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Original Research Article Outline:

RELATIONSHIP BETWEEN SYNTHETIC COTTON DUST EXPOSURE AND SYMPTOMS OF RESPIRATORY DISORDERS IN TEXTILE FACTORY WORKERS AT PT X IN EAST JAVA

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ABSTRACT

Introduction. Respiratory disorders, which range from 1 to 100 μm, are a significant concern in the textile industry. Typical symptoms of cotton dust exposure include chronic cough with or without phlegm, painful breathing, wheezing, nasal congestion, and chest pain. While most research has focused on natural cotton fibers, there is a growing need to investigate the health risks associated with synthetic cotton dust, such as that derived from petroleum-based resources such as polyester. **Method.** This research employed a cross-sectional design, with 76 respondents. **Result & Analysis.** The results showed that 21.1% of the workers experienced respiratory symptoms, and 43.4% of the workers were exposed to high levels of synthetic cotton dust. Chi-square test analysis indicated a significant relationship between synthetic cotton dust exposure and respiratory symptoms ($p < 0.001$; OR 15.1 [3.17 – 73.21]). **Discussion.** Workers with high synthetic cotton dust exposure had a 15.1 times greater risk of experiencing respiratory symptoms than those with low synthetic cotton dust exposure.

Keywords: Synthetic Cotton Dust Exposure, Respiratory Symptoms, Textile Industry

INTRODUCTION

A significant issue in the textile industry is the occurrence of respiratory symptoms due to exposure to cotton dust (Kemenko Bidang Perekonomian RI, 2023). The industry comprises various divisions, including spinning, weaving, knitting, and finishing, with the spinning section particularly exposed to higher levels of cotton dust. Dust particles in this environment can range in size from less than 1 μm to at least 100 μm (Oo et al., 2021). A small fraction of inhaled dust can reach the alveolar regions of the lungs and penetrate the terminal bronchioles, triggering histamine release and narrowing of the airways, gradually making breathing more difficult (Ekambaram et al., 2022). leads to narrowing of the airways, gradually making breathing more difficult (Ekambaram et al., 2022). These symptoms typically subsided by the end of the workday and reappeared on the morning of Monday after a break from the dust (Dangi & Bhise, 2017).

The textile industry uses two primary types of raw materials: natural and synthetic. Natural fibers, such as cotton, can contain endotoxins that can trigger inflammatory reactions if inhaled. In contrast, synthetic fibers, including synthetic cotton derived from petroleum-based resources like polyester, can cause pathological changes in the respiratory tract directly linked to dust inhalation (Boondaeng et al., 2023; Malakouti, 2015; Pimentel et al., 1975)

Respiratory disorders resulting from both types of fibers disrupt the oxygen-binding process within the respiratory tract, leading to impaired airflow and carbon dioxide accumulation, significantly affecting quality of life (Whited et al., 2024). A longitudinal study in China found higher incidences of byssinosis and chest tightness among cotton workers than among silk textile workers, particularly smokers, with symptoms being mostly intermittent; cessation of exposure improved respiratory health, especially over time (Wang et al., 2003). A more recent study (Kammoolkon et al., 2022) found a strong association between respiratory dust exposure and an increased prevalence of respiratory symptoms such as cough, phlegm, chest tightness, and dyspnea among 146 indigo-dyed cotton weavers in northeastern Thailand.

The typical symptoms of cotton dust exposure include chronic cough (with or without phlegm), painful breathing, wheezing, nasal congestion, and chest pain. Notably, exposure to cotton dust can lead to a chronic respiratory condition marked by chest pain, particularly noticeable on the first day of work after a holiday, known as "Monday Morning Dyspnea" (Nafees et al., 2023).

Research conducted on the textile industry in Semarang City in 2023 reported a prevalence rate of 65.8% for respiratory symptoms among workers (Berlian et al., 2023). Although developed countries have seen a significant reduction in lung disease prevalence owing to cotton dust, studies in developing countries have indicated an increasing incidence. Rapid industrialization in several developing nations has rendered lung diseases caused by cotton dust a global health issue (Hinson et al., 2016). For instance, research in Pakistan found that higher concentrations of cotton dust are associated with decreased lung function capacity among textile factory workers (Nafees et al., 2023).

