Original Research Article

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Prevalence of work-related asthma among Egyptian farmers in Great Cairo

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Abstract

Work related asthma (WRA) refers to asthma induced by exposure to sensitizing agents and/or irritants in the workplace leaving health and economic consequences. Early diagnosis can improve the prognosis of WRA permitting sometimes full recovery. This study aimed to assess the prevalence of WRA among Egyptian adult agriculture workers. A multi-center cross sectional study included 150 adult workers from 4 different farms, during the period from 2019 and 2021. All participants were subjected to full medical history, clinical examination, chest x-ray, skin prick test and CBC to detect absolute eosinophilic count. Spirometry with post bronchodilatation test (reversibility test) at the farm (in the day of insecticide aerosol and without aerosol) and after a week off the farm was also done. Age, median ± SD, was 37.67 ± 9.75 years, duration of farming occupation was 21.84 ± 10.18 years. Of the 150 participants, 11 had WRA. Of these, 6 had allergic occupational asthma, 3/11 had work exacerbated asthma and only 2/11 had irritant occupational asthma. Of the allergic subjects, 7.3% tested positive to mixed pollens, 4.7% to *Alternaria*, 2% to penicillium and 2% to the farm pollens. The onset of respiratory symptoms was 13.45 ± 6.93 months after start working in the farm. A statistical significance was observed between WRA and non-WRA individuals regarding age, duration of farming occupation and asthma symptoms during workday (P <0.001). There was a statistical significance between WRA group and non-WRA group regarding FEV1, FEV1/FVC ratio carried out at work, during holidays and during spraying (P <0.001). Absolute eosinophilic count, mean among WRA group was 0.55 ± 0.13 ($\times 10^3$cells/mm^3) with significance between WRA and non-WRA (P= 0.001). Farming occupation may cause WRA, therefore, more attention should be given to minimize exposure and risk of inducing WRA.

Keywords: Work Related Asthma, Farming, Occupational Asthma.

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Introduction

Work related asthma (WRA) refers to asthma induced or exacerbated by sensitizers or irritants at workplace.[1] WRA involves two different entities occupational asthma and work exacerbated asthma. Occupational asthma is characterized by variable airflow limitations induced by different factors confined to the workplace environment.[2] Occupation asthma (OA) may be caused by sensitizing agents with latency period and called allergic OA[3] or can be without latency period due to single high exposure to irritants including vapors, aerosols or gases and called non allergic or irritants OA.[4] Allergic OA is triggered by wide numbers of high molecular weight (HMW) and low molecular weight (LMW) antigens.[5] HMW agents include proteins derived from animals, plants, fungi, and enzymes.[6] They act as complete antigens able to induce T helper 2 response with secretion of interleukins IL4, IL5, IL13 leading to allergen-specific immunoglobulin E (IgE) antibodies. Later, at the second exposure to the same allergens, basophils and mast cells loaded with IgE start to degranulate with release of mediators leading to asthma symptoms.[7] LMW agents include acid anhydrides and platinum salts which act as incomplete antigens (haptens), which need to bind to heterologous or autologous proteins, induce complete immune response.[8] Diagnosis of OA include detailed medical history of asthma symptoms worsened or induced at workplace and after exposure to agents that is known to induce asthma, deterioration of forced expiratory volume1 (FEV1) or peaked expiratory flow (PEF) at workplace in contrast to periods away from work.[9] Serial measurements of bronchial hyperresponsiveness to methacholine or histamine challenge are useful for WRA diagnosis.[10] Evaluation of sputum eosinophils using induced sputum techniques are found to be a good noninvasive procedure to detect airway eosinophilic inflammation in WRA.[11] The current study aimed to assess the prevalence of WRA among agriculture adult workers in great Cairo area.

Subjects and Methods

This cross-sectional study involved 150 adult workers ≥ 18 years old from four different farms, two grape farms and two strawberry farms, in great Cairo in the period from 2019 to 2021.

