Prevalence of Allergic diseases in Mayan Population of Lake Atitlan, Guatemala: a cross-sectional pilot study

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Faculty of Medicine

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Abstract

Background: Allergic diseases in Latin America are often underestimated by patients and underdiagnosed by physicians and paediatricians and only there are few studies available on their occurrence frequency. The diverse socio-demographics and social inequalities in Latin America can cause obstacles in data collection and analysis. This knowledge gap is particularly pronounced in difficult-to-reach indigenous communities across the continent, including Guatemala, where there is a lack of information regarding the prevalence of allergic diseases and the environmental and societal factors that might be of relevance for these diseases.

Objective: The primary aim of this pilot study was to assess the frequency of allergic diseases among the indigenous population residing in the Sololá region of Guatemala. The study sought to achieve the following specific objectives:

1. To determine the prevalence of nasal and skin allergies, and of skin prick test (SPT) positivity to selected allergens in a population of the Sololá region in Guatemala.
2. To provide an overview of environmental and demographic characteristics of this study population.
3. To pilot the approaches and feasibility to undertake research in such a difficult-to-reach and under-investigated population.

Methods: We conducted a pilot cross-sectional study among indigenous Mayans residing in communities surrounding Lake Atitlan in Guatemala. We gathered data from 292 participants using a standardized interviewer-led questionnaire. To ensure participation from weavers and their families, four weavers' organizations in the area informed and invited them to take part in this study. The questionnaire covered demographics, work-related and home-related exposures, as well as nasal and skin allergies. Additionally, we performed a skin prick test on 91 subjects. The test involved allergens, *i.e.,* timothy grass, cat, ambrosia, house dust mites, and cockroach allergens. Descriptive analyses were conducted on the collected data to assess the prevalence of nasal and skin allergies and describe the environmental and demographic characteristics of the study population.

Results: This study revealed notable findings regarding the prevalence of nasal and skin allergies in the indigenous population of the Sololá region in Guatemala. Eczema (10%) and itchy rashes (11%) were found to be the most prevalent allergic conditions among women. Stratifying the data by gender showed that overall, women reported a higher prevalence of allergic diseases compared to men. In addition to assessing the prevalence of allergic symptoms, the study also investigated SPT positivity to five allergens. Notably, SPTs for ragweed and house dust mite allergens yielded negative results, indicating a low prevalence of sensitization to these allergens. The frequencies of SPT positivity were also low for timothy grass (8%), cat (2%), and cockroach (1%) allergens. This pilot study provides valuable insights into the prevalence of allergic symptoms and skin prick test positivity in a under-investigated indigenous population. Despite the challenges of conducting interviews and skin prick tests in this difficult-to-reach population, the study demonstrates the feasibility of these methods in gathering data on allergic diseases.

Conclusions: This pilot study aimed to determine the prevalence of allergic sysmptoms in indigenous communities residing in the Lake Atitlan region of Guatemala. The findings indicated that nasal and skin allergies were infrequent in this population and was supported by the low prevalence of positive skin prick tests. Notably, the study demonstrated the feasibility of recruiting participants through community organizations, facilitating the inclusion of this difficult-to-reach population in research studies. Moreover, the study demonstrates the feasibility of utilizing methodologies such as interviews and skin prick tests in difficult-to-reach populations, making it possible to study allergic diseases in such areas. These findings provide valuable insights into the prevalence of allergic conditions in indigenous communities and lay the foundation for future research in this field in such hard-to-reach regions.

Acknowledgements

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Finally, I would like to dedicate my thesis to the Iranian children, women, and men who have sacrificed their lives in pursuit of what is most essential in life - freedom.

List of Abbreviation

BAU	bioequivalent allergy units
BMI	Body mass index
CO	Carbon monoxide
COPD	chronic obstructive pulmonary disease
DEPs	diesel engine particles
EC	epithelial cells
ECRHS	European Community Respiratory Health Survey
EU	European Union
Ig E	Immunoglobulin E
IL	Interleukin
INCAP	Nutrition of Central America and Panama
ISAAC	International Study of Asthma and Allergies in Children
LMIC	Low- and Middle-Income Country
mm	millimiter
NK	Natural killer
NO_2	nitrogen oxide
NCD	non-communicable disease
PAH	polycyclic aromatic hydrocarbon
PVC	polyvinyl chloride
RHINESSA	Respiratory Health In Northern Europe, Spain and Australia
SO_2	sulphur dioxide
SOP	Standard Operation Procedures
SPT	Skin prick test
Th1/2	type 1/2 helper T
WAO	World Allergy Organization

Part A: The Mantle

1 LITERATURE REVIEW

1.1 Allergic diseases as global health issues

In the recent years, allergic diseases are showed to be a primary cause of morbidity in children and adults under the age of 40, and their prevalence has been on a steady rise globally, and in low- and middle-income countries (LMICs) in particular as they are moving more and more towards urbanization [1]. Furthermore, their severity appears to be increasing, especially in children and young adults, who are bearing the highest burden of these trends [2]. It has been estimated that asthma and allergic diseases affect 30% of the global population [1]. Worldwide, 200 to 250 million people suffer from food allergies, and 400 million suffer from rhinitis [2].

Allergic diseases include life-threatening anaphylaxis; asthma; rhinitis; drug, food, and insect allergies; eczema; and urticaria (hives); angioedema; and eosinophilic esophagitis [3]. These diseases can cause long-term immune dysfunction and inflammation, which can form an underlying susceptibility for many other non-communicable diseases (NCDs), such as diabetes, obesity and cardiovascular diseases [3]. In addition to the health complications, such diseases can result in high socio-economic burden to the affected families and countries due to health care costs, morbidity, reduced quality of life and poorer work performance. Every year, asthma and allergic rhinitis alone are estimated to result in a loss of 100 million workdays and missed school days only in the European Union (EU). When these diseases are not treated adequately, their economic burden is estimated to be between 55 billion and 151 billion euros annually in the EU [4]. In LMICs, the economic burden of such diseases has even more profound effect on the daily lives of individuals, resulting in poverty due to loss of workdays and wages [3]. For instance, in India, it has been reported that the monthly cost of medication for an asthmatic child can be as much as one-third of an average family's monthly income [3].

In LMICs, the environmental risk factors, such as outdoor and indoor pollution (*e.g.,* cooking and tobacco smoke), are believed to contribute the most to the rise of prevalence of this category of diseases. Indoor pollution is estimated to be as much as five times more severe in LMICs than in high-income countries [5]. Furthermore, similar to high-income countries, other environmental risk factors such as climate change, reduced biodiversity and changes in the weather patterns can have direct and indirect consequences on the population health in LMICs, in part by contributing to allergic disease [3].

Despite the growing burden of allergic diseases, in high-income and low- and middle-income countries, the efforts targeting allergic diseases remain fragmented. Allergic diseases have not been given the same level of public and governmental attention as other chronic diseases, such as cancer and cardiovascular diseases. This is surprising given the burden of allergic diseases even from childhood and onwards. This highlights the need for more epidemiological studies to assess the actual prevalent of these diseases, worldwide, in particular in LMICs.

1.2 Epidemiology of allergic diseases in Latin America

Generally, in Latin America, allergic diseases are under-estimated by the patients and underdiagnosed by physicians and paediatricians. Their general concern of allergic diseases is limited; and treatment only focuses on reducing symptoms and not on identification on causes of disease, even in cases with moderate to persistent allergic diseases. Despite growing evidence that prevalence of allergic diseases on the rise in Latin America, there are only a few studies available on the prevalence of these diseases as well as their association with environmental and genetic risk factors in Latin American countries. Social inequalities and diverse socio-demographics in this continent can introduce challenges in collecting data and interpreting it. In 2009, Neffen *et al.* [6]reported that 7% of the Latin American population suffers from one or more type(s) of allergic diseases. Allergies in a Latin America Survey quantified the quality-of-life impact. Nearly two-thirds of patients in this survey reported that their nasal allergy symptoms were associated with increased fatigue and irritability, and over 40% stated that their condition had a significant impact on their everyday life. The incidence of allergic rhinitis is increasing and has become a major cause of morbidity, absenteeism, and restricted activity resulting in reducing the life quality of the affected [7,8].

Asthma and Allergies in Childhood (ISAAC) conducted a series of studies in Latin America to address the knowledge gap on the association of dietary factors with asthma and allergic diseases [9]. This study, which was a multi-centre epidemiological study including eleven Latin American countries, found that the overall prevalence of allergic symptoms in children aged 6–7 years varied between 9.9% (eczema) and 12.5% (wheeze) [9]. In another study, it was shown that 40% of Latin American infants had wheezing in the first two years of life, and almost 20% had recurrent episodes [10].

In general, it is suggested that in this region, socioeconomic factors have a profound impact on allergic diseases. Lower parental education and factors related with poverty and infections have also been associated with a higher prevalence of such diseases in children, Endara *et al.* (2015), in a case-study, compared populations of urban and rural school children in Latin America, and concluded that the association between IgE sensitization to house dust mite and wheeze was stronger in urban compared to rural populations [11].

1.3 Environmental factors exposure

1.3.1 Environmental pollutant exposure

The impact of environmental pollutants on the development of allergic diseases remains controversial despite being investigated extensively. Association between outdoor air pollutants, such as nitrogen oxide (NO_2), sulphur dioxide (SO_2), carbon monoxide (CO) and diesel engine particles (DEPs) and development of respiratory allergic diseases, particularly in children, has been shown [12–14]. In a study conducted on 2506 Japanese children to explore the impact of NO_2 levels (*i.e.,* a good indicator of vehicle exposure) on developing allergic asthma over four years, the authors found that children who lived at a distance of less than 50 m from the roads with heavy vehicle loads were more prone to developing asthma [15]. In particular, NO_2 has been attributed to an increase in the developing wheezing and allergic asthma [16]. In other studies, SO_2 and CO levels was found to be associated with the increase in the risk of allergic rhinitis and asthma in children [17]. DEPs, which consist of different sized particles, are also known to be main contributors to urban air pollutions. These particles can be suspended in the air for a long time, and easily drawn into the lungs where they stimulate the airways epithelial cells to produce cytokines, leading to inflammation [18]. Furthermore, other environmental contaminants, such as polycyclic aromatic hydrocarbon (PAH) metabolites, can increase the formation of oxygen reactive species, resulting in oxidative damage of DNA. Such alteration in the genotype could results in heterogeneous endotypes of asthma [19,20].

Indoor air pollutants are also be suggested to cause allergenic diseases, such as rhinitis and eczema. The sources of indoor pollutants are mainly from smoke, combustion products (*e.g.,* candles or incense), and volatile organic compounds emitted by building materials, paints, furniture with sponge cushions and products containing polyvinyl chloride (PVC). In a study, it was shown that a higher number of children who were exposed to volatile organic compounds, were diagnosed with asthma, rhinitis, and eczema [21]. Other aeroallergens, such as pollen, mould and spores, can also cause allergenic reactions in a large segment of the population [22]. In 2013, the World Allergy Organization (WAO) reported that pollen allergy prevalence is about 10-40% in the whole population [2].

1.3.2 Smoking exposure

From various cohort [23–25] case-control [26–28] and cross-sectional studies [29–33], it emerges that there is a positive association between active and passive smoking and the risk and prevalence of wheeze, asthma and allergic rhinitis [34–39]. Immunological profiling shows that tobacco smoke increases the levels of proinflammatory cytokines and reduces those of anti-inflammatory cytokines [34].

1.3.3 Exposure to food allergens and diet

In the last 2-3 decades, there are accumulating data to suggest that food allergies prevalence is on the rise. They are more common in children, in particular, in industrialised regions. Egg, fish, nuts and milk are examples of food, which can cause allergies [40]. For instance, systematic review and meta-analysis on the prevalence of fish and shellfish allergy concluded that fish allergy ranged from 0-7% and shellfish allergy ranged from 0-10.3% [41]. Similar to other allergens, determining the prevalence of food allergies remains inconclusive due to geographic variations, diet exposure effects, age, race, and ethnicity [42]. In case of milk allergies, the Netherlands and United Kingdom (1%) have the highest prevalence, and the lowest rates are observed in Lithuania, Germany, and Greece (<0.3%) [43]. In an Australian cohort study, in which 5276 children at age one year were recruited, it was reported that 11% of these children have a food allergy, only considering three foods: peanut allergy prevalence of 3.0% (95% CI, 2.4%-3.8%), raw egg allergy prevalence of 8.9% (95% CI, 7.8%- 10.0%), and sesame allergy prevalence of 0.8% (95% CI, 0.5%-1.1%) [44]. In the follow-up study at age four years old, the overall allergy rate was decreased to 3.8%, with a peanut allergy prevalence of 1.9% (95% CI, 1.6%-2.3%), egg allergy prevalence of 1.2% (95% CI, 0.9%-1.6%), and sesame allergy prevalence of 0.4% (95% CI, 0.3%- 0.6%) [45]. Furthermore, food additives (chemical substances), such as preservatives, antioxidant agents and colouring agents, can also develop allergic reactions [42]. Food contamination with herbicides, pesticides, antibiotics and hormone drugs can be other causes of allergy reactions to food [42].

