# Respiratory health of workers exposed to polyacrylate dust

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# ABSTRACT

**Background:** Polyacrylate (PA) powder dust formed in PA manufacturing units is fine sized, i.e., in nanosize. Although several previous studies reported possible significant adverse effects of nanomaterials, studies on the harmful effect of small-sized PA particles on the respiratory health of the workers are scarce. The present study was carried out to assess the effect of PA on respiratory health and lung volumes/rates among the workers of PA manufacturing unit. **Materials and Methods:** The present cross-sectional study included 84 workers of PA manufacturing unit. Using interview technique as a tool for data collection, demographic, occupational, and clinical details of the workers were recorded on the predesigned pro forma. This was followed by detailed clinical examination, spirometry, chest X-ray (posteroanterior [PA] view), and high-resolution computed tomography (HRCT) examination of each worker. **Results:** On the basis of clinical examination, chest radiography, and HRCT, 17.9% of the workers were found to have fibrotic and cavitary changes in lung parenchyma. The production department workers had a higher proportion of respiratory morbidities as compared to supervisory or office staff. Age, gender, smoking habit, and duration of exposure were nonsignificant risk factors for respiratory morbidity. The overall mean forced vital capacity, forced expiratory volume in 1<sup>st</sup> s, Peak Expiratory Flow Rate (PEFR), (Maximal Mid Expiratory Flow Rate) MMEFR<sub>0.2=1.2</sub>, and MMEFR<sub>25%-75%</sub> were 3.19  $\pm$  0.77 L, 2.72  $\pm$  0.67 L, 6.82  $\pm$  1.86 L/s, 5.79  $\pm$  2.03 L/s, and 3.16  $\pm$  1.19 L/s, respectively. Females and those having respiratory morbidity had significantly lower values of all spirometric parameters as compared to their counterparts. **Conclusions:** The workers exposed to engineered fine dust of PA may be at risk of respiratory ill-health.

KEY WORDS: Fibrosis, lung volumes, pharmaceuticals, polyacrylate

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## INTRODUCTION

India is the largest provider of generic drugs globally. Indian pharmaceutical sector industry supplies over 50% of global demand for various vaccines, 40% of generic demand in the US, and 25% of all medicine in the UK. The pharmaceutical sector was valued at US\$ 33 billion in 2017 which is expected to expand further. Pharmaceutical exports include bulk drugs, intermediates, drug formulations, biologicals, Ayush and herbal products, and surgical.<sup>[1]</sup>

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Pharmaceuticals, the most common medical intervention, though bring healing to patients, also increase the risk of illness among workers manufacturing, handling, and administering pharmaceutical products with inadequate attention to personal safety. During manufacturing and preparation of pharmaceuticals, workers can be exposed to various chemicals, including the potent active pharmaceutical ingredients, chemical intermediates, as

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well as other chemicals such as solvents, catalysts, acids, and bases.  $\ensuremath{^{[2]}}$ 

In pharmaceutical industry, many chemicals that are used are nanomaterials as they generate new superior properties and meet current and future demands. Polyacrylate (PA)/ silica nanoparticles are a nanosilica-containing nanocomposite that has broad applications in the pharmaceutical industry. The PA is a form of engineered nanoparticles which may enter the respiratory system of the workers through inhalational mode. For the reason of small size, these particles in the form of dust may enter the deep part of the human respiratory system with breathing and harm the respiratory system, mainly by the injury of the epithelium<sup>[3]</sup> and by inducing the oxidative stress.<sup>[4,5]</sup> The adverse effects happen not only in the respiratory system but also in extrapulmonary organs. Once these smaller particles reach pulmonary alveoli, some of them may pass through the alveolar epithelium and capillary endothelial cell and then enter the cardiovascular system and other internal organs.<sup>[6]</sup>