Exclusion criteria

Patients with history of chronic obstructive pulmonary disease (COPD) or history of smoking two packs cigarettes per day for 20 years or more were excluded from the study. Patients with history of dermographism or drugs interfere with skin pick test (SPT) results such as on antihistamines were also excluded.

Ethical approval

The study protocol was reviewed and approved by the Ethical Committee of the Faculty of Medicine, Ain Shams University (Approval No. FMASU MD 110/2019). A written informed consent was obtained from each participant included in our study.

Methods

Each participant was subjected to detailed medical questionnaire, including history of pre-existing asthma, symptoms suggestive of asthma including wheezes, dyspnea, and chest tightness induced during the work periods and improved during weekends or holidays and symptoms of asthma developed during spraying days,[12] smoking history with determination of smoking index[13] and history of other associated atopic diseases. Clinical examination and laboratory tests including, asthma control test (ACT) determined according to the Global Initiative on Asthma (GINA) guidelines,[14] complete blood count (CBC) for detection of absolute eosinophilic count, SPT for common aeroallergens and farm allergens, spirometry with bronchodilator was also done at workplace, during vacations and at spraying days.

Spirometry

The appropriate technique was explained to all participants before the test. Age, weight, and height of all subjects were determined then we instructed them to take full inhalation before beginning the forced exhalation.[15] Spirometry was performed at the workplace, after one week away from the work and during insecticide spray day with determination of the first second of forced expiration (FEV1), FEV1/ FVC (forced vital capacity) then all participants were subjected to spirometry with bronchodilatation test for 15 minutes after we asked them to inhale four puffs of 100 µg salbutamol *via* metered dose inhaler. The test was considered positive if there was ≥ 12% in FEV1 baseline values.[16]

Skin prick test (SPT)

We used a standardized SPT panel provided by Hamilton (Omega, Allergy OVERSEAS consultants Inc, Canada). Drops of tested allergen were placed on the volar aspect of the forearm then we did skin prick using a lancet and, the test results were interpreted after 20 minutes. The test was positive when SPT resulted in a wheal with diameter ≥ 3 mm.[17] Common environment aeroallergens involved in the test were Molds including (*Alternaia*, aspergillosis, penicillium, *Cladosporium*), Mites (*Tyrophagus putrescentiae*, *Dermatophagoides farinae*, *Dermatophagoides pteronyssoides*) and extract of mixed pollens. We also prepared and tested extracts from the farm corps at the Allergy Laboratory, Ain Shams University and used positive and negative controls.

Preparation of the farm pollen extract

The plants leaves and, flowers were washed then left to dry for two days at temperature 48^{o}C. Defatting by diethyl ether was done. This was followed by soaking plant leaves and flowers in a solution made of 0.5% sodium chloride, 0.25% sodium bicarbonate and 0.4% phenol, in a ratio of 1 gram of the plant to 9 ml of the solution, then left for incubation for two days at temperature of 2-8 ^{o} C. The obtained solution was filtered by filter paper followed by filtration through Seitz filter (microbiological filter) for removal of microorganisms.[18]

Statistical analysis

Collected data were revised, coded, tabulated, and introduced to a PC using the Statistical Package for Social Sciences (SPSS 25). Data were presented and analyzed according to the type of data obtained for each parameter. Regarding descriptive statistics, mean ± standard deviation and range are presented for numerical data, whereas non numerical data are presented as percentage and frequency. The chi-squared test was used to examine the relation between two qualitative variables. Student T test was used to access the significance between two groups mean. A $p \leq 0.05$ was considered statistically significant. Fisher test was used to examine relation between two variables when the count was less than 5 in more than 20 % of cells.

Results

All 150 cases recruited in this study were males and their mean age was 37.67 ± 9.75 years. Of these, 138 (92.7%) participants were farmers and most of them were nonsmokers (62.7%) with smoking index 8.72 ± 4.39 pack/year. Regarding previous history of other atopic diseases, 6 patients (4%) had allergic rhinitis while only 2 (1.3%) reported history of asthma. The overall mean time of working in farms was 21.84 ± 10.18 years.