1.4 Allergic reactions

In general, allergic reactions are categorised into four types; however, hypersensitive (allergic) disorders often involve more than one type. The brief overview of allergic reactions is summarised in Figure 1.1.

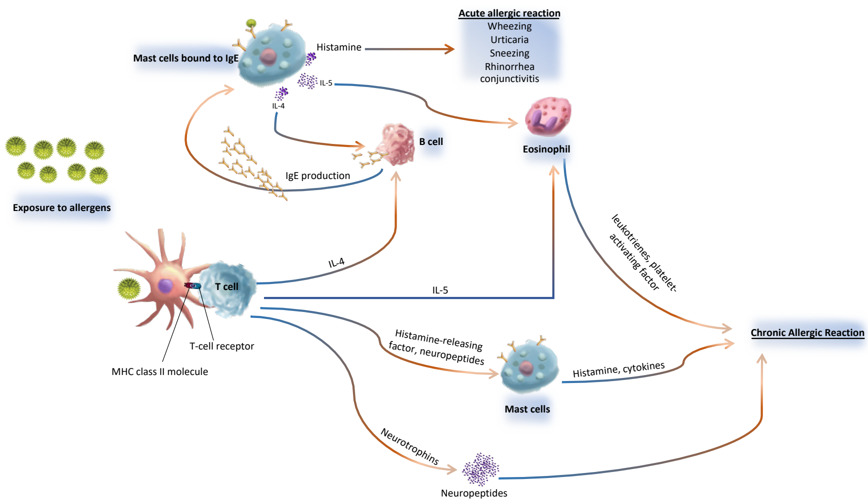

Figure 1.1. An overview of acute and chronic reaction pathways (Adapted from Kay, 2001) [46].

1.4.1 Type I reactions (Immediate or IgE-mediated reactions)

Type I reactions or immediate hypersensitivities are mediated by IgE antibodies. Allergen-specific IgE antibodies might be produced in response to allergens present in the environment (3), foods (4) and drugs [47]. Upon exposure to allergens, they bind to IgE antibodies, which are bound to a high-affinity receptor, called FcεRI, on mast cells and blood basophils. This activates the release of histamine, proteases and chemotactic factors, and synthesis of other mediators, such as prostaglandins, leukotrienes, platelet-activating factor and cytokines [47]. The release of such mediators results in vasodilation, increased capillary permeability, mucus hypersecretion, smooth muscle spasm, and tissue infiltration with eosinophils, type 2 helper T (Th2) cells, and other inflammatory cells. On re-exposure, the allergen is recognized by IgE antibodies bound to mast cells and basophils, which leads to triggering of these cells, and an immediate hypersensitivity reaction with eosinophils, Th2 cells [48].

1.4.2 Type II reactions (antibody-dependent cytotoxic hypersensitivity)

Type II reactions, *i.e.,* antibody-dependent cytotoxic hypersensitivity, takes place when antibodies bind to cell surface antigens, or a molecule bound to a cell surface. Such an antigen-antibody complex activates complements and cells such as natural killer (NK) cells, eosinophils, macrophages, which participate in antibody-dependent cell-mediated cytotoxicity. This activation results in damaging cells and tissues. Disorders involving type II reactions are Hashimoto thyroiditis Coombs-positive hemolytic anaemias [48].

1.4.3 Type III reactions

Type III reaction is a response to antigen-antibody complexes deposited in vessels or tissue. Antigen-antibody complexes can activate the complement pathway, which leads to the release of inflammatory mediators. The activated complement components recruit and activate neutrophils, resulting in inflammation and tissue injury. Accumulation of antigen-antibody complexes can be deposited in the tissues, such as renal glomeruli, blood vessels, synovial of joints causing systemic reactions [47]. Examples of type III disorders are systemic lupus erythematosus, rheumatoid arthritis, leukocytoclastic vasculitis, cryoglobulinemia, acute hypersensitivity pneumonitis, and several types of glomerulonephritis. This reaction develops 4-10 days after exposure to antigen, and continuous exposure to the can result in chronic. *e.g.,* allergic asthma, IgE-mediated components of allergic bronchopulmonary aspergillosis [48].

1.4.4 Type IV reactions (delayed hypersensitivity)

Type IV reactions, also known as delayed hypersensitivity, are mediated by CD4+T helper cells, *i.e.,* Th1 type of response [47]. Following the initial exposure to a specific antigen, T cells can be sensitized and activated by continuous exposure to the antigen. The tissue injury is mostly caused by lysosomal enzymes, reactive oxygen intermediates, and proinflammatory cytokines, secreted by activated macrophages. Disorders involving type IV reactions include contact dermatitis (*e.g.,* poison ivy), subacute and chronic hypersensitivity pneumonitis, allograft rejection, the immune response to tuberculosis, and many forms of drug hypersensitivity [48].

1.5 Allergy Diagnosis

For accurate diagnosis of allergies, the factors, such as detailed clinical history, and knowledge about local environment, are crucial. Additionally, the association between allergen exposure and onset of clinical features, periodicity of symptoms (*i.e.,* seasonal/ perennial, diurnal), animal or insect exposure, the affected body systems, familial atopy and occupational history should be investigated.

1.5.1 In vitro diagnosis tests (Immunoglobulin (Ig)E antibody levels)

In many routine allergy diagnostics, IgE level are used to detect and monitor the reaction of the immune system to the allergen (Kos and Sanders, 2018). IgE molecules produced against specific antigens are labelled as serum specific IgE (sIgE) [49]These can be detected by enzyme conjugated antihuman IgE antibodies. However, raised levels of IgE may also be due to conditions such as parasitic infestations, immunodeficiency disorders (e.g., AIDS, hyper IgE syndromes etc.) and Ebstein Barr virus (EBV) infection [10]. The major downside of sIgE estimation is false positivity with high total IgE levels (>300 kIU/L) due to non-specific binding to test allergens [11].

1.5.2 In vivo diagnosis tests (Skin prick test)

SPT is first described by Charles Harrison Blackley (1860s) in patients of 'hay fever'. SPT, which is the most frequent method for diagnosis of IgE mediated allergic diseases (14), should be administrated to patients with either recurrent or persistent symptoms which cannot be adequately controlled by therapy. Generally, clinical conditions where SPT is indicated are asthma, rhinitis, eczema/atopic dermatitis, suspected occupational exposure to selected potential allergens.

In this test, once the allergens are introduced into the skin, dermal mast cells begin to degranulate due to cross-linking of sIgE bound to their membrane receptors, leading to the immediate release of histamine which can be clinically characterised by wheal erythema (flare) that can be measured to assess the degree of cutaneous sensitivity, hence, SPT represents a surrogate indicator of systemic allergic sensitization (*i.e.,* nose, lungs, eyes, gut) through the presence of cutaneous reactivity to specific allergens.

Since blood vessels and pain receptors are located in deep dermis, SPT is pain-free and associated with minimal risk of bleeding or infection if performed appropriately [15]. Selection of antigens should be based upon patient's clinical and environmental history, occupation and socio-economic factors. Among the most common allergen to be used in SPT include house dust, house dust mite, relevant pollens (grass, tree or weeds), fungus (Alternaria, Aspergillus), insects (Cockroach) and pet animals (dog, cat, buffalo), milk, egg, peanut, soya, wheat, tree nut, fish and shellfish. Patients on anti-histaminics and immunomodulators, on b-blockers, with unhealthy skin condition, within 4 weeks of anaphylaxis and extremes of age are not suitable for SPT. As positive and negative control, histamine and normal saline ae used, respectively and read after 10 minutes and 15 minutes [16]. Positive reaction is suggested by appearance of a wheal at the prick site (Fig. 1.2). The maximum diameter of the wheal is measured, and reaction interpreted in millimetres (mm) of wheal diameter [19, 20]. Positive control should be at least 3 mm or more than negative control to establish test validity. Any allergen showing a wheal size of ≥3 mm than the negative control is considered to be positive indicator of hypersensitivity.

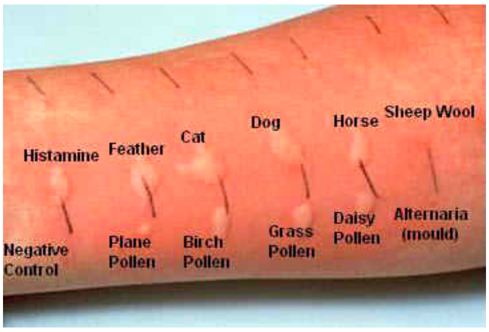

Figure 1.2. An example of skin prick test (SPT) (https://www.aashwas.in/diagnostic-services/skin-prick-test-spt/)

1.5.3 Factors Influencing on SPT result

1) Medications – Certain medications such as antihistaminics, Astemizole and long-term systemic steroids may affect the results of SPT [16].

2) Age – SPT is currently practiced beyond 6 months of age though no lower or upper age limit cut-off is recommended [16]. Skin reactivity declines after 60 years.

3) Test area – Generally, left forearm is the preferred area for this test. The mid and upper back are 33% more reactive than the lower back. The back as a whole is more reactive (53%) than the forearm. An area approximately 5 cm away from the wrist and 3 cm from the antecubital fossa, on the forearm is usually used [16].

4) Distance between two pricks – A minimum of 2 cm gap should be present between two adjacent test sites.

5) False positives – Skin conditions such as dermatographism and acute or chronic urticaria, naturally occurring histamine in some allergen extracts (insect venom, mold, foods), non-standard allergen preparations, cross-reactivity with homologous proteins.
6) False negatives – Recent use of (within 4 weeks) anaphylaxis, some medications, and UV exposure.

1.5.4 Comparison of in vitro test with in vivo test

The main advantages of *in vitro* tests over *in vivo* test include no effect of anti-histaminics or steroids, feasibility with any skin condition and no risk of systemic reactions. Furthermore, serum sIgE has better specificity with higher positive predictive value to identify allergens (e.g., pollen and insects) sensitization [21]. On the other hand, SPT have an advantage over *in vitro* tests in terms of faster result (15-20 minutes), no interference with high IgE levels and cost effectiveness [16].

1.6 Health in Guatemala

Guatemala is the most populated country in Central America. Almost half of the country's 15.2 million citizens live in urban areas [50]. Among Latin American countries, Guatemala has relatively poor health outcomes. The estimated life expectancy at birth is 74 years [51], and the health status is worst among the poor, rural and indigenous populations. As the country is at a pre-transition stage, the proportion of communicable diseases as the cause of death is about 61%, which is high compared to many other Latin American countries [52]. Furthermore, Guatemala has the highest prevalence of chronically malnourished children in Latin America (44%) [53]. Similar to many other Latin American countries, the prevalence of non-communicable diseases such as chronic obstructive pulmonary disease (COPD) is on the rise [50]. However, the records on NCDs are not well registered in this country.

1.7 Challenges in conducting Research in hard-to-reach Regions of Latin America

Conducting research in hard-to-reach regions, particularly among indigenous communities such as the Mayans in Latin America, presents unique challenges. In addition to geographical challenges, conducting research in hard-to-reach regions, particularly among indigenous communities like the Mayans in Latin America, can be challenging and involves addressing cultural and language barriers. These communities may have distinct cultural practices, beliefs, and languages that require researchers to work closely with local community leaders and translators. Effective engagement and participation of community members in the research process are essential to ensure their trust, understanding, and cooperation.

Furthermore, limited availability of healthcare facilities and trained personnel can pose significant challenges to conducting research in these regions. The lack of adequate infrastructure and healthcare resources can hinder the implementation of research protocols and data collection processes. Researchers may need to adapt their methodologies to work within the constraints of the available resources or develop alternative strategies to ensure data quality and participant safety.

Overcoming these challenges necessitates careful planning and consideration of the unique circumstances and needs of the community. Engaging with local stakeholders, including community leaders, healthcare providers, and relevant organizations, is crucial for understanding the local context and obtaining support for the research initiatives. Collaborating with these stakeholders can help overcome logistical barriers and ensure the successful execution of research activities.

In addition, building capacity within the community by providing training and support to local healthcare workers or research assistants can enhance the feasibility and sustainability of research efforts. This approach not only empowers the community but also promotes the long-term benefits of the research by strengthening local expertise and resources.

