Conference Paper

Lipopolysaccharides Endotoxin-containing Paddy Dust Leads to Cross-shift Lung Function Decline and Respiratory Complaints in Paddy Milling Machine Operators

M. Farid Dimjati Lusno, Khuliyah Candraning Diyanah, and Soedjajadi Keman
Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia

Abstract

Lipopolysaccharides (LPS) LPS endotoxin-containing paddy dust leads to airway inflammation, lung function decline, and pneumonitis. Therefore, this study aimed to analyze the effect of LPS endotoxin-containing paddy dust on the cross-shift lung function decline and respiratory complaints of paddy milling machine operators. This environmental epidemiology study has an analytic observational design and used a cross-sectional approach. The study was conducted in the Bulubrangsi and Godog Villages in the Laren Sub-district of the Lamongan District. The study population was entirely made up of paddy milling machine operators from the Bulubrangsi and Godog Villages with certain inclusive criteria. This study used 18 samples, and results showed that the average personal paddy dust inhalation level was $5.68 \pm 1.28 \text{mg/m}^3$ with the LPS endotoxin level at $232.22 \pm 18.41 \text{EU/m}^3$. Interestingly, there was a very significant positive correlation between the personal paddy dust levels, the LPS endotoxin levels, and the cross-shift Forced vital capacity (FVC) and Forced expiratory volume (FEV$_1$) declines (Spearman correlation test, all $p < 0.01$). There was also a positive correlation between the personal paddy dust levels, the cross-shift FVC% decline, and the respiratory complaints (Spearman correlation test, all $p < 0.05$). In conclusion, LPS endotoxin-containing paddy dust leads to cross-shift lung function decline in paddy milling machine operators. Smoking habits also correlated to a cross-shift decline in FVC. It is recommended to reduce exposure to indoor endotoxin-containing paddy dust levels through measures of engineering, administrative, and wearing appropriate personal protective equipment at the workplace.

Keywords: LPS Endotoxin containing paddy dust, Lung function decline, Operator respiratory complaints
1. INTRODUCTION

Development in industry, could lead to the contamination of the air, water, and other environmental components that affect human lung health. A person’s work environment also seriously affects their health. Workers in the agriculture industry are exposed to hazardous materials from their work environment, such as dust, unfavorable climatic conditions, noise, and insufficient light. Dust is the most influential hazard and is often assumed to be a cause of respiratory system disease. Occupational respiratory disease is usually caused by exposure to substances that can be irritating or toxic. Even a single exposure to such substances can cause acute or chronic respiratory diseases. Occupational lung disease is most likely due to the presence of dust in the lungs, and the severity of the disease can be affected by the type of dust, the period of exposure, and the concentration and size of airborne dust particles in the respiration zone [14]. Dust exposure can be detrimental to workers’ happiness with their jobs and may also cause issues with the workers’ pulmonary function. In general, issues with lung function occur before the onset of respiratory diseases, such as occupational lung disease [13].

Ross et al.’s (1994) study in the UK included 3,276 cases of occupational diseases, 941 of which were occupational asthma. In Medan’s (1996) study, the milling of grains, including paddy milling, was the fourth main cause of occupational asthma following isocyanate, paints, and laboratory animals.

Cotton dust exposure is associated with both acute and chronic respiratory inflammation, which can cause organic dust toxic syndrome, byssinosis, asthma, bronchitis, and chronic respiratory tract obstruction (Merchant et al. 1973; Beck et al. 1982). The effects of acute and chronic respiratory inflammation experienced by cotton workers is dose-dependent and can be triggered by the microbiological contamination of cotton fibers. The main bacterial contaminant is endotoxin (Castellan et al. 1984; Kilburn, 1984; Rylander, 1990). After being exposed to high levels of cotton dust, there is a significant change in lung function, which can be a precursor to a decline in long-term lung function (Christian et al. 1994). However, cotton dust exposure in moderate levels (<1.0 mg/m³) causes very little change in lung function without direct physiological effects (Rylander 1990).