Most studies have focused on natural cotton fibers or have not distinguished between natural and synthetic cotton. Therefore, this study aimed to determine the relationship between exposure to synthetic cotton dust and the respiratory symptoms experienced by textile industry workers. By clarifying the specific health risks associated with synthetic cotton dust, this study seeks to inform policymakers about the need for stricter safety standards and improved protective measures for workers. Additionally, the findings provide a foundation for future research and contribute to a global understanding of occupational health challenges in rapidly industrialized regions.

METHOD AND ANALYSIS

This study was conducted in the spinning section of a textile factory, PT. X in East Java with 76 respondents. The inclusion criteria were textile factory workers in the spinning, weaving, knitting, or finishing sections, who were willing to participate, and aged between 18 and 60 years. Exclusion criteria included workers who were classified as heavy smokers according to the Brinkman Index and those with a history of or currently experiencing lung disease.

The sample size was calculated using the following formula for a single proportion:

$$n = \frac{Z_{1-\alpha/2}\left(p_0(1-p_0)\right)}{d^2}$$

Where:

- *where n* is the required sample size
- $Z_{1-\alpha/2}$ is the critical value for a given confidence level. For $\alpha = 0.05$, $Z_{1-\alpha/2} = 1.96$
- p_0 is the expected proportion
- d is effect size

Based on a prior work of (Berlian et al., 2023), p_0=0.66 and d = 0.1, thus the minimum sample size was 86.39 which

rounds to 87. However, since the number of workers in the spinning department was less than 87, we conducted total sampling by recruiting all 76 workers who met the criteria in that department.

This study employed the American Thoracic Society (ATS) respiratory disorder symptom questionnaire, specifically the ATS-DLD-78-A type (Karnagi, 1996). This instrument is a standardized tool used to assess respiratory symptoms and lung health. It includes questions about symptoms such as cough, phlegm production, chest tightness, wheezing, and shortness of breath, helping researchers and clinicians evaluate the prevalence and severity of respiratory disorders in study populations.

Table 1 shows the variables, operational definition, and scales used in this study

Variabel	Operational Definition	Scale
Independent:		
Exposure to dust cotton	Exposure of dust cottin at department of *ring spinning frame* and *winding* (Berlian et al., 2023)	Nominal - High - Low
Dependent:		
Respiratory Symptoms disorders	Respiratory disorders are characterized by symptoms such as cough, sputum production, episodes of coughing with sputum, wheezing, and a feeling of chest tightness or pressure (Broaddus et al., 2022)	Nominal - Have Do not have
Confounding factor		
Age	The respiratory system undergoes many changes with age, increasing the frequency of common symptoms such as cough and dyspnea (Wang et al., 2003)	Category - ≤ 30 - 31-40 - 41-50 - >50
Working hours	Working in an environment with high dust concentrations has a negative impact on the duration of exposure (Berlian et al., 2023)	Numeric - > 8 hours - ≤ 8 hours
Length of employment	The longer workers remain in the workplace, the greater their risk of exposure to dust particles (Berlian et al., 2023)	Numerics - > 5 years - ≤ 5 years
Smoking	Distribution of smoking habit based on Brinkman	Nominal - Smoking - Not Smoking
Gender	Gender is a risk factor for respiratory symptoms, particularly in males (Oviera et al., 2016)	Nominal - Female - Male
Use of PPE	Not using personal protective equipment (PPE) increases the risk of experiencing respiratory symptoms (Berlian et al., 2023)	Nominal - Use - Do not use

The researchers obtained informed consent from the participants and explained the research aims, objectives, benefits, and instructions for completing the questionnaire. More detailed information on the consent process, duration of data collection, and measures to ensure data accuracy should be included. The questionnaires were then distributed and the researchers assisted the respondents in filling them out.

The collected data were processed using the Statistical Package for the Social Sciences (SPSS) version 27 with both univariate and bivariate analyses. This research was approved by the Health Research Ethics Commission (KEPK) FKIK Untirta on April 17, 2024 (approval number 50/UN43.20/KEPK/2024).