Ultimately, conducting research in hard-to-reach regions requires a comprehensive and culturally sensitive approach that emphasizes community involvement, collaboration, and adaptability. By addressing cultural and language barriers and working within the limitations of available resources, researchers can navigate the challenges and contribute valuable knowledge to improve the health and well-being of these marginalized populations.

1.8 Research questions

1. What is the prevalence of allergic symptoms within Mayan communities in Guatemala?
2. Which allergic symptoms are more commonly observed in this population?

1.9 Hypotheses and Objectives

1.9.1 Hypotheses

Our initial hypothesis for this study was that allergies would be prevalent among Guatemalan indigenous population, primarily due to the potential exposure to allergens from textile work and the presence of immunomodulatory agents such as disinfectants and pesticides.

1.9.2 Objectives

The main objective of this study was to describe the frequency of allergies, in terms of nasal and skin allergies as well as skin prick test positivity, in a difficult-to-reach indigenous population residing in the area of Lake Atitlan, Guatemala. To achieve this, the following primary objectives were:

1. To determine the prevalence of nasal and skin allergies, and of skin prick test positivity to selected allergens in a population of the Sololá region in Guatemala.
2. To provide an overview of environmental and demographic characteristics of this study population.
3. To pilot the approaches and feasibility to undertake research in such a difficult-to-reach and under-investigated population.

2 METHODOLOGY

To achieve the objectives of this study, we designed a cross-sectional study to be conducted through an interviewer-led questionnaire, and skin prick test.

2.1 Study population

This study was carried out in the region of Sololá in Guatemala (Fig. 1.3), focusing on the municipalities around Lake Atitlan, with a population of 55, 410 inhabitants of whom 70% live in rural areas [54]. There are many villages around Lake Atitlan from which we selected two villages to establish two study sites. The majority of the inhabitant in these villages belong to Mayan populations. These villages are well known for their traditional textile industry which is mainly operated by indigenous women. In addition to the textile industry, the majority of the families in this area are subsistence farmers, earning part of their cash supplement from selling their agricultural products.

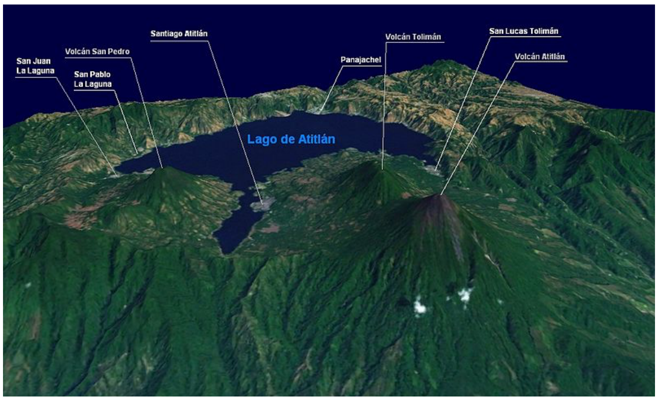

Figure 1.3. The location of the study site in the surrounding villages of the area of Lake Atitlan, Guatemala.
(https://commons.wikimedia.org/wiki/File:Volcano_Atitlan,_San_Pedro,_Toliman_%26_Lago_Atitlan_3D_version_1.jpg).

The study presented herein is a pilot study conducted during the 2019 Covid-19 pandemic under the constraints of limited participant recruitment. The study was conducted by Fernando Jerez (FG), an experienced project coordinator with extensive knowledge working with rural communities in Guatemala, particularly those involved in the informal weaving industry. FG assembled a team to implement the study in accordance with the protocol developed by the research team at the University of Bergen. This team was composed of a local social worker, Paulina Collum (PC), and several other health workers (HWs).

2.2 Approach for Engaging Communities in this Study

In collaboration with the Center for Equity and Governance for Healthcare in Guatemala (CEGSS) (https://cegss.org.gt/en/), our co-investigator Ana Lorena Ruano initiated the first contact with our target population. To assess their interest in participating in our research, an exploratory informal survey was conducted among several weavers' organizations. The participants expressed a great interest in the study and provided feedback that emphasizing the

importance of investigating lung health, as well as asthma and allergic diseases, in this population.
After obtaining reference information from PC, we were provided with the names of specific weavers' organizations in the area that had previously collaborated with ALR, FJ, and PC. The organizations that ultimately participated in our project were the "Red de Defensores Comunitarios por el Derecho a la Salud (REDC Salud)," "Red de Mujeres Estrella Tzutujil," "Asociación de Mujeres Ixoq Ajqne," and "Fundación Tradiciones Mayas". In early March 2021, FJ and PC carried out a recognition trip to different villages where the weavers and their families live and work. During this trip, meetings were held with some of the organizations' members, and an introduction to the study was given, along with an invitation to participate. FJ and PC maintained regular communication with the weavers' organizations until the fieldwork took place. The information obtained from PC proved to be invaluable in establishing contact with these organizations.

2.3 Data collection

The data was collected through standardised questionnaires. The participants (n=291) were invited to complete an interviewed-led questionnaire. The questionnaire (Appendix A), which is a modified version of earlier studies, i.e., ISAAC and **E**uropean **C**ommunity **R**espiratory **H**ealth **S**urvey (ECRHS), included the following groups of items:

(a) Personal details are, *i.e.,* age, gender, occupation tenure and its duration, daily hours, number of children, smoker/non-smoker, and family history of diseases.

(b) Allergic symptoms and diseases – type, onset, duration and frequency. Questions concerning other diseases such as other respiratory diseases, physical disorder and other diseases.

(c) Exposures of the participants at their work and home environments.

The interviews and the clinical measurements were carried out by trained health workers, by following the standard operation procedures (SOPs). In addition to the questionnaire, anthropometric measurements (*i.e.,* height and weight). Furthermore, SPT was performed to verify the sensitivity to allergen: timothy grass, cat, ambrosia, house dust mites, and cockroach allergens.

3 LIMITATIONS OF THIS STUDY

This study has encountered several limitations that should be acknowledged. One of the main limitations is the small population size. Due to the constraints imposed by the Covid-19 pandemic, limited budget, and time restrictions, the study was conducted with a small sample size, which may hinder the generalizability of the findings and the ability to draw definitive conclusions based solely on the results of this study. However, despite the small sample size, this study has laid the groundwork for future research with larger populations.

The Covid-19 pandemic posed significant challenges to the study. Travel restrictions and safety concerns prevented us from physically visiting the study site, which limited our ability to gain a comprehensive understanding of the area, its population, and the cultural context during the data collection process. Additionally, suboptimal communication with the physician who conducted the SPT and inadequate training for the field workers administering the questionnaires due to the inability to be physically present at the study site further added to the limitations. Furthermore, the complexity of the questionnaire and the translation of medical terms into local languages presented difficulties in fully comprehending certain exposures and allergic symptoms. This may have impacted the accuracy of the data and hindered the ability to conduct thorough analyses of exposure-outcome association analysis.

Another limitation is the potential for selection bias. As with many studies of this nature, there is a possibility that the participants included in the study may not fully represent the broader population. This could affect the validity and generalizability of the study findings.

4 CONCLUSIONS AND RECOMMENDATIONS FOR THE FUTURE STUDY

Our study aimed to investigate the prevalence of nasal and skin allergies, as well as SPT positivity, in the indigenous Mayan population residing in the area of Lake Atitlan, Guatemala, and to evaluate any potential home and work exposures. We further examined the feasibility of conducting such studies in hard-to-reach regions in Guatemala.

Despite the aforementioned limitations, this study has yielded valuable preliminary findings that serve as a foundation for further investigations in the indigenous Mayan population of Guatemala and in fact our study is one of the very few studies to describe allergic symptoms in one of the Mayan populations of Latin America.

In line with our ethical responsibility towards the participating communities and in adherence to the Ministry of Ethics in Health guidelines, we are committed to sharing the results of this study with the involved communities, accompanied by potential recommendations. We believe that this dissemination of knowledge will contribute to a better understanding of allergic diseases within their communities and aid in the development of strategies for prevention and control. Initial efforts in this regard have already been initiated during the winter of 2023. To enhance our understanding of this population, the team has plans to analyse biological samples collected during the study. The principal investigator, Cecilie Svanes, has secured grants to further advance this research and will continue to seek additional funding for future studies. Furthermore, we are actively preparing to submit this paper to the Journal of Epidemiology and Community Health, an international peer-reviewed journal in the field.

During this study, we have established collaborative partnerships with local Guatemalan health authorities, including the Institute of Nutrition of Central America and Panama (INCAP) and the Rafael Landívar University. These collaborations have facilitated ongoing studies, and several graduate students have been recruited to contribute to various aspects of this project. The knowledge gained from this study, coupled with the experience in data collection tools and community collaborations, will greatly benefit future research endeavours.

To improve future studies and build on the learnings of the current study, several recommendations can be made. Firstly, a larger and more diverse sample size should be recruited to increase the generalizability of the findings. Additionally, bilingual and culturally competent staff should be utilized to ensure accurate translation and interpretation of study materials. This is particularly important given the linguistic and cultural diversity of the region. Furthermore, we recommend incorporating a longitudinal study design to provide more insight into the temporal relationship between environmental exposures and the development of allergic symptoms. This would enable researchers to investigate the causal relationship between exposure to specific allergens and the development of allergic symptoms over time.

Overall, despite the limitations encountered, this study has provided valuable insights and set the stage for continued investigations in this population. Our commitment to community engagement, further research, and knowledge dissemination underscores our dedication to advancing our understanding of allergic diseases and improving the health and well-being of the Mayan population in Guatemala.

Part 2: The Manuscript

5 Prevalence of nasal and skin allergies in Mayan Population of Lake Atitlan, Guatemala: a cross-sectional pilot study*

Shokouh Makvandi-Nejad, Juan Pablo Lopez Cervantes, Fernando Jerez, Ana Lorena Ruano, Cecilie Svanes

ABSTRACT

Background This cross-sectional pilot study aimed to assess the prevalence of allergic symptoms in the hard-to-reach indigenous population of the Sololá region in Guatemala.

Methods A total of 292 participants were enrolled, with an average age of 32 years (ranging from 14 to 77 years old). The study gathered data on symptoms of nasal and skin allergies and background characteristics through a standardized questionnaire, and skin prick tests (SPT) including the allergens, *i.e.,* timothy grass (*Phleum pratense*), cat (*Felis catus*), ragweed (*Ambrosia*), mites (*Dermatophagoides pteronyssinus*), and cockroach (*Blattodea*) allergens were performed in a subsample (n=91).

Results The study revealed that symptoms of nasal and skin allergies were relatively rare, with hay fever (5%), nasal allergies (5%), eczema (8%) and itchy rashes (10%) being the most prevalent allergic diseases. Moreover, the results showed negative SPT for ragweed and house dust mite allergens, with low frequency of SPT positivity observed for timothy grass (8%), cat (2%), and cockroach (1%) allergens.

Conclusions The study provides important insights into the prevalence of allergic symptoms and skin prick test positivity in a difficult-to-reach and not previously investigated indigenous population of the Sololá region in Guatemala. It appears the occurrence of allergic symptoms are rare in this population. Furthermore, this pilot study indicates that conducting interviews and SPTs in this population is feasible.

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INTRODUCTION

Allergic diseases have a significant impact on the quality of life globally, affecting individuals across all age groups and genders. However, in Latin America, there is often a lack of proper diagnosis and treatment of allergic diseases, resulting in limited management of symptoms rather than addressing the underlying causes [55]. Research by Neffen et al. (2009) [6] revealed that 7% of the Latin American population suffers from one or more types of allergic diseases, with allergic rhinitis leading to morbidity, absenteeism, and restricted activity. A recent survey demonstrated that a majority of patients with nasal allergies reported increased fatigue and irritability, while more than 40% stated that their condition significantly impacted their daily lives (Neffen, 2010) [56]. In children aged 6-7 years, the prevalence of allergic symptoms ranged from 9.9% for eczema to 12.5% for wheeze, with socio-economic factors playing a crucial role in the development of respiratory allergic diseases [57].

Environmental factors, including outdoor and indoor air pollution, contribute to the development of allergic diseases. Exposure to outdoor pollutants such as nitrogen oxide (NO2), sulphur dioxide (SO2), carbon monoxide (CO), and diesel engine particles (DEPs) has been associated with an increased risk of respiratory allergic diseases, particularly in children [58] [13]. Indoor pollutants like smoke, combustion products, and volatile organic compounds (VOCs) can also trigger allergenic reactions, with higher exposure levels linked to a greater incidence of asthma, rhinitis, and eczema [21]. Other aeroallergens such as pollen, mold, and spores also contribute to allergic reactions among a significant portion of the population [59].