A recent examination on the pathogenesis of grain dust was conducted, but the results were similar to the pathogenesis of other organic dusts. Early inflammatory response is related to endotoxin hypothesis. Spirometry abnormalities are more closely related to levels of endotoxin in the air than levels in respirable dust concentrations.
(Clall et al. 1993). The examination of lung function has an important role in diagnosing obstructive pulmonary disease, looking at the severity and pathway of the disease, and determining the prognosis for the patient (Yunus 1992).

A previous environmental epidemiology study showed changes in respiratory and pulmonary function from the long-term inhalation of paddy dust, specifically in the prevalence of chronic bronchitis, which increased 23%–33% ([1], Dosman et al. 1980), and in the increase of bronchial reactivity [17]. Long-term exposure to paddy dust decreases lung function and is affected by the dose-response relationship between them [7, 8]. One of the agents responsible for the inflammatory effect of paddy dust is endotoxin. Endotoxin was consistently measured at significant levels in dust samples from paddy grains [6]. Endotoxin is a proven cause for the average decrease in Forced Expiratory Volume (FEV₁) and causes respiratory inflammation [6, 19]. Respirable of LipoPolysaccharide solution (LPS) and constitutive decay element (CDE) with a high endotoxin concentration cause a significant decrease in FEV₁ [9, 11].

Respiratory diseases often found among workers who are exposed to air pollution or dust are chronic bronchitis, emphysema, and asthma. These conditions are characterized by a decrease in lung function (such as dysfunctional ventilation), a significant decrease of FEV₁, and dysfunctional oxygenation ([13], Young 1993). Such symptoms affect work productivity, quality of life, and often increase a person’s health care costs.

The Bulubrangsi and Godog Villages of Laren District, Lamongan are paddy-producing areas and have a lot of paddy mills. Air pollution and dust can affect the lung function of paddy-milling machine operators and even the community around the mill. This can decrease productivity and increase treatment costs.

There is a high frequency of lung disease among workers, especially paddy-milling machine operators. To learn and anticipate the effects of endotoxin-containing dust from paddy milling on cross-shift lung function, a test was conducted among paddy milling machine operators in rural and industrial areas who have risk factors for lung disease.

2. METHODS

This study was designed as an environmental epidemiological observation with a cross-sectional design. The location of this study was in the Bulubrangsi and Godog Villages in the Laren District of Lamongan. The study population was contrived of male paddy milling machine operators between 20–40 years-old who were willing to participate in the study, had at least two years of work experience, and whose
past work experience did not include working in areas that could cause respiratory disease, such as cement factories or asbestos factories. There were three paddy mills in each village, and each mill had three machine operators, so the total sample was 18 individuals.

The independent variables in this study were paddy mill dust and LPS endotoxin-containing paddy dust. The dependent variables were the cross-shift lung function decline and the worker’s respiratory complaints. Personal dust levels were measured using the Personal Dust Sampler, so the levels of paddy dust inhaled by each worker could be seen. LPS endotoxin-containing paddy dust levels were analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Lung function was measured with a spirometry test, and respiratory complaints were obtained with a standard questionnaire from the American Thoracic Society. Spearman’s correlation statistical test was used for data analysis with the value of $p < 0.05$ considered as a significant result.

3. RESULTS

Each operator’s personal paddy mill dust inhalation levels were measured. The mean of those measurements amounted to $5.68 \pm 1.28$ mg/m$^3$. Only one sample was within the range of paddy dust inhalation levels allowed for workers. The lowest paddy mill dust level was $3.98$ mg/m$^3$, and the highest was $8.01$ mg/m$^3$. Paddy mill dust levels are acceptable when $\leq 4$ mg/m$^3$ (SNI 19-0232-2005). The sample of endotoxin-containing paddy dust levels averaged $232.22 \pm 18.41$ EU/m$^3$ with the lowest score being $208$ EU/m$^3$, and the highest being $260$ EU/m$^3$.

Table 1 shows the correlation between personal paddy dust levels, lung function decline, and respiratory complaints among the paddy milling machine operators.