Out of 150 cases, 11 (7.3%) were diagnosed as WRA. According to the WRA sub-types, allergic OA was the most frequent (54.5%, n=6), followed by work-exacerbated asthma (WEA) (27.3%, n=3) and only 2 participants had irritant OA (18.2%, n=2) Figure 1. Their mean time of work at the current farm was 4.91±2.02 years. They reported asthma symptoms 78.18 ± 41.91 minutes daily after starting the working day.

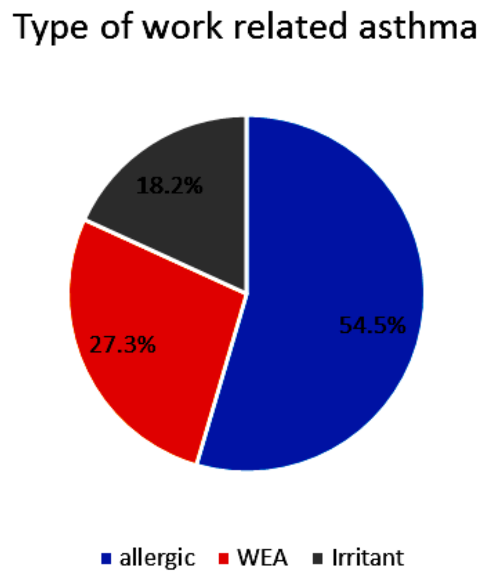

Figure 1. Subtypes of work-related asthma.

All the WRA group reported improvement in their respiratory symptoms at home. The mean duration of respiratory symptoms since they started working at the farms was 13.45 ± 6.93 months. Respiratory symptoms usually started after 78.18 ± 41.91 minutes during working days. The mean score of ACTs was 14.55 ± 5.07.

The age and duration of working in the farm were significantly different between WRA and non-WRA individuals (P <0.001). Symptoms suggestive of asthma during workday including wheeze, cough, dyspnea during work, and presence of wheeze during examination at work were also significantly different between WRA and non-WRA individuals (P <0.001). Table 1 shows comparison of studied parameters between WRA and non-WRA individuals including peripheral eosinophilia count and, SPT of different studied pollens.

Table 1. Comparison between work related asthma (WRA) group and non WRA group

Item		Non WRA Mean ± SD	WRA Mean ±SD	*P*-value (Student t test)
Age		38.42 ± 9.7	28.27±3.41	<0.001
Duration in the farming industry (years)		23.2 ± 9.36	4.91±2.02	<0.001
Duration of work at the current farms (years)		5.1 ± 2.7	4.91±2.02	NS
Smoking index (pack/ year)		8.91 ± 4.34	3.5 ± 2.12	NS
Symptoms suggestive of asthma		N (%)	N (%)	*P*-value
Wheeze at work (symptom)	No	139(95.86%)	6 (4.14%)	<0.001
	Yes	0 (0%)	5 (100%)	
Cough at work	No	138 (95.83%)	6 (4.17%)	<0.001
	Yes	1 (16.67%)	5 (83.33%)	
Dyspnea at work	No	119 (100%)	0 (0%)	<0.001
	With effort	20 (71.43%)	8 (28.57%)	
	With effort and rest	0 (0%)	3 (100%)	
Asthmatic attack during work	No	139 (100%)	0 (0%)	<0.001
	Yes	0 (0%)	11 (100%)	
Wheeze at work (sign)	No	139 (97.18%)	4 (2.8%)	<0.001
	Yes	0 (0%)	7 (100%)	
	Non WRA Mean ± SD	WRA Mean ± SD	*P*-value Student t-test	
Absolute eosinophils ($\times 10^3$cells/mm^3)	0.18±0.09	0.48±0.21	0.001	
Pollen type		No N (%)	Yes N (%)	*P*-value Fisher's Exact test
Alternaria	No	135 (94.41%)	8 (5.59%)	0.009
	Yes	4 (57.14%)	3 (42.86%)	
Mixed pollens	No	135 (97.12%)	4 (2.88%)	<0.001
	Yes	4 (36.36%)	7 (63.64%)	
Penicillium	No	137 (93.2%)	10 (6.8%)	NS
	Yes	2 (66.67%)	1 (33.33%)	
Cladosporium	No	138 (92.62%)	11 (7.38%)	NS
	Yes	1 (100%)	0 (0%)	
Farm pollens	No	137 (93.2%)	10 (6.8%)	NS
	Yes	2 (66.67%)	1 (33.33%)	