However, there is limited data available on the prevalence and trends of allergic symptoms in Latin America, particularly in hard-to-reach regions, and the existing studies have yielded mixed results. The factors contributing to the variation in prevalence and trends are complex, encompassing genetic, environmental, and socio-economic factors. Furthermore, the lack of standardized diagnostic criteria and methodologies across studies hampers result comparison and the accurate estimation of true prevalence rates. To fully comprehend the current status and trends of allergic symptoms in Latin America, further research is required. Therefore, the primary objective of this pilot study was to describe the frequency of allergies, specifically nasal and skin allergies and skin prick test positivity, in a difficult-to-reach indigenous population residing in the Lake Atitlan area of Guatemala.

METHODS

Amidst the challenges posed by the Covid-19 pandemic, this pilot study was conducted. Although the researchers were unable to travel from Norway to Guatemala due to pandemic restrictions, a committed team led the study under the guidance of an experienced project coordinator with extensive knowledge and expertise in working with rural communities in Guatemala. The team consisted of a local social worker and several healthcare workers who played crucial roles in facilitating the study activities.

Study design

The project was designed as a descriptive cross-sectional study. The study utilized a detailed interviewer-led questionnaire, clinical investigations, including anthropometry and skin prick tests.

Location and study population

Guatemala is a Central American country that consists of 22 regions or departments, with Solola being one of them. This region encompasses several villages surrounding Lake Atitlan, where indigenous Mayan people renowned for their traditional textile products. For the purposes of this study, San Pablo la Laguna, a village near the lake, was selected as the study site. Participants from San Pablo la Laguna and nearby villages were invited to travel to the study site to complete the interviews and clinical assessments.

The Solola region is home to an estimated population of 430,000 people, of which approximately 90% identify as belonging to an indigenous ethnicity. Our study aimed to target the indigenous Mayans who reside in communities surrounding Lake Atitlan.

Approach for Engaging Communities in this Study

In collaboration with the Center for Equity and Governance for Healthcare in Guatemala (CEGSS) (https://cegss.org.gt/en/), the first contact with our target population was initiated. To assess their interest in participating in our research, an exploratory informal survey was conducted among several weavers' organizations. The participants expressed a great interest in the study and provided feedback that emphasizing the importance of investigating lung health, as well as asthma and allergic diseases, in this population.

After obtaining reference information from the local social worker, the names of the interested weavers' organizations were listed and contacted. The organizations that ultimately participated in our project were the "Red de Defensores Comunitarios por el Derecho a la Salud (REDC Salud)," "Red de Mujeres Estrella Tzutujil," "Asociación de Mujeres Ixoq Ajqne," and "Fundación Tradiciones Mayas". The project coordinator and the local social worker carried out a recognition trip to different villages where the weavers and their families live and work. During this trip, meetings were held with some of the organizations' members, and an introduction to the study was given, along with an invitation to participate. Regular communication with the weavers' organizations continued until the fieldwork took place. The information obtained from the local social worker proved to be invaluable in establishing contact with these organizations.

Number of participants and sampling of the study population

The number of participants for the pilot study was determined based on budget constraints. The leaders of the weavers' organizations, *i.e.,* "Red de Defensores Comunitarios por el Derecho a la Salud (REDC Salud)", "Red de Mujeres Estrella Tzutujil", "Asociación de Mujeres Ixoq Ajqne", and "Fundación Tradiciones Mayas" were responsible for the cohort selection. They invited weavers from their respective organizations and encouraged them to invite three family members, including offspring, husband, siblings, or parents, to participate in the study. To estimate the prevalence of allergic diseases in the surrounding areas of the lake, participants from several small villages were included. Initially, the age range for participants was planned to be over 4 years old. However, after discussing with the weavers' organizations and collaborators, the age cut-off was increased to 14 years due to concerns about any possible negative effects on younger participants, even if fully explained in the informed consent. The pilot study invited 94 weavers, each representing a household, and ultimately included 292 consented (Appendix D) participants (Fig. 1).

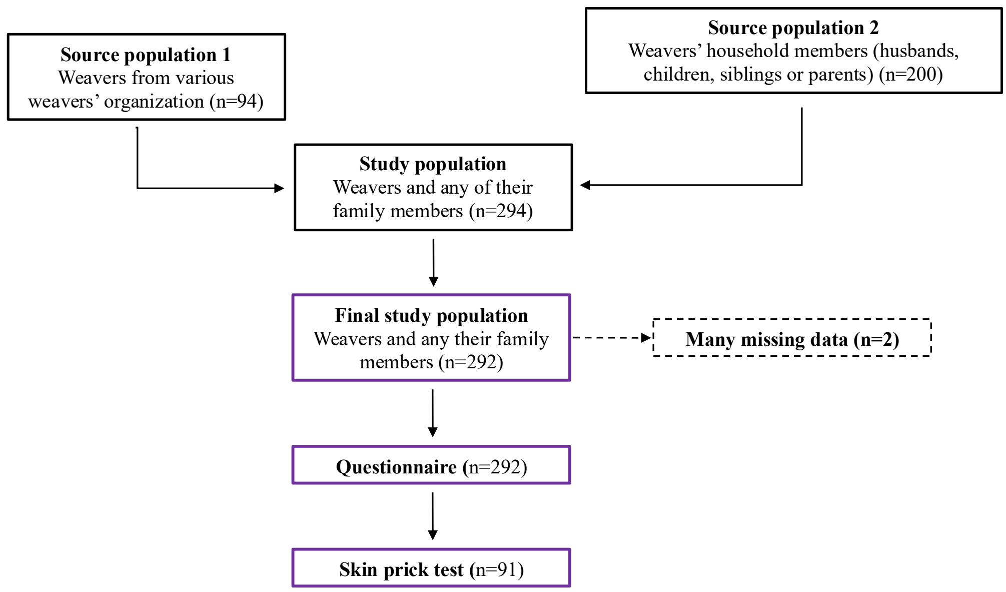

Figure 1. Flowchart depicting sample selection and completion of questionnaire and skin prick test (SPT) in the study population. Weaver organizations: Red de Defensores Comunitarios el Derecho a la Salud (REDC Salud), Red de Mujeres Estrella Tzutujil, Asociación de Mujeres Ixoq Ajqne and Fundación Tradiones Mayas.

Inclusion and exclusion criteria

The index participants for the study comprised of mainly Guatemalan female weavers who were members of a weavers' organization and residing in any village in the Solola region and were 18 years old or above. Additionally, we included family members residing in the same household as the index participant, including offspring aged 14 years or older of any gender, the husband (father of the offspring), and the weavers' parents or siblings of any gender. However, individuals with a serious health condition were excluded from participating.

Research tools

Various research tools were utilized in the implementation of this project, which was planned and developed based on the protocol employed in the Respiratory Health In Northern Europe, Spain and Australia (RHINESSA) studies in multiple countries (www.rhinessa.net). The study protocol consisted of an in-depth standardized interviewer-led questionnaire (Anni, anthropometric measurements that included height, weight, and abdominal circumference, blood pressure measurement, spirometry for assessing lung function, skin prick tests for identifying common local allergens, and the collection of blood and urine samples. The project coordinator supervised the data collection, which was conducted by a team of trained local healthcare workers.

Health workers' training

The project coordinator recruited a team of health workers from the Guatemalan region where the study was conducted. The health workers had a nursing background or similar qualifications and were fluent in both Spanish and the local indigenous languages (*i.e.,* Tzutujil or Kaqchikel). Prior to the study, the team underwent training which included didactic videos and an informative presentation on the various steps involved in the protocol. The skin prick tests were performed by a local allergologist.

Standardized interview

For the standardized interview, the project utilized questionnaires (Appendix A) that were adapted to standardised questionnaires previously used in multinational studies such as European Community Respiratory Health Survey (ECRHS), ISAAC, and RHINESSA. These were adapted to fit the requirements of the current project and different versions were created to cater to different age groups. The questionnaires included personal information such as age, gender, occupational history and duration, daily working hours, number of children, smoking habits, and family medical history. They also covered questions related to allergic symptoms, including type (*e.g.,* eczema) and frequency, as well as other physical disorders. In addition, questions were asked about chemical exposures in the participants' work and home environments, their access to and utilization of traditional and non-traditional medicines and health facilities, and, for index participants, questions about their weaving occupation. It is worth noting that not all of the collected data was analyzed and included in the current study.

The paper-based questionnaires were completed through face-to-face standardized interviews conducted by health workers. The questionnaires were translated into either Tzutujil or Kaqchikel, the two prominent local languages, by the health workers. For participants under 18 years of age, a parent or legal representative was present during the interview.

Clinical assessments

The project utilized Standard Operating Procedures (SOPs) (Appendix C) based on procedures used in the previous RHINESSA studies and with similar equipment. The SOPs were followed to measure the participants' blood pressure, height, weight, waist and hip circumference, as well as skin prick test.

Skin prick test

The primary diagnostic method for allergen skin testing in this study was the skin prick test. A local allergologist administered the test using the same allergen battery that he typically utilizes in his private clinical practice. To perform this test, droplets of 1:10 weight/volume allergen extract solutions were applied on the volar surface of the forearm, after cleaning the skin with a 70 percent alcohol solution. The allergenic extracts used in the test were standardized and labelled by potency unit, i.e., bioequivalent allergy units (BAU). Each droplet contained a single allergen extract and was placed at least 2 centimetres apart to prevent overlapping reactions. Following the application of allergens, a lancet or needle was used to make a linear excoriation in the skin. Both positive histamine dichloride (10 mg/mL for epicutaneous use) and a negative control of diluent identical to that of the allergen extracts, i.e., glycerinated saline.

Definition of positive test: When someone has a positive reaction to an allergen skin test, a raised wheal with redness around it will appear. To record the results, the largest diameter of both the wheal and the redness in millimetres is measured at 10 minutes for the histamine control and 15 minutes for the allergen extracts. In this study, a weal of 3 mm or more in diameter was generally considered to represent a positive response (indicating sensitisation to the allergen).

Fieldwork and data collection and analysis

The municipality provided a multipurpose room for the project, where various stations were set up for the execution of the protocol over the course of one week. The project was coordinated by the project coordinator, local social worker and the health care works. Participants were received in family groups and given informed consent forms (Appendix D), which were explained to them in detail in the local languages. Once the participants signed the consent forms and their questions were answered, they were guided through each of the stations to complete the four parts of the protocol (*i.e.,* questionnaire, anthropometry/blood pressure, spirometry, and bio sampling) one by one. After the protocol was completed, each participant received a financial compensation as previously agreed upon in the informed consent. Ethical concerns were considered, as well as the restrictions and recommendations announced by the local government regarding Covid-19, in order to minimize risks for the participants and health workers. The data analyses and plotting the figures in this study was performed using R Studio packages.

Ethical approval and considerations

Approval for this study was obtained from the Regional Committees for Medical and Health Research Ethics (REK nord with reference 203917) in Norway and from the Ministry of Ethics in Health in Guatemala (Reference 29-2020) (Appendix E). The project was presented to and agreed upon by local authorities and the weavers' organizations prior to protocol development and fieldwork.

Informed consent was obtained from all participants, or from a parent or guardian for participants aged 16 years or younger, after providing a thorough explanation of the study in the local languages, Tzutujil or Kaqchikel (Appendix D). As part of the informed consent process, participants were given a detailed description of the study protocol, including information about bio-sampling and data security. Participants aged 15 years and older received economic compensation (170 NOK or equivalent in local currency) to partially cover transportation expenses, meals, and any potential loss of working hours during the study visit. Compensation was provided to all participants who fully or partially participated in the project.

To ensure the security of collected information, paper-based questionnaires, consent forms, bio-samples, and SPT results were coded with unique IDs and securely stored by the project coordinator at the study site. Scanned copies of the questionnaires and consent forms, along with the SPT results, were sent to the research team in Norway through a secure file server.

Prior to initiating the study procedures, a "Getting ready questionnaire" (Appendix B) was administered to ensure that participants did not have recent respiratory infections or other conditions that could pose risks to their health, or the health of the personnel involved.

RESULTS

General characteristics of the study sample

A total of 292 participants took part in this study and were interviewed using a questionnaire administered by the health workers. All participants were given a core questionnaire, while specific sections of the questionnaire varied based on the participant's occupation as a weaver or their age group. The study population's demographic and anthropometric characteristics are presented in Table 1, with nine subgroups classified according to gender, age, weight, height, body mass index (BMI), ethnicity, education, health condition, and smoking habits.

