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Occupations and Causative Agents among Work-Related Asthma Patients in Easy Asthma Clinic, Srinagarind Hospital, Khon Kaen, Thailand

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Abstract **Background:** Work-related asthma (WRA) is the most common chronic occupational lung disease in developing countries and the second most common in developed countries. The median attributable risk of occupational asthma for the population is estimated to be 25%. In Thailand, there are no details on occupational and causative agents vis-à-vis WRA. **Aims:** Our aim was to describe the occupational and causative agents for WRA patients who attended the Easy Asthma Clinic (EAC), Srinagarind Hospital, Khon Kaen, Thailand. **Methods:** This was a descriptive study: 323 participants at the Easy Asthma Clinics were identified and interviewed prior to obtaining information related to WRA symptoms and its suspected causative agents. Descriptive statistics were used for proportions. **Results:** The proportion of asthma patients with WRA was 16.7%. The top three occupations that carried the highest risk were (a) school workers, (b) skilled agriculture, forestry, and fishery workers, and (c) manufacturing and wood workers. The top three most identified causative agents were chalk powder, smoke from burning grass/tree, and fumes from stainless steel production. Some 63.0% of WRA patients did not wear respiratory protection equipment at work and among those who did, none wore it correctly. **Conclusions:** Occupational history, causative agents, and history of asthma symptoms related to work help to determine the proportion of WRA patients. The results of the current study should thus encourage physicians to record patient occupation(s) and job descriptions, so as to remove identifiable factors, before airway remodelling occurs, which makes treatment more difficult and costly.

Keywords: *work-related asthma, lung diseases, occupational, causative agents*

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1. Introduction

Work-related asthma (WRA) is the most common chronic occupational lung disease in developing countries and second most common in developed countries [1]. Based on North American and European studies, the median population occupational attributable risk for asthma is estimated to be 25% [1,2]. WRA is divided into new onset asthma (NOA) (i.e., asthma induced after starting to work with triggering agents in the workplace) and work-exacerbated asthma (WEA) (i.e., pre-existing asthma or concurrent asthma exacerbated by triggering agents in the workplace exposure) [3,4]. Previous studies have demonstrated certain occupations elevate the risk of asthma including general manufacturing, cleaners [5], skilled agriculture and fisheries, spray painters [6], health care, and teacher [7]. To date, more than 250 agents capable of causing WRA have been reported [7,8,9]. Substances that induce WRA are classified as either high molecular weight allergens (> 5 kDa)-usually protein derived allergens-or as low molecular weight compounds [10] and also classified as sensitizing and irritant agents in the workplace [11]. The primary causative agents are grain dust, latex protein, epoxy resin, di-isocyanate [12,13], animal proteins, wood dust [14], biological dust, textile dust [7], and welding fumes [15].

For a diagnosis of WRA, specific inhalation challenge (SIC) testing is the most commonly used as the gold standard; as this most closely represents a single exposure at work. The advantage is that the specific cause for WRA is identified. Likewise, the serial peak expiratory flow (PEF) measurement is also accomplished, which is currently recommended as a confirmatory test [16,17]. SIC testing, however, is not available in many countries and self-measurement of PEF is not without its problems. For example, there is a variable time delay between exposure and asthma and workers vary in their ability to perform unsupervised recording and often show a learning

effect at the start of a record [18]. In several countries, the medical and occupational history are the gateway to the diagnosis of WRA, which should indicate whether a patient's asthma began during a work period and whether the asthma worsens during work periods or improves on days away from work (i.e., on holiday). Despite low specificity, the high sensitive indicators helps doctors achieve early detection and early treatment [19,20].

In Thailand, surveillance systems for WRA are as yet unclear because of a lack of serial reporting, which would be needed to know the number of WRA patients under-diagnosed and/or improperly treated [21]. Early detection and advice on how to avoid work triggers could have potential to decrease disease severity, improve control, and prevent disease expression [19]. Although WRA is a relatively common illness, very little is known about at-risk occupations and triggering agents in Thailand. The current study used medical and occupational history to determine the proportion of WRA patients attending the Easy Asthma Clinic at a university hospital in Khon Kaen, Thailand

2. Methods

The study population included patients over 18 years of age who underwent hospital treatment and follow-up at Srinagarind Hospital, Khon Kaen University, Thailand. Patients who had never had a job were excluded. There were 10,206 patients who underwent treatment and follow-up at EACs in Khon Kaen province. A total of 4,606 patients met the inclusion criteria. The required sample size was calculated to be 323 patients according the finite population proportion described by Ngamjarus et al. [22].

The interview questionnaire included general personal biodata, underlying diseases, and four questions aimed to diagnosis WRA. It included 1) a history of asthma symptoms that improved or disappeared when away from work; 2) a history of asthma symptoms that worsened on days in which the patient was at work; 3) evidence of sensitizing or irritant agents in the workplace previously studied and known to cause WRA; and, 4) evidence of exposure to sensitizing or irritant agents in the workplace previously studied and found to cause WRA.