P value > 0.05 is not significant (NS)

Spirometry results done at workplace showed a statistical significance difference between WRA group and non WRA group regarding FEV1, FEV1/FVC and post bronchodilator FEV1 values (P<0.001). All spirometry results, compared between WRA and non-WRA groups, are shown in Table 2.

Table 2. Comparison of spirometry results between WRA and non WRA groups at different times.

	Group		*P*-value Student t-test
	Non WRA Mean ±SD	WRA Mean ±SD	
FEV1 % at work	87.92±4.21	68.55±7.99	<0.001
FEV1/FVC at work	87.41±2.01	77.27±4.28	<0.001
Post bronchodilator FEV1% at work	91.05±4.39	81.09±5.01	<0.001
FEV1% on holiday	91.27±4.89	85.73±4.1	<0.001
FEV1/FVC on holidays	88.59±2.3	85.3±1.25	<0.001
Post bronchodilator FEV1% on holiday	94.86±4.83	94.91±4.35	NS
FEV1% during spraying aerosols	86.03±3.36	64±2.14	<0.001
FEV1/FVC during spraying	86.05±1.92	74.39±2.24	<0.001
Post bronchodilator FEV1% during spraying	89.81±8.3	78.91±3.36	<0.001

P value > 0.05 is not significant (NS).

When comparing FEV1 between the different types of WRA, including allergic OA, WEA, and irritant OA, there were statistical significance difference between the three types during spraying days (*P*<0.001). Also, the FEV1/FVC ratio was statistically significance different between them at work and during holidays (*P*<0.001), (Figures 2, 3).

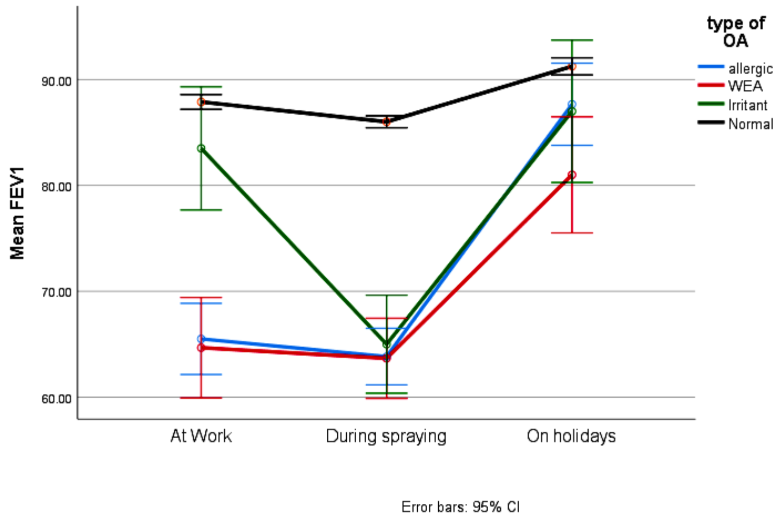

Figure 2. Comparison between FEV1% of different types of work-related asthma at different times.