The majority of the participants were female, with 240 (82%) women and 53 (18%) men included in the study. The median age of female participants was 34 years, ranging from 16 to 77 years old, while the median age of male participants was 32 years, ranging from 18 to 65 years old. The median height for female participants was 145 cm, ranging from 135 to 158 cm, and the median height for male participants was 154 cm, ranging from 147 to 164 cm. The median weight for both female and male participants was similar at 63 and 60 kg, respectively. However, the median body mass index (BMI) was higher for female participants (31) compared to male participants (26), indicating that the female participants had a higher prevalence of overweight status. These findings may have implications for analysing specific health outcomes. Additionally, the majority of the participants (95%) were identified as Indigenous, while only 5% were non-Indigenous.

Out of the 67 participants, who answered the question regarding the education level, 18 (27%) had no education, 26 (39%) had incomplete primary education, four (6.0%) had completed primary education, 18 (28%) had incomplete secondary education, and only 1% had completed secondary education. It is evident that the majority of the participants did not have a formal education beyond primary level. It is important to note that this data is limited in scope and may not be representative of the education level of the broader population.

The data on health conditions in the study population reveals that out of the 257 participants, 2 (0.8%) reported having heart disease, 6 (2.3%) reported a history of stroke, 4 (1.5%) reported hypertension, and 10 (4.0%) reported having diabetes. The prevalence of diabetes was higher among female participants (5.8%) than male participants (1.9%), while the prevalence of stroke was higher among male participants (5.7%) than female participants (1.7%).

The study included a larger proportion of female participants, with a relatively young median age for both females and males. The majority of participants had a BMI within the normal range, and a considerable proportion identified themselves as indigenous. The education level varied, with a higher proportion of participants having incomplete primary and secondary education. The prevalence of heart disease, stroke, and hypertension was relatively low, while diabetes was more prevalent. A small proportion (2.6%) of participants reported being smokers (Table 1).

Table 1. Characteristics and Demographics of Mayan population in the area of Lake Atitlan, Guatemala. Missing data for ethnicity (n=159); education (n=225); health conditions (n=35); and smoking (n=20).

Characteristics	Number	Median (interquartile range)	Percentage
Total	292		
Female	240		82%
Male	53		18%
Age			
Total		32 (16-77)	
Female		34 (16-77)	
Male		32 (18-65)	
Hight (cm)			
Total		146 (135-164)	
Female		145 (135-158)	
Male		154 (147-164)	
Weight (kg)			
Total		63 (46-110)	
Female		63 (46-110)	
Male		60 (49-104)	
BMI			
Total		30 (21-54)	
Female		31 (21-54)	
Male		26 (21-39)	
Indigenous			
Yes	127		95%
No	6		5%
Education			
None	18		27%
Primary incomplete	26		39%
Primary complete	4		6%
Secondary incomplete	18		27%
Secondary complete	1		1%
Health condition			
Heart disease	2		0.8%
Stroke	6		2.4%
Hypertension	4		1.5%
Diabetes	10		4.0%
Smoking	7		2.6%

Assessment of Environmental Exposures in the Study Population

This study further examined several environmental exposures, including career, home heating system, house animal, house cleaning reagents, pesticide exposure, and hand disinfectant frequency (Table 2). First, we analysed the number of women and men in the most common careers, *i.e.,* weavers, farmers as well as other occupations, such as construction workers, cooks, drivers, administrators, handcraft persons, housewives, tailors, and unemployed individuals. As expected, the majority of female participants were weavers, as this industry is popular among Mayan women.

The type of home heating system used was also investigated, and out of 135 participants who answered the associated questions, 90% (121 individuals) reported exposure to solid fuel, while only 2.3% (three individuals) reported exposure to gas fuel (Table 2). The third exposure factor examined in the study was house cleaning reagents, which encompassed four categories:

never, less than 1 per week, 1-3 times a week, and 4-7 times a week. Of the 206 participants, who answered these questions, 1% reported never using house cleaning reagents, 37.4% reported using them less than once a week, 14.5% reported using them 1-3 times a week, and 47% reported using them 4-7 times a week (Table 2).

The pesticide exposure factor included exposure at home exposure (never, sporadically, depending on season, whole year), and at work exposure (never, sporadically, depending on season, whole year). A total of 250 individuals (81%) reported being exposed to pesticides, with 48 (19%) reporting never being exposed at home, 167 (67%) reporting sporadic exposure at home, and 19 (7.6%) reporting exposure depending on the season (Table 2).

Finally, Table 2 provides data on hand disinfectant frequency, with 259 individuals (88%) reporting disinfecting their hands. Among those who reported disinfecting their hands, 14 (5%) reported never, 192 (70%) reported 1-5 times per day, 44 (16%) reported 6-10 times per day, and 13 (4.8%) reported 11-20 times per day. There were also 10 individuals (3.7%) who reported disinfecting their hands more than 20 times per day.

Table 2. The exposure characteristics in Mayan population in the area of Lake Atitlan, Guatemala. Other occupations include Construction worker, cook, driver, administrator, handcraft person, housewife, tailor and unemployed.

Exposure	Total	Female	Male
What is your career?			
Weaver	82/277	72/82	2/82
Farmer	20/277	1/20	17/20
Other	179/277	116/179	24/179
Which home heating system do you use?			
Solid fuel	121/135	110/121	11/121
Gas fuel	3/132	3/3	0
How often do you use house cleaning reagents?			
Never	2/205	2/2	0
Less than once per week	77/205	59/77	18/77
1-3 times a week	30/205	22/30	8/30
4-7 times a week	97/205	79/97	18/97
How often do you use pesticide at home?			
Total	201/249	160/201	41/201
Never	48/249	41/48	6/48
Sporadically	167/249	132/167	35/167
Depending on season	19/249	15/19	4/19
Whole year	15/249	13/15	2/15
How often do you use pesticide at work?			
Total	186/248	148/186	38/186
Never	62/248	52/62	10/62
Sporadically	160/248	127/160	33/160
Depending on season	16/248	12/16	4/16
Whole year	10/248	9/10	1/10
How often do you use hand disinfect?			
Total	259/273	210/259	49/259
Never	14/273	14/14	0
1-5 times per day	192/273	152/192	40/192
6-10 per day	44/273	36/44	8/44
11-20 times per day	13/273	12/13	1/13
>20 times per day	10/273	10/10	0

Allergic symptoms prevalence in Mayan population in Guatemala

The study conducted questionnaire-based surveys on a sample population to investigate the prevalence of various allergic conditions among different age groups and genders. The objective was to assess the prevalence of hay fever, nasal allergies, watery eyes, eczema, and itchy rash, while examining their distribution across gender and age categories.

The survey sample includes 277 participants, with 224 females and 53 males. The study revealed that hay fever was more prevalent among females (6%) respondents reporting symptoms, compared to male respondents (2%), with the highest incidence in the 31-45 years age group among females (9%) (Table 3). The data indicates that nasal symptoms are more prevalent among females, with 6% of female respondents reporting ever experiencing nasal symptoms. Similarly, in the last 12 months, 4.5% of female respondents reported experiencing nasal symptoms, compared to none of the male respondents. Nasal symptoms were also more common among females, in the 31-45 years age group, where the prevalence reached 11%.

Eczema was also more prevalent among females (10%) than males (8%), with the highest incidence in the 31-45 years age group among females (12%). Finally, the study investigated itchy rashes, both ever and in the last 12 or 6 months. The prevalence of ever itchy rash was higher among females (11%) than males (5%), with the highest incidence among females aged 31-45 years (13%). The prevalence of itchy rashes in the last 12 and 6 months was also more frequent among females, particularly on the wrist and hands, and it was reported by a small percentage of males only (Table 3).

Overall, the data suggests that allergic conditions are more prevalent in females than males, and the prevalence is highest in the 31-45 years age group for most conditions. The study also shows that eczema and itchy rash are more prevalent in females, whereas itchy rash on hands is more prevalent in males. This data provides valuable insights into the prevalence and distribution of various allergic symptoms among different age and gender groups.

Table 3. Prevalence of allergic reactions in Mayan population in the area of Lake Atitlan, Guatemala. The values in the table are the outcome out of total number of participants who answered this question. In this study, a weal of 3 mm or more in diameter is generally considered to represent a positive response (indicating sensitisation to the allergen).

	Total (all ages)	15-30 years old	31-45 years old	>45 years old
Have you ever experienced hay fever?				
Total (female and male)	15/277 (5%)	6/127 (5%)	8/101 (8%)	0/49
Female	13/224 (6%)	5/99 (5%)	8/85 (9%)	0/40
Male	1/53 (2%)	1/28 (3%)	0/16	0/9
Have you ever had nasal allergies when you did not have a cold or flu?				
Total (female and male)	13/275 (5%)	2/127 (1.5%)	9/99 (9%)	3/49 (6%)
Female	13/222 (6%)	2/99 (2%)	9/83 (11%)	3/40 (7.5%)
Male	0/53	0/28	0/16	0/9
Have you had nasal symptoms in the last 12 months?				
Total (female and male)	10/275 (4%)	2/127 (1.6%)	6/100 (6%)	2/48 (4%)
Female	10/222 (4.5%)	2/99 (2%)	6/84 (7%)	2/39 (5%)
Male	0/53	0/28	0/16	0/9
Have you ever experienced watery eyes?				
Total	7/275 (2%)	3/127 (2%)	3/100 (3%)	1/48 (2%)
Female	7/222 (3%)	3/99 (3%)	3/84 (3%)	1/39 (2%)
Male	0/53	0/28	0/16	0/9
Have you ever had eczema?				
Total (female and male)	22/264 (8%)	9/122 (7%)	10/95 (10%)	3/47 (6%)
Female	22/213 (10%)	9/94 (9%)	10/81 (12%)	3/38 (8%)
Male	0/51	0/28	0/14	0/9
Have you had eczema on your hands?				
Total (female and male)	17/271 (6%)	7/125 (6%)	7/98 (7%)	3/48 (6%)
Female	16/220 (7%)	7/97 (7%)	7/84 (8%)	2/39 (5%)
Male	1/51 (2%)	0/28	0/14	1/9 (11%)
Have you had itchy rashes in the last 12 months?				
Total (female and male)	20/207 (10%)	11/97 (11%)	6/79 (7%)	3/31 (10%)
Female	18/164 (11%)	10/76 (13%)	6/64 (9%)	2/24 (28%)
Male	2/43 (5%)	1/21 (5%)	0/15	1/7 (14%)

Allergic symptoms prevalence based on the skin prick test

In this study, we further investigated the prevalence of different types of allergies among different age and gender groups using skin prick tests. The study included five different types of allergens, namely timothy grass, cat, Ambrosia (ragweed), house dust mite (*Dermatophagoides pteronyssinus*), cockroach.

It was found that the prevalence of allergies was generally low among the study population, with the highest prevalence observed for timothy grass (8%). Notably, none of the participants tested positive for mite and ragweed allergens (Table 4 and Figure 1). Looking at the gender differences, the prevalence of timothy grass and cat allergies was slightly higher among females than males, although the difference was not substantial. However, cockroach allergy was more prevalent among males than females, with 7% of males aged 15-30 years testing positive for this allergen (Table 4). Regarding age groups, the prevalence of allergies did not vary much among different age groups for most allergens, except for timothy grass allergy, which was most prevalent among females aged 31-45 years (8%) (Table 4).

Overall, the study provides important insights into the prevalence of allergies among different age and gender groups. The results suggest that timothy grass and cat dander are the most prevalent allergens among the tested population, with the highest prevalence among females aged 31-45 years old. The absence of positive reactions to ragweed and house dust mites suggests a lower prevalence of allergies to these allergens in the tested population. It is important to note that the sample size in each age and gender group is relatively small, which may limit the generalizability of these findings.

Table 4. Skin prick test (SPT) results for common allergens in different age and gender groups in Mayan population in the area of Lake Atitlan (Guatemala) (n=91).