Data were recorded using a double data entry program (Epi-info Version 3.4.3) and analyzed using SPSS version 19.0 (IBM, Armonk, NY). Descriptive statistics were used to analyze characteristics of the sample such as sex, health benefit schemes, atopy history, occupational history, agents that cause WRA, and proportion of WRA. Our study results were presented as percentages.

The study was reviewed and approved by Khon Kaen University Ethics Committee for Human Research (Ref No: HE601441).

3. Results

A total of 323 participants were interviewed from Srinagarind Hospital. Most of them (51.1%, n=165) were between 45 and 64 years of age. Most of the participants were female (n=228; 70.6%). The CSMBS, UC, and SSS medical insurance scheme covered 128 (39.6%), 115 (35.6%), and 80 (24.8%) of the participants, respectively (Table 1).

Atopic diseases were presented in 215 participants (66.6%); among whom 57.0% (n=184) had allergic rhinitis, 17.3% (56) allergic conjunctivitis, and 15.2% (49) eczema. Ninety-eight participants (30.3%) had a family history of asthma (Table 1).

The top three occupational categories as classified by the ISCO-08 were professionals (n=143; 44.3%); skilled agricultural, forestry and fishery workers (n=71; 22.0%); and services and sales workers (n=41; 12.7%) (Table 2).

Table 1. General characteristics of participants

Characteristics	N=323 n (%)
Age range (yr)	
- 18 - 44	34 (10.5)
- 45 - 64	165 (51.1)
- >= 65	124 (38.4)
Sex	
- male	95 (29.4)
- female	228 (70.6)
Health benefit schemes	
- UC	115 (35.6)
- SSS	80 (24.8)
- CSMBS	128 (39.6)
Atopic diseases (yes)	215 (66.6)
Type of diseases	
- allergic rhinitis	184 (57.0)
- allergic conjunctivitis	56 (17.3)
- eczema	49 (15.2)
- hey fever	13 (4.0)
Family history of asthma	98 (30.3)

Table 2. Proportion of occupation classified by ISCO-08 in participants

International Standard Classification of Occupation 2008	N=323 n (%)
1) Managers	16 (5.0)
2) Professionals	143 (44.3)
3) Technicians and associate Professionals	1 (0.3)
4) Clerical support workers	9 (2.8)
5) Services and sales workers	41 (12.7)
6) Skilled agricultural, forestry and fishery workers	71 (22.0)
7) Craft and related trades workers	22 (6.8)
8) Plant and machine operators and assemblers	7 (2.2)
9) Elementary occupations	13 (4.0)

Of the 323 participants, 54 (16.7%) had WRA (diagnosed by medical and occupational history). The rank of most common occupational category was: (a) school workers (n=15; 27.8%) comprising 14 primary school-teachers and 1 vocational education teacher; (b) skilled agricultural, forestry and fishery workers (n=11; 20.4%) including 8 field crop and vegetable growers, 2 mixed crop growers and 1 mixed farmer; and (c) manufacturer and wood workers (n=11; 20.4%) including 6 welders/flame cutters, 2 spray painters/varnishers, 2 rubber products machine operators, and 1 carpenter/joiner (Table 3).

The WRA triggering agents among (a) school workers were chalk powder and whiteboard markers; (b) skilled agricultural, forestry and fishery workers smoke from burning grass/trees and pesticides; and (c) manufacturer and wood workers stainless steel production fumes, isocyanate, diesel exhaust, and wood dust (Table 4).

Sixty-three percent of WRA patients did not wear respiratory protective equipment (RPE) (n=34). None of the school workers or services workers wore RPE (100%, n=20). Among the patients with WRA, those who did use RPE, none wore it correctly and/or had the proper type vis-à-vis the triggering agents in the workplace (Table 5).

Table 3. Proportion of defined occupation in WRA patients

Defined occupations	N=54
	n (%)
1) Health workers	**0 (0.0)**
- nursing professionals	0 (0.0)
2) School workers	**15 (27.8)**
- vocational education teacher	1 (1.9)
- primary school teachers	14 (25.9)
3) Skilled agricultural, forestry and fishery workers	**11 (20.4)**
- field crop and vegetable growers	8 (14.8)
- mixed crop growers	2 (3.7)
- apiarists and sericulturists	0 (0.0)
- mixed crop and animal producers	1 (1.9)
4) Manufacturer and wood workers	**11 (20.4)**
- carpenters and joiners	1 (1.9)
- spray painters and varnishers	2 (3.7)
- welders and flame cutters	6 (11.1)
- motor vehicle engine assembler	0 (0.0)
- musical instrument makers	0 (0.0)
- rubber products machine operators	2 (3.7)
5) Textile workers	**3 (5.6)**
- cloth weavers	3 (5.6)
- dressmakers	0 (0.0)
- sewers	0 (0.0)
6) Services workers	**4 (7.4)**
- hairdressers	3 (5.6)
-hairdressing teachers	1 (1.9)
7) Office workers	**0 (0.0)**
8) Cleaners and refuse workers	**10 (18.5)**
- domestic housekeepers	2 (3.7)
- cleaners	8 (14.8)
- garbage and recycling collectors	0 (0.0)
9) Food Processing workers	**0 (0.0)**
- street food vendors	0 (0.0)
- bakers	0 (0.0)

