

# Toluene diisocyanate-linked occupational airflow obstruction and peak expiratory flow rate patterns among foam makers

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## Abstract

This study looked at the prevalence of respiratory symptoms and airflow obstruction, and peak expiratory flow rate (PEFR) variation between production workers and control workers (both inside and outside work, linked to the foam-making industry at Onitsha, south-east Nigeria. A cross-sectional case control study was conducted among 199 randomly selected workers from five major foam companies. Subjects were grouped into exposed (production workers) and control, and a modified structured four-part Guidelines for Health Surveillance for Isocyanates questionnaire was administered. The workers had their PEFR values individually assessed during work on Friday and before resumption of work the following Monday morning for a period of 6 months. A total of 199 subjects were recruited (129 production workers, 70 control workers). There was a higher proportion of respiratory symptoms among the exposed group (53%) compared with the controls (34%) ( $p < 0.02$ ). It was concluded that airflow obstruction and respiratory symptoms are common among workers in foam industries exposed to toluene diisocyanate.

## Introduction

The health of workers is affected by their type of occupation, and through the ages man has continued to suffer from hazardous exposures in the work environment. Industrial workers, in particular, are prone to developing respiratory complications.<sup>1</sup> This is to be expected, because the lung, with its extensive surface area, thin alveolar epithelium, and high blood flow rate (450 ml/s or 12% of the body's total volume) constitutes an important site of contact with the various materials contained in the enormous litres of air to which it is exposed daily. Hence,

inhalation is by far the commonest route of entry into the body of occupational agents. This is why the lung is considered the most important organ in occupational medicine.<sup>2</sup>

The effects of exposure of the lung to organic, as well as inorganic dusts/chemicals, have been largely studied, for example, jute;<sup>1</sup> grain, flour, cotton, latex, and tea;<sup>3-8</sup> soap and detergents, wood, and coal;<sup>9-15</sup> asbestos, cement, aluminium, vinyl chloride, and acid anhydrides;<sup>16-20</sup> amines;<sup>21</sup> and diisocyanates.<sup>22-26</sup> Many respiratory diseases may be caused or worsened by lung exposure to these and some other toxic occupational agents. Asthma, however, is the principal cause of respiratory disease linked to the work place environment.<sup>27, 28</sup>

By definition, occupational asthma (OA) is a disease characterised by variable airflow obstruction and airway hyper-responsiveness caused by a specific agent or process encountered in the work place, (and not to stimuli encountered outside the workplace,<sup>7,29,30</sup>) or the presence of respiratory symptoms at work, e.g. symptoms of wheezing, cough, dyspnea, and chest tightness that resolve after time away from work.<sup>31-33</sup>

However, despite being a common problem, OA has been confirmed to be under-diagnosed and under-treated.<sup>34,35</sup> Foam production involves the use of different chemical compounds. These include: toluene diisocyanate (TDI), polyethylene, methylene chloride, calcium carbonate, silicon, delma, stannous octoate, and water.

Of these, although only TDI has been reported in the literature as a cause of OA, toluene and other isocyanates have also been the leading cause of OA for decades.<sup>22,23,36</sup>

The health effects of exposure of the lung to diisocyanates include difficulty in breathing (dyspnoea), wheezing, cough, and chest tightness. Overt exposure, can lead to frank OA, hypersensitivity pneumonitis, rhinitis, and pharyngitis; in addition conjunctivitis and dermatitis, which are non-respiratory conditions, are also common.<sup>26,37</sup> Wheezing and dyspnoea attributable to the air-flow obstruction, the most easily recognised presentations of OA, are the hallmark of asthma. These symptoms alone, however, are not sufficient to arrive at a diagnosis of OA,<sup>38</sup> a history of work relatedness is important. The diagnosis is thereafter confirmed, usually by demonstrating significant variability in peak expiratory flow (PEF) with temporal association with work-place exposure to a suspected agent or process.

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The identification of the specific causative occupational factor, however, is not a *sine qua non* for arriving at a diagnosis of OA.<sup>39</sup>

Tests involving forced expiration, such as PEF, are easily reproducible, and are the most informative tests of ventilatory function.<sup>40</sup> Results of PEF, according to Venables and colleagues,<sup>43</sup> correlate well with bronchial provocation testing, and provide a suitable alternative for the diagnosis of occupational asthma. Tests that depend on inspiratory flow rates, on the other hand, are hardly reproducible because there is no airflow.