	Total (all ages)	**15-30 years old**	**31-45 years old**	**>45 years old**
Timothy grass (*Phleum pratense*)				
Total (Female and male)	7/91	4/35	3/43	0/13
Female	5/77	2/30	3/38	0/9
Male	2/14	2/5	0/5	0/4
Cat (*Felis catus*)				
Total (Female and male)	2/91	0/35	2/43	0/13
Female	2/77	0/30	2/38	0/9
Male	0/14	0/5	0/5	0/4
Ragweed (*Ambrosia*)				
Total (Female and male)	0/91	0/35	0/43	0/13
Female	0/77	0/30	0/38	0/9
Male	0/14	0/5	0/5	0/4
House dust mite (*D. pteronyssinus*)				
Total (Female and male)	0/91	0/35	0/43	0/13
Female	0/77	0/30	0/38	0/9
Male	0/14	0/5	0/5	0/4
Cockroach (*Blattodea*)				
Total (Female and male)	1/91	0/35	0/43	1/13
Female	0/77	0/30	0/38	0/9
Male	1/14	0/5	0/5	1/4
One or more positive SPT				
Total (Female and male)	10/91	4/35	5/43	1/13
Female	7/77	2/35	5/38	0/9
Male	3/14	2/5	0/5	1/4

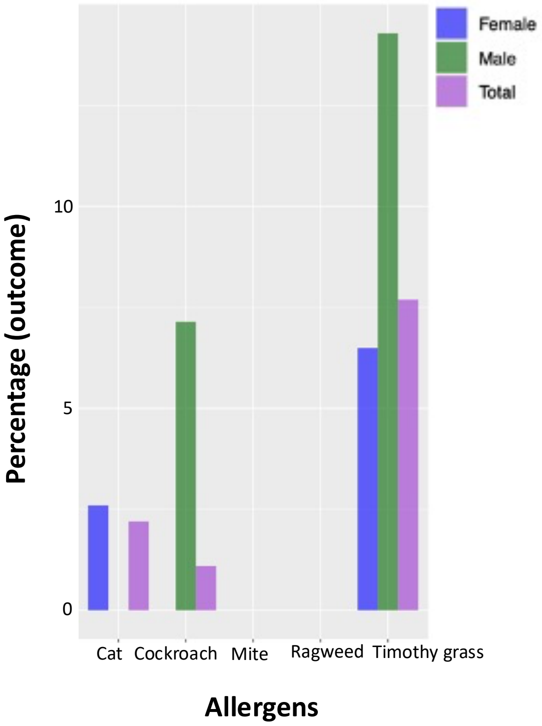

Figure 1. The prevalence of skin prick test (SPT) positivity to common respiratory allergens, including cat, cockroach, mite, ragweed, and timothy grass, among 91 participants of a Mayan population (77 females and 14 males). All participants tested negative for mite and ragweed allergens, as also shown in Table 4. Furthermore, the skin prick test for cat allergen was negative for all 14 male participants, while none of the female participants tested positive for cockroach allergen.

Allergic symptoms according to selected environmental exposures

Initially, our study aimed to investigate the potential association between various environmental (at work and home) exposures and the occurrence of allergic symptoms, *i.e.,* hay fever, nasal allergies, eczema, and itchy rashes, in the target population. However, due to the low prevalence of allergic symptoms observed in this population and small size of the population, we modified the study objective transitioning it into a descriptive study.

The study population was divided into two groups based on their occupation: the weavers' group (81 participants) and the non-weavers' group (194 participants). In the weavers' group, 6% and 9% of the participants reported experiencing hay fever and ever nasal allergies, respectively, while 5% reported watery eyes, 14% reported ever eczema, and 17% reported ever itchy rashes. In comparison, the non-weavers' group had a slightly lower prevalence of these symptoms, with 5% reporting hay fever, 4% reporting ever nasal symptoms, 2% reporting watery eyes, 7% reporting ever eczema, and 8% reporting ever itchy rashes. Overall, there is more prevalence of allergic symptoms in weavers (Figure 2A).

In addition to occupation, the study also examined the use of household cleaning products by the participants, categorizing them into four groups based on their frequency of use. Only two participants reported never using these products, and none of them reported any allergic symptoms. Among those who used the products less than once per week, 4% reported hay fever and ever nasal symptoms, 1% reported watery eyes, 4% reported ever eczema, and 13% reported ever itchy rashes. For participants who used these products 1-3 times per week, 7% reported hay fever, 4% reported ever nasal symptoms, 7% reported watery eyes, 11% reported ever eczema, and 6% reported ever itchy rashes. Among those who used these products 4-7 times per week, 7% reported hay fever and ever nasal symptoms, 4% reported watery eyes, 9% reported ever eczema, and 6% reported ever itchy rashes (Figure 2B). Generally, reported allergic symptoms were more in the participants, who use “home cleaning products”, than the ones who never such products.

The study also investigated the use of pesticides by the participants, both at home and in the workplace. Questions were categorized into four groups based on the frequency of use: never, sporadically, depending on the season, and whole year. In the "never use" category, 48 participants reported not using pesticides, and from whom 4%, 2%, 4%, 11% and 15% reported experiencing hay fever, nasal symptoms, watery eyes, eczema and itchy rashes, respectively.

For those who used pesticides sporadically, 3% reported hay fever and 4% reported ever nasal symptoms, 1% reported watery eyes, 5% reported ever eczema and 9% reported ever itchy rashes. Participants who used pesticides depending on the season reported a higher incident of allergic symptoms, with 16% reported hay fever and 11% reported ever nasal symptoms and watery eyes, while 16% reported ever eczema and 9% reported ever itchy rashes. Finally, participants who used pesticides throughout the year reported the highest incidence of allergic symptoms, with 7% reporting hay fever and 14% reporting ever nasal symptoms. Additionally, 21% reported ever eczema, while none reported ever itchy rashes (Figure 2C).

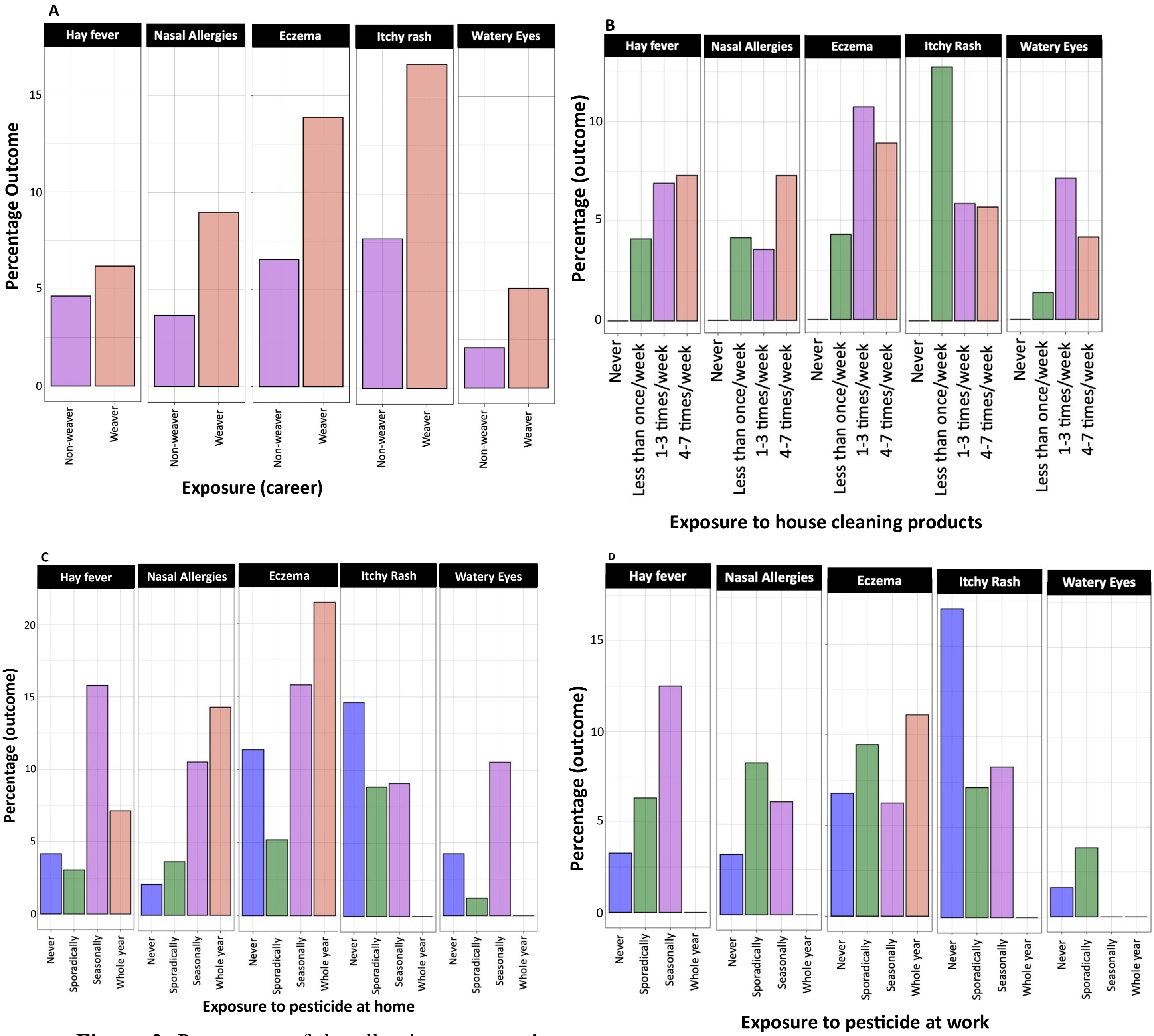

Figure 2. Percentage of the allergic symptoms' occurrence in Mayan population in the area of Lake Atitlan (all age groups and genders), Guatemala. (A) weavers vs other occupations (non-weavers); (B) Frequency of house cleaning products (*i.e.,* never; less than once per week, 1-3 times per week, and 4-7 times per week); (C) Frequency of using pesticides at home (*i.e.,* never, sporadically use, Seasonally use, and all though the year); and (D) Frequency of using pesticides at workplace (*i.e.,* never, sporadically use, Seasonally use, and all though the year).

DISCUSSION

The primary aim of this pilot study was to assess the prevalence of nasal and skin allergies, along with SPT positivity, in an indigenous population residing in the hard-to-reach area of

Lake Atitlan, Guatemala. Surprisingly, our findings revealed that both nasal and skin allergies are infrequent in this population (Tables 3 and 4; and Figure 1). This conclusion is supported by the remarkably low percentage of reported symptoms and the minimal frequencies of positive skin prick test results. Furthermore, our study provided additional insights into the environmental exposures encountered by this population, as outlined in Table 2.

Initially, our study was designed to investigate the potential impact of textile chemical exposure on women weavers and their offspring. However, due to the unforeseen circumstances arising from the Covid-19 pandemic, we were required to modify our study protocol accordingly. As a result, our study encompassed a total of 292 individuals, with an average age of 34 years, and notably, 82% of the participants were women, as indicated in Table 1. The data presented in Figure 1 and Tables 3 and 4 provides valuable insights into the prevalence of allergic symptoms within the Mayan population in Guatemala. Through the use of a questionnaire-based approach, this study aimed to assess the prevalence of hay fever, nasal allergies, watery eyes, eczema, and itchy rash across different age groups and genders. In this population, the prevalence of rhinitis is relatively low, with a rate of 5%. This falls on the lower end when compared to the wide range of prevalence observed in other regions worldwide, which can vary from 1% to over 60% (Median: 29%)[60].

The findings reveal that allergic conditions tend to be more prevalent in females compared to males, with the highest incidence observed in the 31-45 years age group for most of the assessed symptoms (Table 3). Specifically, hay fever exhibited a higher prevalence among females, particularly in the 31-45 years age group, indicating a potential age-related susceptibility to this condition (Table 3). Similarly, nasal allergies were reported more frequently in females, with a substantial prevalence of 11% observed in the 31-45 years age group. Eczema and itchy rash also displayed a higher prevalence in females compared to males. This is consistent with studies conducted on other populations, there is evidence indicating higher prevalence of allergies and allergic conditions in females compared to males. For instance, studies on allergic hay fever have consistently found a higher prevalence in women [61]. Similar gender disparities have also been observed in other allergic conditions such as eczema [62][63][64][65]. The underlying reasons for this gender difference in allergies are not fully understood, but several factors have been suggested as potential contributors. Hormonal influences have been implicated, with evidence suggesting that progesterone, androgens, and glucocorticoids may possess immunosuppressive properties, while estrogens have been shown to enhance mast cell reactivity, delayed type IV allergic reactions, humoral responses, and autoimmunity[66] [67]. Additionally, differences in environmental exposures between males and females have also been proposed as potential explanations [68]. However, the specific reasons underlying the observed differences in prevalence between genders and age groups within the Mayan population require further investigation.