RESULT

Table 2 presents the characteristics of the 76 workers at the PT X textile factory in East Java. The majority of the

respondents were male (51.3%) and fell within the 31-40 years age group (39.5%), with a median age of 39. More than 60% of workers have more than five years of work experience, and all work less than eight hours per day. Most of the workers were non-smokers (75%). Additionally, 16 workers (21.1%) reported respiratory symptoms. Low exposure to cotton dust is defined as workers involved daily in blowing, carding, drawing, and simplex activities (56.6%), whereas high exposure refers to workers engaged in ring spinning and winding activities (43.4%). Detailed data are shown in Table 2.

Table 2. Characteristics of Respondents

Gender	**Median or frequency (%)**
Males	39 (51.3%)
Females	37 (48.7%)
Age (years) (min-max)	39 (21-56)
Age Category	
≤ 30 y.o	15 (19.7%)
31-40 y.o	30 (39.5%)
41-50 y.o	24 (31.6%)
> 50 y.o	7 (9.2%)
Length of Employment (years) median (min-max)	12 (1-23)
Length of Employment	
> 5 years	53 (69.7%)
≤ 5 years	23 (30.3%)
Working hour	
≤ 8 hours	76 (100%)
Smoking	
Do not smoke	57 (75%)
Light Smoker	17 (22.4%)
Heavy Smoker	2 (2.6%)
Use of PPE	
Using PPE	76 (100%)
Symptoms of Respiratory Disorders	
Do not experience symptoms	60 (78.9%)
Experience symptoms	16 (21.1%)
Cotton dust exposure	
Low exposure (*Blowing, carding, drawing, simplex)*	43 (56.6%)
High exposure (*Ring Spinning, Winding)*	33 (43.4%)

For the bivariate analysis, seven variables were studied, but only five could be analyzed because variables ‘working hours and 'use of PPE' were too homogeneous for statistical testing.

Table 3 shows the analysis of the relationship between synthetic cotton dust exposure and respiratory symptoms using the chi-square test. The analysis yielded a significant *p*-value and odds ratio (OR) of 15.1 (3.17 – 73.21), indicating a significant relationship between synthetic cotton dust exposure and respiratory symptoms.

Table 3. Relationship between Cotton Dust Exposure and Respiratory Disorder Symptoms

	Respiratory Disorders Symptoms			
	Yes	**No**	***p-value***	**OR (95% of CI)**
	***n* (%)**	***n* (%)**		
High	14 (42.4%)	19 (57.6%)	<0.001	15.1 (3.17 – 73.21)
Low	2 (4.7%)	41 (95.3%)		

Table 4 presents the results of the analysis of confounding variables with respiratory symptoms. The relationship between age and respiratory symptoms was analyzed using the chi-square test, resulting in a p-value of 0.423 (p>0.05), suggesting no significant relationship. For the variables of smoking and respiratory symptoms, Fisher's Exact Test yielded a p-value of 1.00 (p>0.05), indicating no significant relationship. Similarly, the gender variable tested with the chi-square test yielded a p-value of 0.213 (p>0.05), showing no significant relationship with respiratory symptoms. Lastly, the variable of work experience and respiratory symptoms tested with Fisher's Exact Test

produced a *p*-value of 0.363 ($p>0.05$), indicating no significant relationship between work experience and respiratory symptoms.

Table 4. Relationship between age, smoking, gender and length of employment with experience of symptoms of respiratory problem

	Respiratory Disorders Symptoms			
	Yes *n* **(%)**	**No** *n* **(%)**	***p-value***	**OR (95% of CI)**
Age				
> 39	14 (42.4%)	19 (57.6%)	<0.001	15.1 (3.17 – 73.21)
≤ 39	2 (4.7%)	41 (95.3%)		
Gender				
Male	6 (15.4%)	33 (84.6%)	0.213	2.03 (0.65 – 6.32)
Female	10 (27%)	4 (73%)		
Smoking Habit				
Smoke	4 (21.1%)	15 (78.9%)	1.00	1.00 (0.28-3.57)
Not smoke	12 (21.1%)	4 (78.9%)		
Length of Employment (years)				
≤ 5	3 (13%)	20 (87%)	0.363	2.16 (0.55 – 8.48)
> 5 ye	13 (24.5%)	40 (75.5%)		