A better approach, which is gaining acceptance, is the definition of airflow obstruction based on the standard deviation (SD) of the estimate obtained in the analysis of the population under reference. Those PEF values that fall outside the range in which 95% of the population lie (i.e. less than 2 SD below the measured mean values for the study population) are judged as depicting the presence of airflow obstruction.<sup>42-44</sup>

With the high rate of industrialisation in developed countries of the world the prevalence of OA as expected, has been on the increase.<sup>45-47</sup> This is also true of developing countries, where Kabu and Holgate<sup>48</sup> also found a rising prevalence. The true prevalence of OA, however, remains unknown<sup>49</sup> and is difficult to ascertain due to lack of a standard definition of asthma and what constitutes work relatedness. The difficulty also arises from the variations in epidemiology being adopted by the different investigators.<sup>47</sup> Surveillance-based methods, for example, which depended on the questionnaire account of wheezing only in diagnosis, generally have found the lowest rate of prevalence of OA, ranging from 1% to 8% of cases.<sup>47</sup>

Other types of studies using exposed/unexposed methodology with application of spirometric/PEF indices in diagnosis of the variable airflow obstruction, typical of asthma, have reported various prevalence figures; for example, 10% to 25% of asthma cases have been found by such studies to be work related.<sup>45,47</sup>

The prevalence of OA also varies depending on the offending agent and industry at risk. The prevalence of occupational asthma due to TDI among exposed workers has been reported as being between 5% and 30%.<sup>9,22,30</sup>

Unlike data obtainable in developed countries, there is a paucity of data on lung function in Nigeria's industrial workers. There is the need for data on the prevalence of airflow obstruction linked to the foam-making industry in this part of the country; our study is intended to generate such data, which could then be compared with estimates from other countries.

## Materials and methods

This study was conducted over a period of 6 months from June to November 2005 in Onitsha, Anambra State,

south-east Nigeria. There are about 30 foam manufacturing industries located within the Onitsha area of which 12 major businesses employ between 40 to 90 workers. The production processes involve the use of different machinery, with attendant high production output.

One hundred and ninety-nine (199) workers took part in the study, of which 121 were less than 29 years and 2 were 70 years and above (see Table 1). The subjects were made up of 129 production (101 male and 28 female), and 70 control (32 male and 38 female) workers. The mean age of the production workers was 26.11±11 years and that of the control 28±14 years. There was a statistical difference in the ages of the production and control workers  $p < 0.04$ . The inclusion criteria included:

- a willingness to participate in the study;
- workers who had been in the industry for more than 1 month;
- healthy subjects (no anatomic defects, no signs and symptoms of asthma, no cardiopulmonary disease);
- nil smoking history.

Institutional ethical approval was obtained from the Research and Ethical Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi, and permission to conduct the study was sought from the foam industry medical directors. Individual written informed consent was obtained from the workers.

## Data collection and measurement of PEF

Data collection and PEF assessment appointments took place over a period of 6 months when the factory's production line was operating. In addition to the written explanations contained in the subjects' consent forms talks were given regarding the aims, benefits, harmlessness, and methodology of the study. Free medical consultations were also made available to those subjects who needed them.

A modified structured four-part 'Guidelines for Health Surveillance for Isocyanates' questionnaire<sup>50</sup> was administered in turns to the participating workers. Section A was for the purpose of collecting socio-demographic

Table 1: Distribution of subjects (production vs control) by age and gender

Age group (years)	Production workers		Control workers		Total
	Males (%)	Females (%)	Males (%)	Females (%)	
≤29	64 (63)	18 (64)	10 (31)	29 (76)	121
30-49	30 (30)	10 (36)	13 (41)	9 (24)	62
50-69	6 (6)	-	8 (25)	-	14
≥70	1 (1)	-	1 (3)	-	2
Total	101 (100)	28 (100)	32 (100)	38 (100)	199
Mean age±SD (yrs)	28±13	26±10	31±17	24±9	
Mean age±SD (yrs) (Production control)	26±11		29±14		
z-score=0.58 $p > 0.4$					

data; section B dealt with occupational and medical history; and section C with physical examination and post-examination findings.