To further have an insight in the prevalence of allergic symptoms, we performed SPT on 91 participants. The results of this study (Table 4 and Figure 1) provide valuable information regarding the prevalence of specific allergens among the study population. Our findings indicated that the highest prevalence of sensitivity was observed for the timothy grass allergen (8%), which is lower than other geographic regions. Among the European population, the highest prevalence of sensitization, ranges from 18.5 to 28.5%. with a median prevalence of 16.9% [69] [70] [71]. In Canada, the prevalence of sensitivity to timothy grass pollen usually varies between 20 % to 23% with a median prevalence of 22% [72]. We further found that the prevalence of sensitivity to timothy grass allergen was higher in males than females. However, we performed SPT on only 14 male participants, which is a very small sample size, and therefore, limits the generalizability of our findings. On the other hand, we found a relatively low prevalence of sensitivity to cat allergens among the Mayan population in Guatemala, which is in contrast to other studies conducted in Western countries, where the prevalence of cat allergy is reported to be 10-20% [73]. Interestingly, none of the male participants tested positive for cat allergens, whereas only 3% of female participants showed a positive SPT result for cat allergens. Similarly, none of the female participants tested positive for cockroach allergens, while 7% of male participants showed a positive SPT result for this allergen. Notably, none of the participants tested positive for house dust mite and ragweed allergens. This finding is surprising comparing to the prevalence of house dust mite allergy in many regions of the world reported to be 5-30% [74]. While this data provides valuable insights into the prevalence of specific allergens among the Mayan population in Guatemala, however, future studies with larger populations are necessary to confirm the SPT results to obtain more accurate estimates of the prevalence of allergic sensitivities in this population.

Other findings of this study which is summarised in Table 2 provides important insights into the environmental exposures of the Mayan indigenous population residing in the area of Lake Atitlan, Guatemala. The study investigated various factors that could potentially affect in development of allergic symptoms, such as career, home heating system, house cleaning reagents, pesticide exposure, and hand disinfectant frequency (Table 2). This study revealed that the majority of participants were exposed to solid fuel for heating purposes. In addition, a significant proportion of participants reported exposure to house animals, which can also trigger allergic reactions. The use of house cleaning reagents was common among the participants, with almost half reporting using them 4-7 times per week. Furthermore, the study revealed that most participants reported being exposed to pesticides, both at home and at work. Finally, the study found that most participants reported disinfecting their hands, with a significant proportion reporting doing so 6-10 times per day. This finding is not surprising given the ongoing Covid-19 pandemic and the emphasis on hand hygiene to prevent the spread of the virus.

Finally, to further evaluate the health status of this population we studied the demographic and its anthropometric characteristics. The greater proportion of female participants with overweight status, reflected in the higher median BMI (Table 1) compared to males, may have significant implications for analyzing health outcomes. In another study, it is also showed that women had nearly double the age-adjusted prevalence of obesity as men (30% vs. 17%, respectively) in the Mayan population [75]. Studies have established that overweight and obesity are key risk factors for various chronic diseases such as cardiovascular diseases and diabetes [76] [77]. Consequently, the higher proportion of overweight females in the study population may increase their risk of long-term health complications. Further follow-up studies will be necessary to explore the potential relationship between overweight status and long-term health outcomes among this population. Interestingly, the prevalence of heart disease, stroke, and hypertension was relatively low, while diabetes was more prevalent among the study population (4%), with higher prevalence among female participants (Table 1). This finding is not consistent with the study by [75] conducted in similar settings and population that have reported a high prevalence of these diseases among the two indigenous municipalities in rural Guatemala in a population-representative survey. They reported the crude prevalence of diabetes was 12.5%, hypertension 20.3%, obesity 23.7%. In our target population, the low prevalence of heart disease, stroke, and hypertension may be due to underdiagnosis or lack of access to healthcare in the study population.

It is important to note that this study has various limitations such as its cross-sectional design, which does not allow for the establishment of a causal relationship between the studied factors and the observed allergic symptoms. Furthermore, the sample size was relatively small, and the study was limited to a specific geographic region and ethnic group. Therefore, the findings may not be generalizable to other populations. Additionally, the study relied on self-reported symptoms, which could be subject to recall bias or misinterpretation, in particular, due to the translation from Spanish to the local languages. Further research is needed to confirm these findings in larger and more diverse populations.

The study encountered numerous practical limitations and obstacles due to the fact that this is a hard-to-reach population, and the Covid-19 pandemic situation made it even more difficult. Our inability to travel to the study site posed a significant challenge, hindering our ability to gain a thorough understanding of the area and its population. During the study's preparation and fieldwork, we relied heavily on the Guatemalan project coordinator to perform crucial activities. Consequently, we missed out on first-hand knowledge of the population's characteristics, social environment, and cultural experience during our study fieldwork. Nevertheless, our collaborators assisted us in comprehending our study population and the challenges associated with working with a new culture.

Another limitation of this study was the insufficient training sessions for the field workers on the use of assessment tools, including questionnaires, due to our inability to be present at the study site, posed another limitation to this study. Although we provided interactive videos with detailed explanations of the procedures, and all field workers had prior experience in health facilities, specific sensitization to the questionnaires was necessary. This included training on the proper translation of medical terms into local languages, as well as more intensive training on the standard procedures for medical equipment use.

Furthermore, during the data analysis, we identified suboptimal continuous quality control of procedures at the study site, which may have been resolved had we been physically present. These issues were evident in missing data in the interviews and the misinterpretation of questions. Although we customized the questionnaire based on feedback from our Guatemalan collaborators and translated it into local languages, they faced challenges in fully comprehending some of the exposures and allergic symptoms. The questionnaire's complexity, combined with the translation of complex medical terms from Spanish to the local languages, contributed to these difficulties. As a result, we may have underestimated the true prevalence of allergic symptoms in the target population and difficult to study the exposure and outcome associations. This, in turn, reduced the possibility of providing useful recommendations as feedback to the participants.

To further improve future studies, a larger and more diverse sample size should be recruited to increase the generalizability of the findings. Additionally, more considerations are required in using bilingual and culturally competent staff to ensure accurate translation and interpretation of study materials. Finally, a longitudinal study design may provide more insight into the temporal relationship between environmental exposures and the development of allergic symptoms.

Despite the limitations, this study provides valuable insights into the prevalence and distribution of various allergic symptoms among different age and gender groups in one of the Mayan indigenous populations in Latin America. Further, these findings are particularly significant as little is currently known about this population's allergic disease. It is important to note that allergic diseases represent a burden on public health worldwide. The increasing prevalence of allergic conditions is a major public health challenge, particularly in low-income countries. Such information is essential for developing effective prevention and treatment strategies for allergic diseases in this population, and further, they may help to inform public health efforts aimed at reducing the burden of allergic disease in this population. Overall, this study highlights the need for more research in this field and the importance of public health interventions to reduce the burden of allergic diseases in vulnerable and hard-to-reach populations.

COMPETING INTEREST

The research team declares no conflicts of interest.

AUTHORS CONTRIBUTION

CS, ALR, SMN, and JPLC contributed to the study design. ALR and FJ facilitated collaboration and communication with the weavers' organizations and community leaders in Guatemala. FJ collected the data at the study site, while SMN and JPLC processed the data. SMN analysed the data for the allergy study and drafted the manuscript. CS supervised the study and provided manuscript revisions.

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6 REFERENCES*

1 Stróżek J, Samoliński B, Kłak A, *et al.* The indirect costs of allergic diseases. *International Journal of Occupational Medicine and Environmental Health* 2019;**32**:281–90. doi:10.13075/ijomeh.1896.01275

2 Blaiss, MS, Canonica, GW, Holgate, ST, Lockey, RF and Pawankar R. *White Book on Allergy (Update: 2013)*. 2013

3 Pawankar R. Allergic diseases and asthma: A global public health concern and a call to action. *World Allergy Organization Journal* 2014;**7**:1–3. doi:10.1186/1939-4551-7-12

4 Zuberbier T, Lötvall J, Simoens S, *et al.* Economic burden of inadequate management of allergic diseases in the European Union: A GA2LEN review. *Allergy: European Journal of Allergy and Clinical Immunology* 2014;**69**:1275–9. doi:10.1111/all.12470

5 Organization WH. Chronic Respiratory. *WHO Library* 2007;:1–37. doi:ISBN 978 92 4 156346 8

6 Neffen H, Sole D and MJ. Rinitis ale´rgica en Latino- ame´ rica. Manejo actual y estratrategias para la adopcio´ n de guías de diagnostico y tratamiento. *Drugs Today* 2009;**45**:1–19.

7 Arshad SH. Indoor allergen exposure in the development of allergy and asthma. *Current Allergy and Asthma Reports* 2003;**3**:115–20. doi:10.1007/s11882-003-0023-8

8 Nathan RA, Meltzer EO, Derebery J, *et al.* The prevalence of nasal symptoms attributed to allergies in the United States: Findings from the burden of rhinitis in an America survey. *Allergy and Asthma Proceedings* 2008;**29**:600–8. doi:10.2500/aap.2008.29.3179

9 Cepeda AM, Thawer S, Boyle RJ, *et al.* Diet and Respiratory Health in Children from 11 Latin American Countries: Evidence from ISAAC Phase III. *Lung* 2017;**195**:683–92. doi:10.1007/s00408-017-0044-z

10 Alvarez-Alvarez I, Niu H, Guillen-Grima F, *et al.* Meta-analysis of prevalence of wheezing and recurrent wheezing in infants. *Allergologia et Immunopathologia* 2018;**46**:210–7. doi:10.1016/j.aller.2016.08.011

11 Endara P, Vaca M, Platts-Mills TAE, *et al.* Effect of urban vs. rural residence on the association between atopy and wheeze in Latin America: Findings from a case-control analysis. *Clinical and Experimental Allergy* 2015;**45**:438–47. doi:10.1111/cea.12399

12 Baldacci S, Maio S, Cerrai S, *et al.* Allergy and asthma: Effects of the exposure to particulate matter and biological allergens. *Respiratory Medicine* 2015;**109**:1089–104. doi:10.1016/j.rmed.2015.05.017

13 Sénéchal H, Visez N, Charpin D, *et al.* A review of the effects of major atmospheric pollutants on pollen grains, pollen content, and allergenicity. *Scientific World Journal* 2015;**2015**. doi:10.1155/2015/940243

14 D'Amato G, Liccardi G, D'Amato M, *et al.* Outdoor air pollution, climatic changes and allergic bronchial asthma. *European Respiratory Journal* 2002;**20**:763–76. doi:10.1183/09031936.02.00401402

15 Y. Nitta MAMS. Air Pollution and Respiratory in Chiba Prefecture, Japan Symptoms in Children Living along Trunk Roads. *Journal of Epidemiology* 2003;**13**:108–19.

16 Hasunuma H, Ishimaru Y, Yoda Y, *et al.* Decline of ambient air pollution levels due to measures to control automobile emissions and effects on the prevalence of respiratory and allergic disorders among children in Japan. *Environmental Research* 2014;**131**:111–8. doi:10.1016/j.envres.2014.03.007

17 Pénard-Morand C, Charpin D, Raherison C, *et al.* Long-term exposure to background air pollution related to respiratory and allergic health in schoolchildren. *Clinical and Experimental Allergy* 2005;**35**:1279–87. doi:10.1111/j.1365-2222.2005.02336.x

18 Provoost S, Maes T, Willart MAM, *et al.* Diesel Exhaust Particles Stimulate Adaptive Immunity by Acting on Pulmonary Dendritic Cells. *The Journal of Immunology* 2010;**184**:426–32. doi:10.4049/jimmunol.0902564

19 Wenzel S. Severe asthma: From characteristics to phenotypes to endotypes. *Clinical and Experimental Allergy* 2012;**42**:650–8. doi:10.1111/j.1365-2222.2011.03929.x

20 Valavanidis A, Fiotakis K, Vlahogianni T, *et al.* Characterization of atmospheric particulates, particle-bound transition metals and polycyclic aromatic hydrocarbons of urban air in the centre of Athens (Greece). *Chemosphere* 2006;**65**:760–8. doi:10.1016/j.chemosphere.2006.03.052

21 Franck U, Herbarth O, Röder S, *et al.* Respiratory effects of indoor particles in young children are size dependent. *Science of the Total Environment* 2011;**409**:1621–31. doi:10.1016/j.scitotenv.2011.01.001

22 Brandt EB, Biagini Myers JM, Ryan PH, *et al.* Air pollution and allergic diseases. *Current Opinion in Pediatrics* 2015;**27**:724–35. doi:10.1097/MOP.0000000000000286

23 Tariq SM, Hakim EA, Matthews SM, *et al.* Influence of smoking on asthmatic symptoms and allergen sensitisation in early childhood. *Postgraduate Medical Journal* 2000;**76**:694–9. doi:10.1136/pmj.76.901.694

24 Brooks AM, Byrd RS, Weitzman M, *et al.* Impact of low birth weight on early childhood asthma in the United States. *Archives of Pediatrics and Adolescent Medicine* 2001;**155**:401–6. doi:10.1001/archpedi.155.3.401