DISCUSSION

Field observations at PT. X's spinning section revealed six stages of the process: blowing, carrying, drawing, simplex, ring-spinning frame, and winding. Research by Berlian et al. (2023) in Semarang revealed that the total dust measurements in the spinning unit at two locations exceeded the quality standard (>230 µg/Nm³) set by the Government Regulation of the Republic of Indonesia. The concentrations were 4111.4 µg/Nm³ and 452.23 µg/Nm³ in the Ring Spinning Frame and Winding sections, respectively. Conversely, the Blowing, Carding, and Drawing sections had dust levels below the standard, measuring 63.95 µg/Nm³, 95.2 µg/Nm³, and 93.38 µg/Nm³, respectively (Berlian et al., 2023; Ekambaram et al., 2022).

PT. X primarily uses polyester staple fibers as a raw material. This synthetic fiber, commonly used in the textile industry, is produced from monomers, such as Purified Terephthalic Acid (PTA) and monoethylene glycol (MEG). These monomers are heated to form a polymer melt, which is then cooled and cut into small pellets called resins (Hamid et al., 2023).

This study found that 21.1% of the PT. X's textile factory workers reported respiratory symptoms and 43.4% were exposed to high levels of cotton dust. Supporting these findings, Ekambaram et al. (2022) reported a prevalence rate of 20% for cough, 16% for chest tightness, and 20% for dyspnea among female textile workers, indicating similar respiratory health impacts despite the differences in location and demographic focus. In contrast, (Berlian et al., 2023) reported a higher prevalence of 65.8% for respiratory symptoms in a different study, Additionally, the study conducted in Ethiopia (Daba Wami et al., 2018) reported a 47.8% prevalence of respiratory symptoms among workers exposed to cotton dust, further highlighting the variability in prevalence rates across different studies and locations. These discrepancies can be attributed to variations in the sample size, research locations, and types of cotton fibers. Another plausible explanation is that workers at PT X adhere to Government Regulation Number 22 of 2021, which mandates strict compliance with PPE usage.

Relationship between Age and Experience of Symptoms of Respiratory Disorders

Analysis of age and respiratory symptoms revealed no significant relationship between the two variables. This result does not support the findings of Dangi and Bhise (2017) in India, which showed a positive correlation between age and duration of exposure, suggesting that aging may contribute to obstructive pulmonary pathology due to a decrease in the FEV1/FVC ratio. However, no spirometry measurements were conducted in this study. Some studies have also reported that the negative impact of cotton dust exposure on lung function depends on workplace dust concentrations and individual factors such as age (Hinson et al., 2016).

Theoretically, aging can reduce the gas exchange surface in the lungs, which can decrease the oxygenation capacity of blood. Additionally, air ducts can collapse more easily, exacerbating the underlying obstructive diseases. In this study, 39.5% of the workers were in the age range of 31-40 years, and only seven workers were over 50 years old, of whom three reported respiratory symptoms.

Relationship Between Smoking and Experience of Symptoms of Respiratory Disorders

The results of the data analysis showed no relationship between smoking and respiratory symptoms. Smoking is not directly related to respiratory symptoms in textile factories, and one-fifth of non-smoking workers experience respiratory problems. Therefore, some respiratory symptoms were not caused by smoking habits. This finding is consistent with research conducted by Berlian et al. (2023) in Semarang, which showed no relationship between smoking habits and respiratory symptoms. Similarly, studies by Silpasuwan et al. (2016) in Thailand and Hinson et al. (2016) found no relationship between smoking habits and respiratory disorders or the prevalence of byssinosis.

In theory, smoking can damage the respiratory system, particularly in workers continuously exposed to dust, thereby posing additional health risks. Smoking causes changes in the tissues and functions of the respiratory tract. Exposure to cigarette smoke can accelerate the decline in FEV1, leading to airflow obstruction, enlargement of mucus cells, and an increase in mucus glands in large airways. Additionally, an inflammatory reaction can occur, causing narrowing of the small airways owing to cell proliferation and mucus accumulation.

Relationship between Gender and Experience of Symptoms of Respiratory Disorders

Data analysis revealed no relationship between sex and respiratory symptoms. These results are consistent with the research conducted by Silpasuwan et al. (2016)in Thailand, which also showed no significant relationship between sex and respiratory disorders or lung function.