Although several previous studies caution against the possible significant adverse effects of nanomaterials,<sup>[7-10]</sup> in their editorial,<sup>[7]</sup> the authors have suggested that as the nanoparticles overlap with the ultrafine particles of air pollution and as the fine air pollutants are known to cause cardiovascular and respiratory morbidity, nanoparticles are concern from toxicity point of view. Similarly, Nel et al.<sup>[8]</sup> have mentioned that only a limited number of nanomaterials have so far been shown to exert toxicity in tissue culture and animal experiments, usually at high doses. However, only a limited number of studies suggest the harmful effect of small-sized PA particles on the respiratory health of the workers involved in manufacturing process. Song et al.<sup>[11]</sup> reported nonspecific pulmonary inflammation, pulmonary fibrosis, and foreign-body granulomas of the pleura on pathological examinations of patients' lung tissue. They further observed on transmission electron microscopy that the nanoparticles were lodge in the cytoplasm and caryoplasm of pulmonary epithelial and mesothelial cells but are also located in the chest fluid. They attributed these changes to PA as they also noticed PA in the workplace. In their animal experiment, Zhu et al.<sup>[12]</sup> again reported that exposure to PA results in pleural effusion/pericardial effusion, pulmonary fibrosis, and granuloma in rats. In another experimental study<sup>[13]</sup> on Wistar rats, it was reported that the exposed rats exhibited various degrees of pleural effusion and pericardial effusion.

The manufacturing process involved polymerization of ethylene dichloride and acrylic acid (monomer) liquid into the reactor, and a slurry of PA is formed in the reaction vessel. The wet PA powder containing 80%–85% PA is then pneumatically transferred into a rotary vacuum drier. The dry powder is then transferred to pneumatic outlet trolley, and batchwise 10–12 kg of PA powder is fed into hopper of pulverizer manually where the PA is finely grounded to <100 mesh size. The PA powder is further fed into

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cyclone separator where the air and powder are separated. Finally, the PA powder is manually filled into HDPE bags and loaded into carboys, labeled, and shifted outside of the packaging section. Thus, the separator and bag filling are processes of potential exposure to dry PA powder.

With this background, the present study was carried out to assess the respiratory health and lung volumes/rates among the workers of PA manufacturing unit.

### **MATERIALS AND METHODS**

The PA manufacturing unit was identified in the Western state of India. All the workers of the PA manufacturing units were included in the present cross-sectional study. Thus, a total of 84 workers participated in the study. After taking approval from the Institutional Ethics Committee of National Institute of Occupational Health, the study began with explaining the purpose of the study to the participants and taking their written informed consent in Hindi and English as applicable. Using interview technique as a tool for data collection, demographic, occupational, and clinical details of the workers were recorded on the predesigned pro forma. This was followed by detailed clinical examination and chest X-ray (PA view) with the help of 300 mA machine at the end of inspiration on a  $12 \times 15$  film. High-resolution computed tomography (HRCT) examination of each worker was carried out on GE 16 Slice Scanner Machine by taking 1 mm thin sections at 1 mm intervals and was reconstructed using a sharp algorithm.

The pulmonary functions of the workers were measured using Spirovit SP-10 (Maker Schiller AG, Switzerland). After calibrating the spirometer according to the procedure given in the catalog, three readings of each ventilatory function of each worker were taken. The readings showing the highest value were recorded, considering that the worker has co-operated at his/her best and used for further analysis. The predicted forced vital capacity (FVC) was calculated according to the regression equation given by Kamat et al.<sup>[14]</sup> On the basis of the observed FVC and forced expiratory volume in 1<sup>st</sup> s (FEV<sub>4</sub>) values, the pulmonary function impairment was classified<sup>[15]</sup> as "normal" (>80% of predicted FVC and >70% FEV,/FVC%), "restrictive" (< 80% of predicted FVC and > 70% FEV./ FVC%), "obstructive" (>80% of predicted FVC and <70% FEV /FVC%), and "combined" (<80% of predicted FVC and <70% FEV,/FVC%).

The study variables included age, gender, smoking habit, years of employment, nature of work, and respiratory morbidity. Age and years of employment were arbitrarily dichotomized into <40 and  $\geq40$  years and <5 and  $\geq5$  years, respectively. The smoking habit was dichotomized into ever smokers and never smokers. There were several departments in the industry such as production, maintenance, office work, packing, and

quality control. The production workers and the workers engaged in packing of material were directly exposed to dust and therefore considered as "direct exposure" group for further analysis while all other departments were considered as "indirect exposure" group as they were employed in the unit but not handling the material. The operational diagnosis of respiratory morbidity was based on the abnormality seen on chest X-ray and HRCT. In case of discrepancy, the findings on HRCT were considered final for labeling the participant as having respiratory morbidity or free from it.