Table 1 shows there was a significant correlation between personal paddy dust inhalation levels, FVC decline (Spearman’s correlation test, $p = 0.000; r = 0.831$), and FEV$_1$ decline (Spearman’s correlation test, $p = 0.000; r = 0.585$). There was also a significant correlation between personal paddy dust inhalation levels, %FVC decline (Spearman’s correlation test, $p = 0.045; r = 0.336$), and respiratory complaints (Spearman’s correlation test, $p = 0.012; r = 0.414$). The other parameters, %FEV$_1$ and FEV$_1$/FVC, had no significant correlations.

Table 2 shows the correlation between LPS endotoxin-containing paddy dust levels, lung function decline, and respiratory complaints among paddy milling machine operators.
Table 1: Correlation Between Personal Paddy Dust Levels, Lung Function Decline, and Respiratory Complaints.

<table>
<thead>
<tr>
<th>No.</th>
<th>Personal Paddy Dust Level (mg/m³)</th>
<th>ΔFVC (L)</th>
<th>Δ%FVC (%)</th>
<th>ΔFEV₁ (L)</th>
<th>Δ%FEV₁ (%)</th>
<th>ΔFEV₁/FVC (%)</th>
<th>Respiratory Complaints</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.01</td>
<td>1.03</td>
<td>16</td>
<td>0.83</td>
<td>18</td>
<td>-2.9</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>5.98</td>
<td>0.65</td>
<td>8</td>
<td>0.39</td>
<td>6</td>
<td>0.5</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>7.65</td>
<td>0.91</td>
<td>25</td>
<td>0.84</td>
<td>26</td>
<td>1.1</td>
<td>68</td>
</tr>
<tr>
<td>4</td>
<td>5.46</td>
<td>0.34</td>
<td>20</td>
<td>-0.07</td>
<td>6</td>
<td>-17.6</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>5.32</td>
<td>0.29</td>
<td>12</td>
<td>0.52</td>
<td>24</td>
<td>13.5</td>
<td>54</td>
</tr>
<tr>
<td>6</td>
<td>5.13</td>
<td>0.2</td>
<td>-6</td>
<td>0.26</td>
<td>-11</td>
<td>5.2</td>
<td>78</td>
</tr>
<tr>
<td>7</td>
<td>4.96</td>
<td>0.13</td>
<td>-2</td>
<td>0.10</td>
<td>-4</td>
<td>-0.9</td>
<td>36</td>
</tr>
<tr>
<td>8</td>
<td>5.88</td>
<td>0.41</td>
<td>10</td>
<td>0.20</td>
<td>3</td>
<td>-12.8</td>
<td>24</td>
</tr>
<tr>
<td>9</td>
<td>3.99</td>
<td>0.04</td>
<td>-4</td>
<td>0.08</td>
<td>-18</td>
<td>7.1</td>
<td>30</td>
</tr>
<tr>
<td>10</td>
<td>4.35</td>
<td>0.33</td>
<td>0</td>
<td>0.51</td>
<td>22</td>
<td>7.1</td>
<td>30</td>
</tr>
<tr>
<td>11</td>
<td>6.99</td>
<td>0.98</td>
<td>8</td>
<td>0.79</td>
<td>19</td>
<td>-1.5</td>
<td>74</td>
</tr>
<tr>
<td>12</td>
<td>4.24</td>
<td>0.19</td>
<td>-2</td>
<td>0.34</td>
<td>-2</td>
<td>0</td>
<td>68</td>
</tr>
<tr>
<td>13</td>
<td>6.76</td>
<td>0.66</td>
<td>0</td>
<td>0.28</td>
<td>-13</td>
<td>-15.7</td>
<td>46</td>
</tr>
<tr>
<td>14</td>
<td>5.66</td>
<td>0.55</td>
<td>6</td>
<td>0.50</td>
<td>7</td>
<td>0</td>
<td>44</td>
</tr>
<tr>
<td>15</td>
<td>4.91</td>
<td>0.71</td>
<td>2</td>
<td>0.64</td>
<td>13</td>
<td>-3.3</td>
<td>32</td>
</tr>
<tr>
<td>16</td>
<td>4.96</td>
<td>0.47</td>
<td>-3</td>
<td>0.35</td>
<td>3</td>
<td>-6.8</td>
<td>54</td>
</tr>
<tr>
<td>17</td>
<td>7.77</td>
<td>0.69</td>
<td>24</td>
<td>0.20</td>
<td>7</td>
<td>-16.5</td>
<td>58</td>
</tr>
<tr>
<td>18</td>
<td>4.21</td>
<td>0.69</td>
<td>3</td>
<td>0.69</td>
<td>2</td>
<td>0</td>
<td>70</td>
</tr>
<tr>
<td>Averages</td>
<td>5.68 ± 1.28</td>
<td>0.51 ± 0.30 **</td>
<td>6.50 ± 9.66 *</td>
<td>0.41 ± 0.27 **</td>
<td>6.00 ± 12.76</td>
<td>-2.42 ± 8.63</td>
<td>51.89 ± 18.70 *</td>
</tr>
</tbody>
</table>