Theoretically, there is a difference in total lung capacity between men and women, with women's total lung capacity being 15%-25% lower than that of men. In men, total lung capacity can reach up to 5800 ml, while in women it only reaches 4200 ml (Hall & Hall, 2020)

Relationship between Length of Employment and Experience of Symptoms of Respiratory Disorders

The data analysis revealed no significant relationship between work experience and respiratory symptoms. This finding aligns with the research by Silpasuwan et al. (2016) in Thailand, which also found no relationship between work experience and respiratory problems. However, research by Daba Wami et al. (2018) in Ethiopia showed that workers with 2-5 years of experience had a 2.38 times higher likelihood of

experiencing respiratory symptoms than those with less than 2 years of experience. Theoretically, the longer a worker remains in a dusty environment, the greater is the likelihood of developing respiratory symptoms.

In contrast, Berlian et al. (2023) demonstrated a statistically significant relationship between work experience and respiratory symptoms in Semarang. Workers with more than 5 years of employment were 1.478 times more likely to experience respiratory symptoms than those with five years or less of experience.

Implication

The study's findings emphasize the crucial need to implement and strictly enforce the use of personal protective equipment (PPE) in textile factories, especially for long-tenured workers. Improving workplace ventilation systems and investing in advanced filtration and regular maintenance can help reduce dust particle concentrations in air. Establishing routine health monitoring programs, including regular medical check-ups and lung function tests, can facilitate the early detection and management of respiratory symptoms. Additionally, job rotation schemes to limit exposure duration and ongoing educational initiatives regarding dust exposure risks and protective measures can further enhance worker safety and health.

CONCLUSION

The results of the analysis indicated a significant relationship between cotton dust exposure and respiratory symptoms. Workers with high cotton dust exposure have a 15.1 times greater risk of developing respiratory symptoms than those with low exposure. Age was found to have an influence on the prevalence of respiratory symptoms, whereas sex, smoking habits, and length of employment did not show a significant effect. This study has several limitations, including the use of convenience sampling, which may have introduced bias. In addition, the study was conducted in a single factory (PT X) in East Java, which may not be representative of other textile factories in different regions or countries with varying environmental conditions and workplace practices. Furthermore, the study might not capture the long-term effects of dust exposure if the duration of the exposure data is limited. Longitudinal data will provide more insights into chronic health impacts.

REFERENCES

Berlian, A., Setiani, O., Sulistiyani, S., Raharjo, M., & Darundiati, Y. (2023). The Relationship of Dust Exposure with Respiratory Disorders Symptoms Among Textile Industry Workers. *Journal of Ecological Engineering*, *24*(3), 35–46. https://doi.org/10.12911/22998993/157389

Boondaeng, A., Keabpimai, J., Srichola, P., Vaithanomsat, P., Trakunjae, C., & Niyomvong, N. (2023). Optimization of Textile Waste Blends of Cotton and PET by Enzymatic Hydrolysis with Reusable Chemical Pretreatment. *Polymers*, *15*(8), 1964. https://doi.org/10.3390/polym15081964

Broaddus, V. C., Schnapp, L. M., Stapleton, R. D., Murray, J. F., & Nadel, J. A. (Eds.). (2022). *Murray and Nade's textbook of respiratory medicine* (Seventh edition). Elsevier.

Daba Wami, S., Chercos, D. H., Dessie, A., Gizaw, Z., Getachew, A., Hambisa, T., Guadu, T., Getachew, D., & Destaw, B. (2018). Cotton dust exposure and self-reported respiratory symptoms among textile factory workers in Northwest Ethiopia: A

comparative cross-sectional study. *Journal of Occupational Medicine and Toxicology*, *13*(1), 13. https://doi.org/10.1186/s12995-018-0194-9

Dangi, B., & Bhise, A. (2017). Cotton dust exposure: Analysis of pulmonary function and respiratory symptoms. *Lung India*, *34*(2), 144. https://doi.org/10.4103/0970-2113.201319

Ekambaram, G., Vara, A., Nileshkumar, S. M., & Sivasubramanian, N. (2022). Effect of cotton dust on lungs among female workers in cotton industry in northern Gujarat, India. *Bioinformation*, *18*(3), 255–260. https://doi.org/10.6026/97320630018255

Hall, J., & Hall, M. E. (2020). *Guyton and Hall Textbook of Medical Physiology* (14th ed.). Elsevier.