The height and weight of each subject were measured along with respiratory and heart rates. The chest was examined for any deformity as well as for signs of cardio-pulmonary diseases, including auscultation for presence of abnormal heart and breathing sounds.

PEFR was done four times per day<sup>51</sup> for the 6-month period of the investigation. Three readings, expressed in litres per minute to the nearest litre were obtained for each subject, and the best of these selected for the purpose of analysis. Workers with PEFR values at work less than 2 SD below the mean value for the subject population, based on their outside work PEFR were classified as having airflow obstruction.<sup>42-44</sup>

### Data management and statistical analysis

Data were entered into the computer, and analysed using Epi Info version 6. Descriptive statistics such as frequencies and percentages were used to describe the categorical variables; while summary statistics, such as mean and standard deviation were used to summarise the numerical variables. Tests of significance to determine the association between groups studied, such as chi-square and z-test, were used where appropriate. Conclusions were drawn based on 0.05 percent level of significance (i.e.  $p \leq 0.05$ ).

Additionally, independent effects of the socio-demographic characteristics (age, sex, height, weight, body mass index (BMI), and length of service in the industry) on PEFR were determined using the correlation coefficient (r-value).

### Results

Based on the presence of at least one respiratory symptom, Table 2 shows that these symptoms were more common (52.7%) in the production workers, which was statistically significant when compared with a value of 34.3% for the symptomatic control workers ( $p < 0.020$ ). The common respiratory symptoms were wheeze, cough, catarrh, dyspnoea, and chest tightness.

Table 2 Respiratory symptoms prevalent among the workers

Clinical condition	Production workers	Control workers	Total
Symptomatic	68 (53%)	24 (34%)	92
Asymptomatic	61	46	107
Total	129	70	199
$\chi^2=6.25$ $p < 0.02$			

Table 3 Summary of all measured variables in production vs control workers

Variables	Production worker (n = 129) mean±SD	Control workers (n = 70) mean±SD	Z-score	p value
Age (years)	26±11	28±14	0.58	$p > 0.4$
Height (cm)	167±22	164±22	1.11	$p > 0.05$
Weight (kg)	72±22	67±7	2.04	$p > 0.05$
PEFR (min <sup>-1</sup> ) (at work)	390±83	400±85	0.76	$p > 0.04$
PEFR (min <sup>-1</sup> ) (outside work)	421±74	427±82	0.63	$p > 0.5$
Length of service (months)	47±21	43±22	1.32	$p > 0.05$

Table 4 Prevalence of airflow obstruction among the production and control workers

Workers	Number with airway obstruction	Number without airway obstruction	Total
Production workers	14 (11%)	115	129
Control workers	0 (0%)	70	70
Total	14 (7%)	185	199
$\chi^2$ (with continuity correction factor)=6.54. $p < 0.001$ .			

Table 3 summarises the significance of the various measured variables in the production and control workers. Table 4 shows that of the 129 production workers, 14 subjects (10.9%) had airflow obstruction, which was quite significant as none of the 70 control workers had airflow obstruction ( $p < 0.001$ ); the overall prevalence of airflow obstruction among the 199 foam industry workers was 7.0%.

### Discussion

A primary objective of this investigation was to determine the prevalence of airway obstruction and PEFR variation between production and control foam workers, both inside and outside the workplace. The mean PEFR value obtained outside the work period/environment is judged to be the nearest to the individual worker's personal best or normal value. Thus, the mean PEFR value of the 133 male workers obtained in this study (456±781/min), was considered as the normal value for the foam industry's male worker population. This was used for determining those male workers with airflow obstruction. All male workers, therefore, whose PEFR values were less than and outside the derived range, 299.3–602.51/min, were considered as having airflow obstruction.<sup>(42-44)</sup>