25 Henderson AJ, Sherriff A, Northstone K, *et al.* Pre- and postnatal parental smoking and wheeze in infancy: Cross cultural differences. *European Respiratory Journal* 2001;**18**:323–9. doi:10.1183/09031936.01.00012401

26 Melsom T, Brinch L, Hessen JO, *et al.* Asthma and indoor environment in Nepal. *Thorax* 2001;**56**:477–81. doi:10.1136/thorax.56.6.477

27 Kilpeläinen M, Koskenvuo M, Helenius H, *et al.* Stressful life events promote the manifestation of asthma and atopic diseases. *Clinical and Experimental Allergy* 2002;**32**:256–63. doi:10.1046/j.1365-2222.2002.01282.x

28 Mommers M, Jongmans-Liedekerken AW, Derkx R, *et al.* Indoor environment and respiratory symptoms in children living in the Dutch-German borderland. *International Journal of Hygiene and Environmental Health* 2005;**208**:373–81. doi:10.1016/j.ijheh.2005.04.007

29 Iribarren C, Friedman GD, Klatsky AL, *et al.* Exposure to environmental tobacco smoke: Association with personal characteristics and self reported health conditions. *Journal of Epidemiology and Community Health* 2001;**55**:721–8. doi:10.1136/jech.55.10.721

30 Al-Dawood K. Parental smoking and the risk of respiratory symptoms among schoolboys in Al-Khobar City, Saudi Arabia. *Journal of Asthma* 2001;**38**:149–54. doi:10.1081/JAS-100000033

31 Miyake Y, Miyamoto S, Ohya Y, *et al.* Association of active and passive smoking with allergic disorders in pregnant Japanese women: Baseline data from the Osaka Maternal and Child Health Study. *Annals of Allergy, Asthma and Immunology* 2005;**94**:644–51. doi:10.1016/S1081-1206(10)61322-1

32 Sturm JJ, Yeatts K, Loomis D. Effects of Tobacco Smoke Exposure on Asthma Prevalence and Medical Care Use in North Carolina Middle School Children. *American Journal of Public Health* 2004;**94**:308–13. doi:10.2105/AJPH.94.2.308

33 Chai SK, Nga NN, Checkoway H, *et al.* Comparison of local risk factors for children's atopic symptoms in Hanoi, Vietnam. *Allergy: European Journal of Allergy and Clinical Immunology* 2004;**59**:637–44. doi:10.1111/j.1398-9995.2004.00463.x

34 Xu F, Yan S, Wu M, *et al.* Ambient ozone pollution as a risk factor for skin disorders. *British Journal of Dermatology* 2011;**165**:224–5. doi:10.1111/j.1365-2133.2011.10349.x

35 Burke H, Leonardi-Bee J, Hashim A, *et al.* Prenatal and passive smoke exposure and incidence of asthma and wheeze: Systematic review and meta-analysis. *Pediatrics* 2012;**129**:735–44. doi:10.1542/peds.2011-2196

36 Been J, Nurmatov UB, Cox B, *et al.* Effect of smoke-free legislation on perinatal and child health: A systematic review and meta-analysis. *The Lancet* 2014;**383**:1549–60. doi:10.1016/S0140-6736(14)60082-9

37 Kantor R, Kim A, Thyssen J, *et al.* Association of atopic dermatitis with smoking: A systematic review and meta-analysis. *J Am Acad Dermatol* 2017;**75**:1119–25. doi:10.1016/j.jaad.2016.07.017.Association

38 Kim SY, Sim S, Choi HG. Atopic dermatitis is associated with active and passive cigarette smoking in adolescents. *PLoS ONE* 2017;**12**:1–11. doi:10.1371/journal.pone.0187453

39 Shinohara M, Matsumoto K. Fetal Tobacco Smoke Exposure in the Third Trimester of Pregnancy Is Associated with Atopic Eczema/Dermatitis Syndrome in Infancy. *Pediatric, Allergy, Immunology, and Pulmonology* 2017;**30**:155–62. doi:10.1089/ped.2017.0758

40 Renz H, Allen KJ, Sicherer SH, *et al.* Food allergy. *Nature Reviews Disease Primers* 2018;**4**. doi:10.1038/nrdp.2017.98

41 Moonesinghe H, Mackenzie H, Venter C, *et al.* Prevalence of fish and shellfish allergy: A systematic review. *Annals of Allergy, Asthma and Immunology* 2016;**117**:264-272.e4. doi:10.1016/j.anai.2016.07.015

42 Takano H, Inoue KI. Environmental pollution and allergies. *Journal of Toxicologic Pathology* 2017;**30**:193–9. doi:10.1293/tox.2017-0028

43 Schoemaker AA, Sprikkelman AB, Grimshaw KE, *et al.* Incidence and natural history of challenge-proven cow's milk allergy in European children - EuroPrevall birth cohort. *Allergy: European Journal of Allergy and Clinical Immunology* 2015;**70**:963–72. doi:10.1111/all.12630

44 Osborne NJ, Koplin JJ, Martin PE, *et al.* Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *Journal of Allergy and Clinical Immunology* 2011;**127**:668-676.e2. doi:10.1016/j.jaci.2011.01.039

45 Peters RL, Koplin JJ, Gurrin LC, *et al.* The prevalence of food allergy and other allergic diseases in early childhood in a population-based study: HealthNuts age 4-year follow-up. *Journal of Allergy and Clinical Immunology* 2017;**140**:145-153.e8. doi:10.1016/j.jaci.2017.02.019

46 Kay A. Allery AND allergic diseases. *The New England Jornal of Medicine* 2001;**344**:30–7.

47 Uzzaman A, Cho SH. Classification of hypersensitivity reactions. *Allergy and Asthma Proceedings* 2012;**33**:96–9. doi:10.2500/aap.2012.33.3561

48 Delves PJ. Overview of Allergic and Atopic Disorders - Immunology; Allergic Disorders. Merck Manuals Professional Edition. 2019;:1–13.https://www.merckmanuals.com/professional/immunology-allergic-disorders/allergic,-autoimmune,-and-other-hypersensitivity-disorders/overview-of-allergic-and-atopic-disorders

49 Ansotegui IJ, Melioli G, Canonica GW, *et al.* IgE allergy diagnostics and other relevant tests in allergy, a World Allergy Organization position paper. *World Allergy Organ J* 2020;**13**:100080. doi:10.1016/j.waojou.2019.100080

50 Checkley W, Ghannem H, Irazol V, *et al.* Management of Noncommunicable Disease in Low- and Middle- Income Countries. *Global Heart* 2014;**9**:431–43. doi:10.1016/j.gheart.2014.11.003.Management

51 Health in Gualtemala. ;:(https://data.worldbank.org/indicator/SP.DYN.LE00.

52 Albala C, Vio F, Yáñez M. Epidemiological transition in Latin America: a comparison of four countries. *Rev Med Chil* 1997;**125**:719–27.

53 Marini A, Gragnolati M. *Malnutrition and Poverty in Guatemala*. 2003.

54 Ruano AL. *The role of social participation in municipal-level health systems: the case of Palencia, Guatemala*. 2012.

55 Baena-Cagnani CE, Canonica GW, Zaky Helal M, *et al.* The international survey on the management of allergic rhinitis by physicians and patients (ISMAR). *World Allergy Organ J* 2015;**8**:10. doi:10.1186/s40413-015-0057-0

56 Neffen HE. How can we improve the management of allergic rhinitis in Latin America? *Allergy Asthma Proc* 2010;**31**:S5–6.

57 Cepeda AM, Thawer S, Boyle RJ, *et al.* Diet and Respiratory Health in Children from 11 Latin American Countries: Evidence from ISAAC Phase III. *Lung* 2017;**195**:683–92. doi:10.1007/s00408-017-0044-z

58 Baldacci S, Maio S, Cerrai S, *et al.* Allergy and asthma: Effects of the exposure to particulate matter and biological allergens. *Respir Med* 2015;**109**:1089–104. doi:10.1016/j.rmed.2015.05.017

59 Brandt EB, Myers JMB, Ryan PH, *et al.* Air pollution and allergic diseases. *Curr Opin Pediatr* 2015;**27**:724–35. doi:10.1097/MOP.0000000000000286

60 Savouré M, Bousquet J, Jaakkola JJK, *et al.* Worldwide prevalence of rhinitis in adults: A review of definitions and temporal evolution. *Clin Transl Allergy* 2022;**12**:e12130. doi:10.1002/clt2.12130

61 Oliveira TB, Persigo ALK, Ferrazza CC, *et al.* Prevalence of asthma, allergic rhinitis and pollinosis in a city of Brazil: A monitoring study. *Allergol Immunopathol (Madr)* 2020;**48**:537–44. doi:10.1016/j.aller.2020.03.010

62 Shaw TE, Currie GP, Koudelka CW, *et al.* Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. *J Invest Dermatol* 2011;**131**:67–73. doi:10.1038/jid.2010.251

63 Silverberg JI, Hanifin JM. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. *J Allergy Clin Immunol* 2013;**132**:1132–8. doi:10.1016/j.jaci.2013.08.031

64 Barbarot S, Auziere S, Gadkari A, *et al.* Epidemiology of atopic dermatitis in adults: Results from an international survey. *Allergy* 2018;**73**:1284–93. doi:10.1111/all.13401

65 Al-Naqeeb J, Danner S, Fagnan LJ, *et al.* The Burden of Childhood Atopic Dermatitis in the Primary Care Setting: A Report from the Meta-LARC Consortium. *J Am Board Fam Med* 2019;**32**:191–200. doi:10.3122/jabfm.2019.02.180225

66 Nowak-Wegrzyn A, Ellis A, Castells M. Sex and allergic diseases. Ann Allergy Asthma Immunol. 2019;**122**:134–5. doi:10.1016/j.anai.2018.12.010

67 Ciccarelli F, De Martinis M, Ginaldi L. Glucocorticoids in patients with rheumatic diseases: friends or enemies of bone? *Curr Med Chem* 2015;**22**:596–603. doi:10.2174/0929867321666141106125051

68 Bereshchenko O, Bruscoli S, Riccardi C. Glucocorticoids, Sex Hormones, and Immunity. *Front Immunol* 2018;**9**:1332. doi:10.3389/fimmu.2018.01332

69 Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, *et al.* EAACI Molecular Allergology User's Guide. *Pediatr Allergy Immunol* 2016;**27 Suppl 2**:1–250. doi:10.1111/pai.12563

70 Pablos I, Wildner S, Asam C, *et al.* Pollen Allergens for Molecular Diagnosis. *Curr Allergy Asthma Rep* 2016;**16**:31. doi:10.1007/s11882-016-0603-z

71 Newson RB, van Ree R, Forsberg B, *et al.* Geographical variation in the prevalence of sensitization to common aeroallergens in adults: the GA(2) LEN survey. *Allergy* 2014;**69**:643–51. doi:10.1111/all.12397

72 Chan-Yeung M, Anthonisen NR, Becklake MR, *et al.* Geographical variations in the prevalence of atopic sensitization in six study sites across Canada. *Allergy* 2010;**65**:1404–13. doi:10.1111/j.1398-9995.2010.02399.x

73 Chan SK, Leung DYM. Dog and Cat Allergies: Current State of Diagnostic Approaches and Challenges. *Allergy Asthma Immunol Res* 2018;**10**:97–105. doi:10.4168/aair.2018.10.2.97

74 Aggarwal P, Senthilkumaran S. Dust Mite Allergy. Treasure Island (FL): 2023.

75 Steinbrook E, Flood D, Barnoya J, *et al.* Prevalence of Hypertension, Diabetes, and Other Cardiovascular Disease Risk Factors in Two Indigenous Municipalities in Rural Guatemala: A Population-Representative Survey. *Glob Heart* 2022;**17**:82. doi:10.5334/gh.1171

76 Kearns K, Dee A, Fitzgerald AP, *et al.* Chronic disease burden associated with overweight and obesity in Ireland: the effects of a small BMI reduction at population level. *BMC Public Health* 2014;**14**:143. doi:10.1186/1471-2458-14-143

77 Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. *BMC Med* 2021;**19**:320. doi:10.1186/s12916-021-02188-x

7 APPENDIXES LIST

Appendix A – Standardized core and secondary questionnaire (English)

Appendix B – “Getting ready questionnaire/Results form” (English)

Appendix C – Standard Operation Procedure (English)

Appendix D – Informed consent (English)

Appendix E – Ethics committee approval (Norway and Guatemala)

Note-The Spanish versions of Appendixes A, B, C and D, translated by Juan Pablo Lopez Cervantes, are also available but not included in this thesis.