*p < 0.05
**p < 0.01

Table 2 shows that there was a very significant correlation between LPS endotoxin-containing paddy dust levels, FVC decline (Spearman’s correlation test, p = 0.000; r = 0.683), and a decrease in FEV₁ (Spearman’s correlation test, p = 0.002; r = 0.508). The other parameters (%FVC, %FEV₁, FEV₁/FVC, and respiratory complaints) showed no significant correlation.

4. DISCUSSION

4.1. Correlation of Paddy Dust Levels, Lung Function Decline, and Respiratory Complaints

Paddy dust exposure causes a spectrum of clinical syndromes that mainly affect the lungs and airways but can also affect skin and mucous membranes. Cough, sputum,
wheezing, dyspnea, and changes in lung function indicate chronic bronchitis and asthma, which are often found after inhaling dust particles ([22]; Corey et al. 1982). In this study, there was a strong correlation between high levels of personal paddy dust inhalation, $\Delta FVC$ (Spearman’s correlation test, $p = 0.000; r = 0.831$), and $\Delta FEV_1$ (Spearman’s correlation test, $p = 0.000; r = 0.585$). There was also a strong correlation between high levels of personal paddy dust inhalation, $\Delta%FVC$ (p = 0.045; r = 0.336), and the respiratory complaints of workers (Spearman’s correlation test, p = 0.012 and r = 0.414). Other parameters, such as $\Delta%FEV_1$ and $FEV_1/FVC$, had no significant correlation.

In an Australian study, 119 newly recruited grain handlers with an average age of 23 years were assessed for respiratory symptoms before and after the harvest of grain.
Their average work period was 18 days. Among the workers, 18% experienced wheezing, shortness of breath, or chest tightness in the workplace and also had significantly lower \( \text{FEV}_1 \) values \((p < 0.05)\) compared to workers who displayed no symptoms.

An observational study conducted by Do Pico et al. (1983) studied 248 grain handlers before and after work (cross-shift) and compared them to 192 city service workers as a control. The workers exposed to grain dust concentrations had personal grain dust inhalation levels of 3.3 mg/m\(^3\). After correcting test results for age, height, and smoking habits, the increase in the total concentration of dust \((p < 0.05)\) correlated significantly with the decrease in FVC, Maximal Expiratory Flow at 50% (MEF\(_{50}\)) and Maximal Expiratory Flow at 75% (MEF\(_{75}\)) and it also increased the number of leukocytes. In that study, grain workers \((n=122)\) who had complaints and respiratory symptoms (such as cough, phlegm, wheezing, and dyspnea) during work shifts had total dust inhalation levels that were higher \((4.1 \pm 8.1 \text{ mg/m}^3)\) that the levels of workers without complaints and respiratory symptoms \((2.1 \pm 4.5 \text{ mg/m}^3)\) (Do Pico et al. 1983).