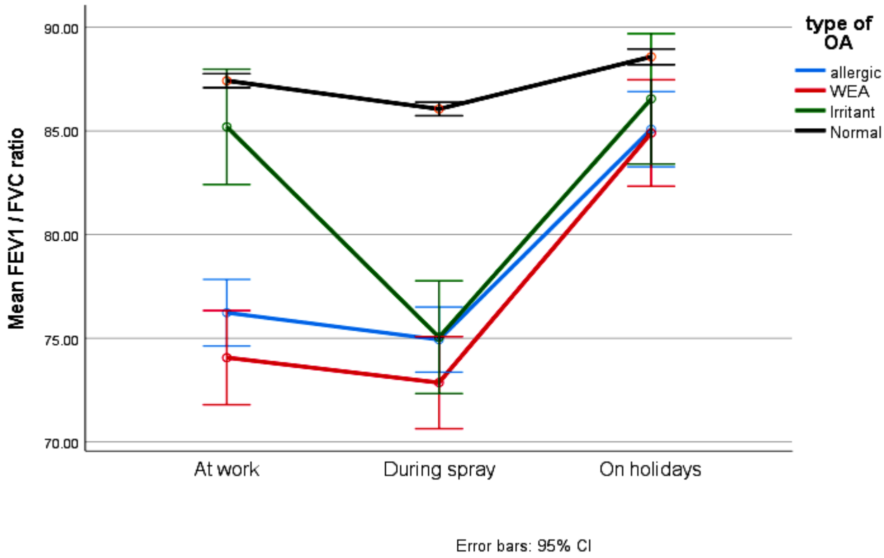

Figure 3. Comparison between mean FEV1/FVC ratio of different types of work-related asthma at different times.

Discussion

The main aim of the current study was to determine the prevalence of WRA among Egyptian adult agriculture workers in great Cairo. A multi-center cross sectional study was done which included 150 adult workers from 4 different farms between the period from 2018 and 2020. All workers were subjected to full history taking, clinical examination, chest x-ray, skin prick test, CBC, and spirometry with post bronchodilatation (reversibility test) at the farm (in the day of insecticide aerosol and without aerosol) and at home after a week off the farm.

The current study showed that 11 out of 150 subjects (7.3%) of study population had work related asthma. These finding agreed with those of Stoleski et al., 2020, who found that WRA prevalence was 8% among crop farmers.[19] Another two studies estimated the prevalence of WRA as 4 % to 5.1% of primary farm operators.[20, 21]

Several theories were suggested to explain the relatively low prevalence of occupational asthma in farmers. They suggested that farming might have protective effects. Authors pointed out that farming conditions may result in a richer microbial environment including, larger families, exposure to livestock (particularly cattle), and exposure to higher levels of endotoxin (a cell wall component of Gram-negative bacteria). All such factors may support the "hygiene" hypothesis (i.e., early in life exposure to bacterial and viral agents through contact with other children or farm animals result in a reduced incidence of atopy and asthma).[22,23,24] Moreover, some authors suggested that susceptible persons may leave dusty work areas early in the course of the job, leaving behind a relatively less susceptible group of workers who are potentially more able to tolerate the work environment.[23,24]

We tried to compare the results of the current study and other studies held in Egypt and worldwide to confirm the relatively low prevalence of WRA in relation to other occupations. Starting with Shaban et al., who assessed the prevalence of occupational asthma among flour mill workers in Giza governorate and found that all 122 studied flour mill workers complained from occupational asthma.[25] Another study conducted by El-Gewily et al., 2018 done in two flour mills at South Cairo, found that more than one quarter of 120 flour mill workers studied, complained of occupational asthma.[26]

In bakery industry, Kitenge et al., 2022 stated that the prevalence of WRA was 5% among bakers[27] and 13% in South Africa.[28] More recently, in a cross-sectional study of 26 bakeries in Parakou, Benin, symptoms of work-related asthma were present in 12.6% of 190 participants.[29] In the study conducted by Ha et al., 2021 studying the prevalence and associated factors among textile workers in Vietnam, they found that in a total of 1082 workers, 80 (7.4%) were diagnosed with asthma, and 46 (4.3%) diagnosed with cotton dust-related allergic asthma.[30] Also in Tunisia, the prevalence of occupational asthma among textile workers was 8% according to a research study compiled by Chaari et al., in 2011.[31]

