae | *Ceanothus* | spp. | Redroot |
| Grasses | Plantae | Poales | Poacea | *Cynodon* | *dactylon* | Bermuda Grass |
| | Plantae | Poales | Poacea | *Lolium* | *perenne* | Rye grass |
| | Plantae | Poales | Poacea | *Phleum* | *pratense* | Timothy grass |
| | Plantae | Poales | Poacea | *Festuca* | *pratensis* | Meadow fescue |
| | Plantae | Poales | Poaceae | *Poa* | *pratensis* | Kentucky blue grass or Meadow grass |

| Aeroallergens | Kingdom | Order | Family | Genus | Species | Common name |
|---|---|---|---|---|---|---|
| | Plantae | Poales | Poaceae | *Sorghum* | *halepense* | Johnson grass |
| | Plantae | Poales | Poaceae | *Holcus* | *lanatus* | Velvet grass or Yorkshire Fog |
| | Plantae | Poales | Poaceae | *Dactylis* | *glomerata* | Orchard grass or cocksfoot |
| | Plantae | Poales | Poaceae | *Anthoxanthum* | *odoratum* | Sweet vernal grass |
| | Plantae | Poales | Poaceae | *Agrostis* | spp. | Bent grass |
| | Plantae | Poales | Poaceae | | | Oat grass |
| | Plantae | Poales | Poaceae | *Avena* | spp. | Wild oat |
| | Plantae | Poales | Poaceae | Bromus | spp. | Bromus |
| | Plantae | Poales | Poaceae | *Agrostis* | spp. | Redtop |
| Trees | Plantae | Lamiales | Oleaceae | *Fraxinus* | *excelsior or americana* | Ash |
| | Plantae | Pinales | Cupressaceae | *Cupressus* | *Arizonica, sempervirens* | Cypress |
| | Plantae | Proteales | Platanaceae | *Platanus* | *Orientalis acerifolia* | Plane tree or sycamore |
| | Plantae | Lamiales | Oleaceae | *OLea* | *europea* | Olive |
| | Plantae | Fabales | Fabaceae | *Prosopis* | *juliflora* | Mesquite |
| | Plantae | Myrtales | Myrtaceae | Eucalyptus | globules | Eucalyptus |
| | Plantae | Fagales | Fagaceae | Fagus | spp. | Beech |
| | Plantae | | Pinaceae | | | Cedar |
| | Plantae | Fagales | Betulaceae | Alnus | spp. | Alder |
| | Plantae | | Adoxaceae | | | Elder |
| | Plantae | Fagales | Betulaceae | Betula | spp. | Birch |
| | Plantae | Fagales | Fagaceae | Quercus | spp. | Oak |
| | Plantae | Fagales | Betulaceae | Corylus | spp. | Hazel |
| | Plantae | Malpighiales | Salicaceae | Poplus | alba | Poplar |
| | Plantae | Rosales | Ulmaceae | Ulmus | spp. | Elm |
| | Plantae | Malpighiales | Salicaceae | *Salix* | spp. | Willow |
| | Plantae | Malpighiales | Salicaceae | *Populus* | *deltoids* | Cottonwood |
| | Plantae | Sapindales | Simaroubaceae | *Ailanthus* | *altissima* | Tree of heaven |
| | Plantae | Fabales | Fabaceae | *Acacia* | *longifolia* | Common Acacia |
| | Plantae | Pinales | Cupressaceae | *Juniperus* | *ashei* | Juniper |
| | Plantae | Pinales | Pinaceae | *Pinus* | spp. | Lodgepole pine |
| | Plantae | Sapindales | Sapindaceae | Acer | spp. | Maple |
| | Plantae | Sapindales | Sapindaceae | Aesculus | spp. | Horse chestnuts |
| | Plantae | Fabales | Fabaceae | Rubinia | pseudoacacia | False acacias |
| | Plantae | Malvales | Malvaceae | Tilia | spp. | Limes |
| | Plantae | Myrtales | Myrtaceae | Eucalyptus | spp. | Red river |
| | Plantae | Fagales | Juglandaceae | Carya | spp. | Shagbark hickory |
| | Plantae | Saxifragales | Altingiaceae | Liquidambar | spp. | Sweetgum |

continued

| Aeroallergens | Kingdom | Order | Family | Genus | Species | Common name |
|---|---|---|---|---|---|---|
| Mold | Fungi | Eurotiales | Trichocomaceae | *Aspergillus* | *Fumigates/niger* | |
| | Fungi | Pleosporales | Pleosporaceae | *Alternaria* | *alternata* | |
| *Indoor and outdoor* | | | | | | |
| | Fungi | Capnodiales | Davidiellaceae | *Cephalosporium* | *Acremonium/ Herbarium* | |
| | Fungi | Eurotiales | Trichocomaceae | *Penicillium* | spp. | |
| | Fungi | Saccharomycetales | Saccharomycetaceae | *Candida* | *Albicans* | |
| | Fungi | Pleosporales | Pleosporaceae | *Bipolaris* | spp. | |
| *Indoor* | | | | | | |
| HDM | Animalia | Sarcoptiformes | Pyroglyphidae | *Dermatophagoides* | *farinae* | |
| | Animalia | Sarcoptiformes | Pyroglyphidae | *Dermatophagoides* | *pteronyssinus* | |
| Cockroach | Animalia | Blattodea | Ectobiidae | *Blattella* | *germanica* | *German Cockroach* |
| | Animalia | Blattodea | Blattidae | *Periplaneta* | *americana* | American cockroach |
| Cat | Animalia | Carnivora | Felidae | *Felis* | *Catus/domesticus* | |

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