Table 4. The agents that cause WRA in participants

Defined occupations	N
School workers (n=15)	
- chalk powder	13
- whiteboard marker	2
Skilled agricultural, forestry and fishery workers (n=11)	
- smoke from grass/tree burning	7
- pesticides	4
Manufacturer and wood workers (n=11)	
- stainless steel fume	6
- isocyanate	2
- smoke from diesel exhaust	2
- wood dust	1
Textile workers (n=3)	
- raw silk	3
Services workers (n=4)	
- persulfafte	3
- dye	1
Cleaners and refuse workers (n=10)	
- chloramine	4
- smoke from cooking	2
- mold	2
- animal protein	1
- house dust mite	1

Table 5. The wear of respiratory protective equipment (RPE) for agents in workplace of WRA patients

Defined occupations	n (%)
School workers (n=15)	
- did not wear	15 (100)
- wear	0 (0.0)
- proper	0 (0.0)
- improper	0 (0.0)
Skilled agricultural, forestry and fishery workers (n=11)	
- did not wear	4 (36.4)
- wear	7 (63.6)
- proper	0/7 (0.0)
- improper	7/7 (100.0)
Manufacturer and wood workers (n=11)	
- did not wear	6 (54.5)
- wear	5 (45.5)
- proper	0/5 (0.0)
- improper	5/5 (100.0)
Textile workers (n=3)	
- did not wear	2 (66.7)
- wear	1 (33.3)
- proper	0/1 (0.0)
- improper	1/1 (100.0)
Services workers (n=4)	
- did not wear	4 (100.0)
- wear	0 (0.0)
- proper	0 (0.0)
- improper	0 (0.0)
Cleaners and refuse workers (n=10)	
- did not wear	3 (30.0)
- wear	7 (70.0)
- proper	0/7 (0.0)
- improper	7/7 (100.0)

4. Discussion

As with other studies of Easy Asthma Clinics in Thailand, most of the participants (70.6%) were female, but there were differences in the proportions covered by the three primary health benefit schemes. The majority of our cases (39.6%) were covered under the Civil Servant Medical Benefit Scheme (CSMBS) followed by the Universal Coverage Scheme (UC) (35.6%). In other studies, most patients were covered by UC [23,24,25]. The difference is explained by the fact that our hospital accepts CSMBS over against other schemes [26].

According to the International Labour Organization (International Standard Classification of Occupations 2008; ISCO-08) [27], we classified occupations based on substances used/or exposed to. As a consequence, school workers (35.9%, n=116) and skilled agricultural, forestry and fishery workers (22.6%, n=73) were the most represented occupations in our study [28]. Thus, it is possible that the sample described in our study is not representative of the total population of asthma patients in Khon Kaen province, but rather only of our EAC at Srinagarind (university) Hospital.

The majority of the participants (66.6%) had a history of atopic disease and 30.3% had a family history of asthma. In a previous related study, Sittipane et al. also found the risk factors most strongly associated with asthma were history of atopic diseases and family history [29].

Further analysis revealed that the proportion of WRA patients with a history of WRA was 16.7% (54/323), including: (a) a history of asthma symptoms that improved

or disappeared when away from work; (b) a history of asthma symptoms that worsened on days in which the patient was at work; (c) evidence of sensitizing or irritant agents in the workplace previously studied and known to cause WRA; and, (d) evidence of exposure to sensitizing or irritant agents in the workplace previously studied and found to cause WRA. Of concern, most of these patients (27.8%, n=15) were school workers who had had exposure to chalk dust and/or whiteboard markers containing volatile substances (i.e., trichloroethylene) [7,30] and/or cleaning agents [31]. This group was followed by skilled agricultural, forestry and fishery workers (20.4%, n=11) who were exposed to grain dust [32], pesticides (i.e., oregano-phosphate) [33] and smoke from burning grass or trees [14] and manufacturer and wood workers (20.4%, n=11) exposed to stainless steel manufacturing fumes [6], isocyanates [14], exhaust [33], and wood dust [34].