Hamid, Md. A., Ahmed, S. T., Parvez, M., & Patwary, S. (2023). Scope, Opportunity and challenges of Polyester Staple Fiber (PSF) Production in Bangladesh. *Journal of Knowledge Learning and Science Technology ISSN: 2959-6386 (Online)*, *2*(3), 106–119. https://doi.org/10.60087/jklst.vol2.n3.p119

Hinson, A., Lokossou, V., Schlünssen, V., Agodokpessi, G., Sigsgaard, T., & Fayomi, B. (2016). Cotton Dust Exposure and Respiratory Disorders among Textile Workers at a Textile Company in the Southern Part of Benin. *International Journal of Environmental Research and Public Health*, *13*(9), 895. https://doi.org/10.3390/ijerph13090895

Kammoolkon, R., Taneepanichskul, N., & Taneepanichskul, S. (2022). Respiratory symptoms and their association with exposure to respiratory dust among indigo-dyed cotton workers. *Archives of Environmental & Occupational Health*, *77*(5), 356–361. https://doi.org/10.1080/19338244.2021.1893633

Karnagi, J. (1996). *Prevalensi bisinosis di pabrik tekstil dan hubungannya dengan konsentrasi debu kapas di lingkungan kerja*. Universitas Indonesia.

Kemenko Bidang Perekonomian RI. (2023). *Encouraging Supply Chain Integration in the Textile and Textile Products (TPT) and Footwear Industries, the Government Prepares Various Policies*. https://ekon.go.id/publikasi/detail/5060/encouraging-supply-chain-integration-in-the-textile-and-textile-products-tpt-and-footwear-industries-the-government-prepares-various-policies

Malakouti, J. (2015). Pulmonary effects of exposure to synthetic fibers: A case study in a textile industry in Iran. *Archives of Hygiene Sciences*, *4*(3), 137–145.

Nafees, A. A., Muneer, M. Z., Irfan, M., Kadir, M. M., Semple, S., De Matteis, S., Burney, P., & Cullinan, P. (2023). Byssinosis and lung health among cotton textile workers: Baseline findings of the MultiTex trial in Karachi, Pakistan. *Occupational and Environmental Medicine*, *80*(3), 129–136. https://doi.org/10.1136/oemed-2022-108533

Oo, T. W., Thandar, M., Htun, Y. M., Soe, P. P., Lwin, T. Z., Tun, K. M., & Han, Z. M. (2021). Assessment of respiratory dust exposure and lung functions among workers in textile mill (Thamine), Myanmar: A cross-sectional study. *BMC Public Health*, *21*(1), 673.

https://doi.org/10.1186/s12889-021-10712-0

Oviera, A., Jayanti, S., & Suroto, S. (2016). Faktor-faktor yang Berhubungan dengan Kapasitas Vital Paru pada Pekerja Industri Pengolahan Kayu di PT. X Jepara. *Jurnal Kesehatan Masyarakat*, *4*(1), 267–276.

Pimentel, J. C., Avila, R., & Lourenco, A. G. (1975). Respiratory disease caused by synthetic fibres: A new occupational disease. *Thorax*, *30*, 204–219.

Silpasuwan, P., Prayomyong, S., Sujitrat, D., & Suwan-ampai, P. (2016). Cotton Dust Exposure and Resulting Respiratory Disorders Among Home-Based Garment Workers. *Workplace Health & Safety*, *64*(3), 95–102. https://doi.org/10.1177/2165079915607495

Wang, X.-R., Eisen, E. A., Zhang, H.-X., Sun, B.-X., Dai, H.-L., Pan, L.-D., Wegman, D. H., Olenchock, S. A., & Christiani, D. C. (2003). Respiratory symptoms and cotton dust exposure; results of a 15 year follow up observation. *Occupational and Environmental Medicine*, *60*(12), 935–941. https://doi.org/10.1136/oem.60.12.935

Whited, L., Hashmi, M. F., & Graham, D. D. (2024). Abnormal Respirations. In *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK470309/