The present study showed that of the 11 WRA subjects, 6 (4%) had allergic occupational asthma, 3 (2%) had WEA, 2 (1.3%) had irritant occupational asthma. Different prevalence of allergic OA was reported in different occupations. In the study conducted by Stoleski et al., 2020 evaluating the influence of occupational exposure on asthma development among crop farmers in the Republic of Macedonia, the prevalence of allergic OA in crop farmers was 2.3%.[19] This was also seen in the study by Minov et al., among workers in the pharmaceutical industry (herbal tea processors and medicines production), showed the prevalence of 1.6% for allergic OA.[32]

There was a statistically significant difference between WRA and non-WRA individuals as regard to age and duration of working in the farming industry (*P* <0.001), as WRA individuals mean age was lower compared to non-WRA individuals 28.27 ± 3.41 and 38.42 ± 9.7 years respectively. In addition, the duration of having an occupation in farms was also significantly lower in WRA individuals compared to non-WRA individuals 4.91 ± 2.02 and 23.2 ± 9.36 years, respectively. The results of our study concerning age were aligned with results shown by Ameille et al., 2003 investigated the incidence of occupational asthma in France and showed that the highest annual rate was in the 15–29 years age group.[33] Also, the study conducted by Mazurek et al., 2015 showed that the mean age at asthma diagnosis was 31.6 years in WRA farm operator individuals in USA.[20] On the other hand, in the study conducted by Kwon et al., 2015, to determine the incidence and epidemiological characteristics of work-related asthma in Korea from 2004 to 2009, workers aged ≥50 years of age had higher rates of WRA compared to younger workers. They explained their results with many reasons. For example, older workers are more likely to have a longer duration of exposure to hazardous substances, and they may have a greater susceptibility to developing asthma. In addition, younger workers may find it easier to change jobs to avoid exposures, and older workers may delay reporting their asthma symptoms.[34]

The current study found that there was no relation between history of atopy and development of WRA as 4% had allergic rhinitis, 1.3% had history of bronchial asthma. These findings came in line with those reported in a study, found that most of WRA patients were not atopic.[21] However, this contrasted with a study by de Meer et al., 2004 who reported a significant association between asthma and atopy in persons exposed to organic dust, suggesting interaction between atopy and exposure to organic dust in the asthma development.[35]

OA occurs after a latency period of occupational exposure, in which there is an allergic sensitization to specific workplace allergen, and development of chronic airway inflammation.[3] This explains the results seen in our study, showed that the mean time of starting respiratory symptoms was 13.45 ± 6.93 months since starting to work at the farm in WRA individuals. Also, such finding agreed with an observation by Beyan et al., 2017 that WRA patients had a latency period around 47 months before the onset of asthma symptoms.[36]

Regarding SPT results, 7.4% of our study population tested positive to mixed pollens, 4.7% to *Alternaria*, 2% to penicillium and 2% of the farm pollens. There was a statistical significance difference between WRA and non-WRA groups in regard to respiratory allergens especially for *Alternaria* and mixed pollens (*P*= 0.009 and <0.001, respectively). In the study conducted by Stoleski et al., 2021 on crop farm workers with allergic asthma the most positive results were to *D. pteronyssinus*, grass and tree mixed pollen, and birch pollen [19]. Kim et al., 1999 revealed that results of skin prick tests in the apple farmers indicated that European red mite was the most common sensitizing allergen (23.2%), followed by

Tyrophagus putrescentiae (21.2%), two-spotted spider mite (16.6%), *Dermatophagoides farinae* (16.3%), *D. pteronyssinus* (14.4%), cockroach (13.1%), and Japanese hop (*Humulus japonicus*) pollen (12.0%).[37]