Statistical analysis was carried out using the statistical software package SPSS 24.0. Distribution of respiratory morbidity according to study variables was compared using Chi-square test and exact test (in case of <5 sample size). The crude odds ratio (OR) was calculated using the single study variable and respiratory morbidity. The adjusted OR was calculated using multiple logistic regression function. The OR thus calculated taking all the dichotomized study variables together for respiratory morbidity was adjusted OR as it has taken into the interaction effect of all study variables for respiratory morbidity. The Shapiro–Wilk test revealed that the data were normally distributed. The mean value of spirometric parameters according to study variables was compared using Student's t-test.

### RESULTS

The present cross-sectional study was conducted among 84 workers of PA manufacturing unit. There were 68 (80.9%) males and 16 (19.1%) females. The mean age for males was found to be  $30.3 \pm 9.2$  years while that for females was  $28.2 \pm 8.3$  years. The median duration of exposure was 2 years. Majority (51.5%) of the workers were educated up to secondary school level while 32.4% of the workers were graduates. Most (45.2%) of the workers belonged to the production department, followed by 10.7% and 9.5% in the office and maintenance department, respectively. 92.9% were nonsmokers and 91.7% were nonalcoholics.

On the basis of clinical examination, chest radiography, and HRCT, 15 (17.9%) workers were found to have respiratory morbidity as per the study criteria. Out of these 15 workers, 7 had fibrotic/fibrocalcified/cavitatory lesion in the right upper lobes, 3 had reticulonodular pattern fibrosis in both upper lobes, and 1 each had ground-glass opacities in both upper lobe, mild bronchiectasis in the right middle lobe, paraseptal emphysema in the right upper lobe, and ground-glass opacities in both upper lobes. Out of those having parenchymal abnormalities, only four had a restrictive type of pulmonary impairment while others had normal spirometric values when compared with their predicted values.

Table 1 shows the distribution of respiratory morbidity according to the study variables. It can be observed that

35.7% of those aged  $\geq$ 40 years had respiratory morbidity as compared to only 14.3% among those aged <40 years. Although more proportion of smokers had morbidity as compared to nonsmokers, the difference was statistically nonsignificant due to a very low number of smokers. Similarly, those in the job for more than 5 years and working in the departments where direct exposure occurs were having more morbidity as compared to their counterparts.

Table 2 shows the multivariate analysis of respiratory morbidity according to study variables. The work in departments resulting in direct exposure to PA dust was a significant risk factor. Age, gender, smoking habit, and duration of exposure were found to be nonsignificant risk factors on univariate as well as multivariate analysis.

The distribution of spirometric values, namely FVC, FEV<sub>1</sub>, PEFR, MMEFR<sub>0.2-1.2</sub>, and MMEFR<sub>25%-75%</sub> according to study parameters, is depicted in Table 3. The overall mean FVC, FEV<sub>1</sub>, PEFR, MMEFR<sub>0.2-1.2</sub>, and MMEFR<sub>25%-75%</sub>

| Table 1: R  | espiratory  | morbidity | according | to study |
|-------------|-------------|-----------|-----------|----------|
| variables ( | (univariate | analysis) | 1         |          |