When analyzing school workers in this study, we found that one of them was a vocational education teacher with a history of pre-existing asthma before starting her job while the others (n=14) were primary school teachers with no history of asthma until they started the job and exposure. Subsequently, all of them had a history of asthma related to agents at workplaces (i.e., chalk dust 13 cases and whiteboard marker 2 cases). None of them wore RPE in the workplace notwithstanding the high risk to agents by inhalation [35]. Previous studies confirmed that school workers had an association with WRA (OR 2.05; 95% CI: 0.71, 5.92) [36] and Gotzev et al. found that the new cases of WRA were rising among education workers every year (2 cases in 2000 and 8 cases in 2017) [37]. Majumdar found that particulate chalk dust size that settled on the classroom floor with dusting and non-dusting chalks within 3 m of the boards was < 2.5 µm [38]. According to the National Institute for Occupational Safety and Health (NIOSH), dust size < 4.0 µm can penetrate deep into the lung (i.e., the bronchi and alveoli) [39] and chalk dusts are irritating agents [40]. So, it was likely that chalk dust will cause irritant induced asthma [7].

Further analysis revealed that 20.4% (11 cases) of WRA occurred among skilled agricultural, forestry and fishery workers, and the majority of whom (72.7%) were field crop and vegetable growers, while the remainder were mixed crop growers (27.3%) and mixed farm operators (10%). All of them had a history of asthma related to workplace triggering agents (viz., smoke from burning grass/trees 7 cases and pesticides 4 cases). Importantly, the use of RPEs was poor (inappropriate or improper) as also reported by Rom (i.e., 15.4% of WRA occurred in farm workers) [41] and Arif et al. (i.e., farm workers had a significant association with WRA (OR 3.37; 95% CI: 1.22, 9.29)) [36].

When analyzing the triggering agents, smoke from burning grass/trees and pesticides were irritating agents [41] and the WRA risk associated with smoke from burning grass/trees and pesticide exposure was greatest among farmer workers (OR 1.13, 95% CI: 0.97, 1.33 and OR=1.69, 95% CI 1.13, 2.52) [14]. As an agricultural country and one of the world's major food exporters, Thailand relies heavily on the use of pesticides to protect crops and increase yields. In the past decade, the Thailand saw an approximate four-fold increase in pesticide use [42].

Surveys evaluating the knowledge, attitude, and practices (KAP) vis-à-vis pesticide use in Thailand revealed that knowledge of the harmful effects of pesticide exposure and methods of safe use differed by crop and farming activity. Although farm workers generally understood the potential risks of pesticides, their attitudes toward pesticide use as well as knowledge and use of PPE especially RPE were poor [43,44]. For example, about three-fourths of chili farmers located in the northeastern region of Thailand surveyed about their KAP did not understand the utility of PPE, did not use PPE, or were not concerned about their overall exposures [43]. The general lack of RPE use by Thai farm workers puts them at increased risk of pesticide exposures and health problem related to those exposures [45].

In the current study, we found the same proportion of WRA (i.e., 20.4%, 11 cases each) occurring among manufacturing and wood workers, and skilled agricultural, forestry and fishery workers. Most the workers (54.5%) were welders and flame cutters, while the remainder were spray painters/varnishers (18.2%), rubber products machine operators (18.2%), and carpenters/joiners (9.1%). All of the workers had a. history of asthma related to triggering agents at the workplace (viz., stainless steel fume 6 cases, isocyanate 2 cases, exhaust 2 cases, and wood dust 1 case).

Karjalainen et al. and Attarchi et al. found that manufacturers had a significant risk for developing WRA (OR 1.56 (95% CI; 1.47, 1.65) and 5.68 (95% CI; 1.41, 13.87), respectively) [46,47] The causes of WRA among manufacturers and wood workers included stainless steel manufacturing fumes (OR= 2.0: 95% CI; 1.5, 3.4) [6], isocyanate (OR= 1.16: 95% CI; 0.99, 1.36) [14], and wood dust (OR= 1.55: 95% CI; 1.08, 2.24) [6]. Although there has been no study on the risk of diesel exhaust, Hoppin et al. found that diesel exhaust was associated with elevated odds of wheezing (OR= 1.31; 95%CI; 1.13, 1.52) [48]. Diesel fuels comprise fine particulates, nitrogen oxides, and sulfur oxide which after combustion release ultra-fine particles (< 1 µm) which are able to reach the bronchial and alveolar regions resulting in allergenicity in both humans and animals [49]. Diesel particulates can also act as allergen carriers, exacerbating the development of asthma [50].

5. Conclusion

Occupational history, causative agents, and history of asthma symptoms related to work are valuable parameters for determining the proportion of WRA patients. The results of the current study should encourage physicians to collect patient occupation(s) and job descriptions; in aid of early treatment by removal from identifiable factors, before airway remodeling, which makes treatment more difficult and costly.

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Statement of Competing Interests

The authors have no competing interests.

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