The Do Pico (1983) study is in line with the cross-over study by Schwarz et al. (1996) that examined lung function among 14 healthy volunteers and 15 wheat workers. There were 14 volunteers who were exposed to grain dust extracts and, three weeks later, to lipopolysaccharide (LPS). Then, 15 workers were exposed to salt wheat and, three weeks later, to extracts of wheat dust. There was a decline in air flow (FEV\(_1\) and FVC) in the volunteer group after exposure to grain dust and LPS. The same result also occurred in the group of wheat workers. The results of other studies on decreased FEV\(_1\) and FVC after exposure to wheat, corn, and paddy dust also were analyzed by Jagielo et al. (1996), Blaski et al. (1996), Revsbech et al. (1989), and James et al. (1986).

### 4.2. Correlation Between LPS Endotoxin-Containing Paddy Dust Levels, Lung Function Decline, and Respiratory Complaints

In this study, there were strong correlations between LPS endotoxin-containing paddy dust levels, \( \Delta \text{FVC} \) \((p = 0.000; r = 0.683)\), and \( \Delta \text{FEV}_1 \) \((p = 0.002; r = 0.508)\). Other parameters, namely \( \Delta \% \text{FVC}, \text{FEV}_1, \Delta \% \text{FEV}_1/\text{FVC}\), and respiratory complaints, had no significant correlations. Viet et al., (2001) conducted a study that examined 98 wheat harvest workers exposed to 0.09–15.33 mg/m\(^3\) of dust and 4.4–744.4 EU/m\(^3\) of endotoxin. Of the workers, 60% had at least one cross-respiratory symptom, such as shortness of breath or wheezing. The results showed that there was no correlation between endotoxin exposure and respiratory complaints because LPS endotoxin-containing paddy...
dust (habituation) had been declined. Thus, the paddy milling machine operators did not suffer from respiratory complaints.

Based on a study of cotton workers, Douwes and Heederik (1997) suggested that exposure to endotoxin levels from 1-20 ng/m$^3$ had a detrimental effect on respiratory health as defined by the American Thoracic Society guidelines. Significant levels of endotoxin had consistently been recorded in dust samples taken from paddy grains [6]. Endotoxin has been shown to cause an average decline in FEV$_1$ and cause inflammation of the respiratory tract [6, 19]. Inhalation of the LPS and CDE endotoxins at high concentrations (6.0 mg/mL) resulted in a significant decline in FEV$_1$ [9].

The short-term effects of inhaled endotoxin included fever with leukocytosis and flu symptoms, such as organic dust toxic syndrome or fever inhalation, within 18 hours after the initial exposure. Without sensitization to endotoxins, the appropriate antibodies did not develop and respiratory symptoms had the opportunity to arise [2]. Chronic effects, such as chronic bronchitis and chronic obstructive pulmonary disease, occurred after repeated exposures to endotoxin [4, 18]. Long-term lung function decline was also observed [22].

Endotoxin exposures in the work environment and their effects on health have been widely investigated. Several studies have specifically examined the effects of exposure to endotoxins associated with paddy dust ([3, 4, 9, 21-24], Blaski et al. 1996). A recent study by Swan and Crook (1999) highlighted the difficulty in determining the health effects of inhaling a mixture of endotoxin-containing organic dust. Various epidemiological studies showed that extended exposure to organic dust in the workplace causes chronic inflammation, which can lead to chronic bronchitis and a decline in lung function. However, more data is needed on the health effects of long-term exposure to endotoxin.

5. CONCLUSION

The levels of LPS endotoxin in inhaled paddy dust significantly correlate with a decline in FVC and FEV$_1$ before and after a worker’s shift (Spearman’s correlation test, both $p < 0.01$; $r = 0.683$ and $r = 0.508$ successive). Meanwhile, the respiratory complaints of workers to the LPS endotoxin-containing paddy dust levels, so the paddy milling machine operators do not experience respiratory symptoms. The reduction of paddy dust and endotoxin at paddy mills can be achieved by creating better ventilation, installing dust collectors, and properly using personal protective equipment, such as respirators.
References