|                             | Respiratory                              | Р                                       |      |
|-----------------------------|------------------------------------------|-----------------------------------------|------|
|                             | Present ( <i>n</i> =15),<br><i>n</i> (%) | Absent ( <i>n</i> =69),<br><i>n</i> (%) |      |
| Age in categories (years)   |                                          |                                         |      |
| <40                         | 10 (14.3)                                | 60 (85.7)                               | 0.07 |
| ≥40                         | 5 (35.7)                                 | 9 (64.3)                                |      |
| Gender                      |                                          |                                         |      |
| Male                        | 12 (17.1)                                | 56 (82.9)                               | 1.00 |
| Female                      | 3 (18.8)                                 | 13 (81.2)                               |      |
| Smoking habit               |                                          |                                         |      |
| Yes                         | 2 (40.0)                                 | 3 (60.0)                                | 0.22 |
| No                          | 13 (16.5)                                | 66 (83.5)                               |      |
| Years of employment (years) |                                          |                                         |      |
| <5                          | 10 (14.5)                                | 59 (85.5)                               | 0.09 |
| ≥5                          | 5 (33.3)                                 | 10 (66.7)                               |      |
| Nature of work              |                                          |                                         |      |
| Direct exposure             | 12 (26.7)                                | 33 (73.3)                               | 0.04 |
| Indirect exposure           | 3 (7.7)                                  | 36 (92.3)                               |      |

# Table 2: Multiple logistic regression for study variables and respiratory morbidity

| Variable           | Crude<br>OR (95%CI) | Р    | Adjusted<br>OR (95%CI) | Р    |
|--------------------|---------------------|------|------------------------|------|
| Age                |                     |      |                        |      |
| >40                | Reference           |      | Reference              |      |
| <40                | 3.33 (0.93-12.01)   | 0.07 | 2.80 (0.54-14.54)      | 0.22 |
| Gender             |                     |      |                        |      |
| Female             | Reference           |      | Reference              |      |
| Male               | 0.93 (0.23-3.77)    | 0.92 | 0.61 (0.12-2.98)       | 0.54 |
| Smoking status     |                     |      |                        |      |
| Never smoker       | Reference           |      | Reference              |      |
| Ever smoker        | 3.39 (0.51-22.30)   | 0.21 | 4.89 (0.44-54.01)      | 0.21 |
| Years of exposure  |                     |      |                        |      |
| <5                 | Reference           |      | Reference              |      |
| >5                 | 2.95 (0.83-10.46)   | 0.09 | 2.89 (0.54-15.57)      | 0.22 |
| Nature of exposure |                     |      |                        |      |
| Indirect           | Reference           |      | Reference              |      |
| Direct             | 4.36 (1.13-16.84)   | 0.03 | 6.17 (1.39-27.33)      | 0.01 |