In this study, all WRA group reported improvement in their respiratory symptoms at home. Respiratory symptoms usually started after 78.18 ± 41.91 minutes during working days. The mean of ACT was (14.55 ± 5.07). Lutzker et al*.,* 2010 stated that adults with WRA reported poorer asthma control and higher health care involvement than non-WRA individuals. This aligned with our study results, showed that according to ACT results, asthma control test ranged from poorly controlled to moderate controlled.[38]

There was a statistical significance difference between WRA and non-WRA groups as regard symptom during workday including wheeze, cough, dyspnea, and asthmatic attacks during work, as well as presence of wheeze during examination at work (P<0.001). Also, there was a statistical significance difference between WRA and non-WRA groups as regard dyspnea and wheeze at home (P=0.002 and 0.005, respectively). In addition, there was a statistical significance difference between WRA group and non WRA group as regard spirometry results carried out at work (on spraying and non-spraying days), during holiday and post bronchodilator reversibility) as regard FEV1, FVC, FEV1/FVC, being higher during the holidays (P <0.001). Irritant OA showed normal spirometry results on holidays and during workdays without spraying, but on the other hand, showed a significant decline in the FEV1 and FEV1 and FVC during the spraying day. Such data was also seen in the study conducted by Stoleski et al., 2021 which showed improvement of respiratory symptoms of tested subjects during holidays compared to working days.[19] According to Nemery, 2004, a very high diagnostic value for WRA was the work history data for improvement or withdrawal of symptoms in the absence of work, apart from the data about their worsening during or after work.[39]

Analysis of induced sputum for detection of sputum eosinophilia is a valid and reproducible method for studying airway inflammation.[40] Although sputum induction is considered a direct and reliable method of assessing airway inflammation, it has a number of limitations, especially during the study period with the COVID-19 pandemic.

In the present study, we detected peripheral absolute eosinophilic count which showed that the absolute eosinophilic count in the peripheral blood was higher in patients with allergic OA and WEA (0.53 ± 0.11 and 0.6 ± 0.18 ×103 cells/mm3, respectively), than in subjects with irritant OA and non WRA (0.12 ± 0.06 and 0.18 ± 0.09 ×103cells/mm3, respectively).

Negewo et al., 2016 assessed the ability of peripheral blood eosinophils for detecting sputum eosinophilia in stable COPD and found that peripheral blood eosinophilic count was able to distinguish patients with sputum eosinophilia from those without, thereby indicating its potential use as a diagnostic biomarker for eosinophilic COPD. Furthermore, they reported that blood eosinophil counts, and their ratios were elevated in eosinophilic COPD and correlated reasonably well with sputum eosinophilia. In addition, blood eosinophil counts of two measurements over a median period of 28 days were found to be stable.[41]

To the best of our knowledge, this is the first study to determine the prevalence of WRA among adult Egyptian agriculture workers in Great Cairo area. Despite the relatively small sample size, the study was a multicenter in four different farms. The current study faced certain challenges as it was done during the COVID-19 era, where many investigations that might increase accuracy of WRA diagnosis, including detection of eosinophilic count through analysis of induced sputum, were restricted for safety concerns.

In conclusion, farming caused a considerable prevalence of OA as 7.4% of the study population had WRA. Many precautions and preventive measures should be taken to lower the risk of WRA among agriculture workers.

Author Contributions

MAE, was responsible manuscript reviewing. RYS, was responsible for data analysis; manuscript editing and review corresponding. NAF, was responsible for

data analysis, methodology. MMY, was responsible for data analysis. SHM, was responsible for review corresponding and manuscript revision. MFM, was responsible for study design, manuscript preparation. OSA, was responsible for data acquisition and analysis, manuscript preparation. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval

The study protocol was reviewed and approved by the Ethical Committee of the Faculty of Medicine, Ain Shams University (Approval No. FMASU MD 110/2019).

Informed consent

A written informed consent was obtained from each participant included in our study.

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