Similarly, the female workers whose PEFR were less than and outside the range, 284.4–490.91/min as determined by their mean PEFR value of 387.0±51.61/min (i.e. mean±SD) were adjudged to have some degree of airflow obstruction in this study. In our study we found

a prevalence of airway obstruction of 7%. In their 2002 retrospective study, a 3.7% prevalence was reported by Arif et al<sup>52</sup> for work-related (physician-diagnosed) asthma, and 11.5% prevalence for work-related wheezing (based on cases of self-reported wheezing by workers). The different environments, i.e. at work and outside work, constitute different exposure situations to TDI. In this study, production workers had significant reductions in their PEFR at work (390±831/min), compared with outside work (421±711/min)  $p<0.001$ . The significantly lower value of mean PEFR in production workers at work compared with the outside work period/environment ( $p<0.001$ ) could be a result of the effect of exposure of these workers to TDI fumes which must have affected the lung function of some of the workers leading to degrees of airflow obstruction and reduction in their PEFR. This is in agreement with observations by Bamidele, who studied soap and detergent industry workers.<sup>10</sup>

In the general population, however, the overall prevalence of OA was found to be 3%,<sup>30</sup> which is lower than the prevalence rate found in our study, though our study was on isocyanate workers.

The mean PEFR values of the 70 control workers, at work (400±851/min) and outside work (428±821/min) were higher than their 129 production counterparts. The lower mean PEFR values among the production workforce compared to the control could also be attributed to their greater exposure to isocyanates fumes on routine bases during work. The findings of lower PEFR values in the production workers compared to controls compares favorably with findings in similar studies in different industries, for example. Bamidele (soap and detergent workers);<sup>10</sup> Oleru (detergent workers);<sup>11</sup> Jinadu (wood furniture workers);<sup>14</sup> and Sofola et al (petrol workers).<sup>53</sup> These investigators, however, drew their unexposed control population from outside the industries studied.

Workers in the foam industry are generally young and the majority of the workers (92%) in this study were between 18 and 46 years with a mean age of production workers of 26+11 years and that of control, 29+14 years.

Of the chemicals used in foam manufacturing, only TDI has been shown to have a deleterious effect on lung function. It has been associated with high prevalence of respiratory symptoms and OA, the latter having a hallmark of airflow obstruction. This study shows that respiratory symptoms are more prevalent in foam production workers (53%) when compared with the control group (34%). This difference is statistically significant ( $p<0.001$ ). Wheeze, cough, catarrh, in that order, were the most common symptoms. Other studies, by Jinadu et al,<sup>14</sup> and Fatusi and Erhabor,<sup>13</sup> have also shown high but differing prevalences of respiratory symptoms in the industrial workers studied. These differences may be explained by the level of exposure of the workers, and the nature of the irritant, as well as by the industrial air hygiene variable obtainable within the particular industry.

In this study, the male workers had significantly higher mean PEFR values than the females at work and outside

the work period/environment. Larger values of PEFR in men have been attributed to their larger lung volumes and muscular power.<sup>54-57</sup> The effect of exposure to TDI on PEFR, therefore, could best be shown by comparison of mean PEFR values for men and women separately, both at work and outside work. In this study, both male and female workers had significant reductions in their PEFR at work, compared to outside work; exposure while at work, invariably, must have affected the lung function of some of the workers leading to degrees of airflow obstruction and reduction in their PEFR.

In this study PEFR was seen to increase with increasing height of workers studied. The correlation was strongly positive. Height is a good indicator of body build, hence, there is always a good correlation between height and ventilatory function<sup>58,59</sup> as was found in this study.

It was observed in this study that PEFR increased with increase in weight of workers. The correlation was significantly positive ( $r=0.61$ ) and ( $p<0.001$ ). This corroborated with the findings of others.<sup>58,59</sup>

This study found a strong, but negative correlation between PEFR and length of service of production workers in the foam industry. The control workers, who were not as exposed to isocyanates as the production workers, did not show such a feature.

In conclusion this study has shown a high prevalence of respiratory symptoms and OA among foam workers. OA often has long-term health, social, and economic consequences and thus early diagnosis is crucial for a favourable and better outcome of the disease. It is important to create and strengthen risk awareness and so increasing the health education impact for the foam industry workers and management staff alike was paramount in the decision to use the 'apparently' unexposed office workers and others inside the foam industry as controls in this study to highlight the dangers of direct exposure.

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