CI: Confidence interval, OR: Odds ratio

| Study variable                  | n  | FVC             | FEV <sub>1</sub> | PEFR            | MMEFR <sub>0.2-1.2</sub> | MMEFR <sub>25%-75%</sub> |
|---------------------------------|----|-----------------|------------------|-----------------|--------------------------|--------------------------|
| Age group (years)               |    |                 |                  |                 |                          |                          |
| <40                             | 70 | 3.26±0.79       | 2.77±0.68        | 6.98±1.90       | $5.92 \pm 2.09$          | 3.18±1.23                |
| ≥40                             | 14 | $2.86 \pm 0.53$ | 2.48±0.53        | 5.98±1.40       | 5.17±1.60                | $3.05 \pm 1.00$          |
| <i>t; P</i>                     |    | 3.18, 0.08      | 2.29, 0.13       | 3.47, 0.07      | 1.59, 0.21               | 0.14, 0.71               |
| Sex group                       |    |                 |                  |                 |                          |                          |
| Male                            | 68 | 3.41±0.65       | $2.89 \pm 0.59$  | 7.31±1.67       | 6.33±1.83                | 3.34±1.23                |
| Female                          | 16 | 2.25±0.44       | $1.99 \pm 0.41$  | 4.69±0.82       | 3.52±1.03                | 2.39±0.57                |
| <i>t; P</i>                     |    | 45.29, 0.00     | 32.24,           | 36.81, 0.00     | 34.93, 0.000             | 8.87, 0.004              |
|                                 |    |                 | 0.000            |                 |                          |                          |
| Duration of exposure (in years) |    |                 |                  |                 |                          |                          |
| <5                              | 69 | 3.24±0.79       | 2.78±0.69        | 6.97±1.89       | 5.95±2.09                | 3.28±1.23                |
| ≥5                              | 15 | 2.95±0.59       | $2.44{\pm}0.46$  | 6.13±1.55       | 5.06±1.62                | 2.61±0.85                |
| <i>t; P</i>                     |    | 1.82, 0.18      | 3.38, 0.07       | 2.55, 0.11      | 2.40, 0.13               | 4.02, 0.04               |
| Smoking habits                  |    |                 |                  |                 |                          |                          |
| Nonsmokers                      | 64 | 3.42±0.67       | 2.90±0.61        | 7.31±1.72       | 6.32±1.88                | 3.36±1.26                |
| Smokers                         | 4  | 3.24±0.53       | $2.74{\pm}0.45$  | 7.39±0.28       | 6.49±0.62                | $3.02 \pm 0.49$          |
| <i>t; P</i>                     |    | 0.27, 0.60      | 0.25, 0.62       | 0.01, 0.92      | 0.03, 0.86               | 0.28, 0.60               |
| Exposure type                   |    |                 |                  |                 |                          |                          |
| Indirect exposure               | 39 | 3.25±0.83       | 2.76±0.71        | 6.92±1.81       | 5.87±1.99                | 3.20±1.26                |
| Direct exposure                 | 45 | 3.14±0.72       | 2.68±0.63        | 6.73±1.91       | 5.73±2.09                | 3.12±1.15                |
| <i>t; P</i>                     |    | 0.42, 0.52      | 0.29, 0.59       | 0.23, 0.64      | 0.09, 0.76               | 0.10, 0.75               |
| Respiratory health              |    |                 |                  |                 |                          |                          |
| Normal                          | 69 | $3.29 \pm 0.74$ | 2.82±0.63        | $7.05 \pm 1.84$ | 6.08±1.91                | 3.32±1.17                |
| With morbidity                  | 15 | $2.73 \pm 0.78$ | 2.26±0.68        | 5.76±1.59       | 4.47±2.1                 | $2.43{\pm}1.01$          |
| <i>t; P</i>                     |    | 6.88, 0.01      | 9.48, 0.003      | 6.28, 0.014     | 8.49, 0.005              | 7.47, 0.008              |

| Table 3: Distribution of lun | a function narameters | according to study variables |
|------------------------------|-----------------------|------------------------------|
|                              | u Tunchon Darameters  | according to study variables |

FVC: Forced vital capacity, FEV,: Forced expiratory volume in 1st s, PEFR: Peak expiratory flow rate, MMEFR: Maximal mid expiratory flow rate

were  $3.19 \pm 0.77$  L,  $2.72 \pm 0.67$  L,  $6.82 \pm 1.86$  L/s,  $5.79 \pm 2.03$  L/s, and  $3.16 \pm 1.19$  L/s, respectively. It can be observed that females and those having respiratory morbidity were having significantly lower values of all spirometric parameters as compared to males and healthy workers, respectively. Further, those aged  $\geq 40$  years, those in the job for  $\geq 5$  years, and those working in departments where direct exposure occurs reported lower values for spirometric measurements in comparison to those younger than 40 years, those in the job for <5 years, and those working in the department other than production and packing, respectively. However, the difference was statistically nonsignificant.

#### DISCUSSION

The present study among workers exposed to PA dust in PA manufacturing unit showed that 17.9% suffered from fibrotic and cavitatory lesions in the lung parenchyma evident on chest radiograph and HRCT. Considering the prevalence of tuberculosis in the country, the possibility of pulmonary tuberculosis cannot rule out. The clinical history did not suggest past tuberculosis, but the site of lesion favors its possibility. However, a multicentric study which used smear test, culture, and chest radiography found the pooled prevalence of pulmonary tuberculosis as 300.7/100,000 population.<sup>[16]</sup> Thus, assuming all the fibrosis cases as past cases of pulmonary cases is still a concern as it is roughly six times of national prevalence. This suggested that exposure at the workplace may have some role in this higher prevalence, and it may be the PA exposure.

Although the concentration of PA dust was not measured, it can be considered engineered fine particles of smaller size. Such smaller particles can penetrate the membrane of pulmonary epithelial cells and lodge in the cytoplasm and karyoplasms<sup>[17]</sup> and aggregate around the membrane of red blood cells and exert toxicity. Patients may develop clinically serious conditions associated with damaged respiratory function, including a progressive pulmonary fibrosis. As suggested in previous studies, the mechanism involved includes direct toxicity of toxic dust<sup>[18]</sup> through promotion of DNA damage<sup>[19]</sup> and through inflammation and oxidative stress (generation of reactive oxygen species).<sup>[19,20]</sup> However some investigators also suggested that PA has low toxicity,<sup>[11]</sup> but some nanoparticles, such as silicon nanoparticles, thin zinc oxide, titanium dioxide, and nanoscale silver clusters, are normally added into the PA emulsion to make the material stronger and more abrasion resistant,<sup>[21-23]</sup> thereby making it more toxic.

The risk factor analysis suggests that those working in the production departments resulting in direct exposure to the finer dust were at increased risk of acquiring the morbidity. Although the concentration and characterization of dust were not done, it may be because of the raw material used and thereby resulting in more concentration of toxic dust causing increased disease in these workers.

In the present study, all the lung function parameters were lower in those having respiratory morbidity as compared to those free from it. This may be attributed either to the parenchymal changes due to past tuberculosis or exposure to the fine dust reaching the terminal parts of the respiratory tract, thereby affecting all the spirometric parameters. All the lung function parameters were found to be significantly lower among females as compared to males. This can be partly attributed to the differences in their anthropometric measurements such as height and weight and partly to the multiple exposures among females. In this society, females are indulged in the cooking process where they are exposed to smoke, if bad fuels are used. Furthermore, by virtue of such occupation, these females are also exposed toxic chemical dust causing damage to pulmonary tissue.

The results of this study need to be considered against the backdrop of certain limitations. First, the measurement of PA dust concentration in the workplace and the characterization of dust particles according to size could not be done. However, the record of the management revealed that the measurement of  $PM_{10}$  done by the third party was 65.1  $\mu$ g/m<sup>3</sup>. Although there are no time-weighted average (TWA)-threshold limit value for PA or polymethacrylate powder as per the Indian Factories Act/ACGIH/OSHA/NIOSH the in the work environment permissible levels used by Germany and The Netherlands, i.e., 0.05 mg/m<sup>3</sup> (8-h TWA) as the maximum allowable concentration<sup>[24]</sup> for the respirable dust of sodium PA (<10 um particle diameter) can be used for prevention of exposure. However, the literature suggests that PA used in such setting are released in very smaller size maybe nanoparticles. Second, the current study includes a smaller sample size resulting in further reduction in size while categorizing the variables.

To prevent the exposure, a multipronged strategy is required. These include installation of local exhaust ventilation at potential processes of exposure to avoid the escape of powder or dust into the work environment, conversion of manual processes such as separation and bag filling into automated process to reduce human-chemical interaction, good housekeeping to avoid the possibility of settled dust to become airborne, and the use of personal protective equipment such as respirator can help in preventing the exposure. Regular environmental monitoring and medical surveillance of workers as done for other dust-related exposures will help in early detection of effects due to exposure.

Thus, to conclude, the present study shows that the workers in the PA manufacturing unit may be exposed to smaller size dust which may cause pathology in lung parenchyma and thereby in the respiratory system. Due to limitations of this study, a more comprehensive study involving larger sample size and environmental monitoring is recommended.

## **Key points**

What is already known about this subject:

- In the PA manufacturing unit, the PA powder dust is often of nanosize
- Very few studies, mostly from animal experiments, are available, which suggest that pulmonary fibrosis may occur due to PA.

What this study adds:

- This is one of the few studies carried out among workers exposed to PA in PA manufacturing unit
- The study reports 17.9% of the workers suffering from lung parenchymal fibrosis
- The spirometric measurement of PA manufacturing unit workers is reported first time in the current study.

What impact this may have on practice or policy:

- The workers handling PA may be exposed to chemical and related health effects
- The workers should be subjected to periodic medical examination as done in other dust or chemical exposures as per the existent law
- In the future, if causal relationship is established, the rehabilitation mechanism should also be developed for these workers, as is suggested for other occupational interstitial fibrosis.

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#### **Conflicts of interest**

There are no conflicts of interest.

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