

Occupational Lung Diseases in Sewage Workers: A Systematic Review

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Abstract

Background: Occupational lung diseases are a global priority and a major source of morbidity and mortality. They include occupational asthma, occupational COPD, pneumoconiosis and pulmonary cancers. While certain occupations have been designated as hazardous, occupational lung diseases in sewage workers have not received sufficient scientific attention, despite chronic exposure to noxious material.

Methods: A systematic review of literature was conducted using STROBE guidelines to determine the evidence base for sewage work as an occupational respiratory hazard. An internet based search was done on Pubmed and Google Scholar for scientific literature in English language using defined MeSH terms singly and in various combinations. The articles were evaluated for comparable methodology and results.

Results: The literature search revealed only 27 studies meeting the criteria for systematic review. The studies revealed significantly higher rates of respiratory symptoms and impaired pulmonary function tests (obstructive pattern) in sewage workers, independent of smoking status, with higher morbidity for those employed in closed channels, drainage systems, pump stations or filter units and sludge handling units and those with longer employment. The findings on occupationally related lung cancers were inconclusive. The proposed pathophysiological mechanisms include oxidative stress and chronic respiratory irritation due to exposure to noxious bioaerosols and endotoxins. Sulf-haemoglobin, surfactant protein A and D, Clara Cell and Malondialdehyde (MDA) have been explored as biomarkers of respiratory injury due to exposure to sewage work.

Conclusion: Sewage work is associated with significant respiratory morbidity. Further systematic studies are required before sewage work is declared as a respiratory hazard.

Key words: Sewage workers, occupational respiratory diseases, occupational COPD, occupational asthma.

Introduction

Occupational lung diseases are a global health issue and have been extensively researched. As per the International Labour Organisation, a third of the 2.78 million deaths per year on account of occupational diseases and accidents are due to occupational lung diseases and respiratory cancers. Therefore, occupationally related lung diseases are a major source of morbidity and mortality.

The common occupational lung diseases include occupational asthma, occupational COPD, pneumoconiosis and pulmonary cancers related to occupational exposure, like asbestos¹.

The aetiopathophysiology of many occupational lung diseases are well understood and amenable to control using established and effective approaches. Rising urbanisation, industrialisation, financial constraint and technological developments have resulted in enhanced occupational exposure to noxious substances as well as obstruction in control of well-researched exposures¹.

Occupation-related respiratory diseases have led to certain

occupations being designated as hazardous like rubber, plastics, and leather manufacturing, building services, textile manufacturing, and construction², though there are insufficient risk reduction measures and regulatory control for even well-established occupational respiratory hazards^{1,2}. (British Thoracic Society and Health and Safety Executive, UK and several independent researchers have also focussed research on work-related COPD^{2,3,4}).

Types of occupational lung diseases

Occupational lung diseases can be classified as occupationally related infectious lung diseases, occupationally related non-infectious lung diseases and occupational lung cancers.

A. Occupationally related infectious lung diseases

Several pulmonary infections have been implicated for specific occupations like health care professionals, miners, poultry workers, farmers, etc^{5,6,7}. While epidemics of avian influenza and SARS do occur periodically, the most prevalent occupationally related infectious disease is tuberculosis.

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The Occupational Safety and Health Administration of USA has defined occupational exposure to tuberculosis as anticipated contact with tuberculosis and not actual exposure thereby reducing the controversy over whether tuberculosis was transmitted at workplace due to contact with a person having infectious tuberculosis or through air that contains *Mycobacterium tuberculosis*. The common occupations associated with occupational tuberculosis are healthcare professionals (doctors, nurses, attendants, prison staff or staff at correctional facilities, funeral directors and miners, factory workers, taxi drivers, security services personnel and farmers in different studies world-wide⁸⁻¹³. Abattoir workers and dairy workers possess occupational risk for bovine tuberculosis¹⁴.

B. Occupationally related non-infectious lung diseases

1. Occupational Asthma

Amongst non-infectious occupational lung diseases, occupational asthma is the most common respiratory illness in the industrialised countries¹⁵⁻²⁰. It accounts for 15% of all cases of asthma in USA as per American Thoracic Society²¹. It is characterised by restriction in airflow or bronchial hyper-responsiveness to workplace exposures. This includes both asthma arising from workplace exposure and pre-existing asthma exacerbated by workplace exposure^{22,23}. It is also responsible for 5% mortality due to workplace related non-malignant respiratory diseases in USA²⁴.

2. Occupational COPD

The next most common type of Occupational Respiratory Disease is Chronic Obstructive Pulmonary Diseases (COPD). Occupational related COPD contributes to 15 to 19% of all COPD cases^{25,26}.

American Thoracic Society determined that the population attributable fraction of COPD due to occupational exposure to dusts, noxious gases/vapours, and fumes (DGVEFs) is about 15%²¹ though this figure may be confounded by concomitant tobacco use, time latency between exposure and development of COPD, nutrition, omitted exposures, (i.e., exposure to other infective and non-infective agents). The confounders have resulted in dilution of effective preventive strategies except in industries like coal mining and silica where the evidence is more robust^{3,27,28}.

However, lack of evidence is not evidence of lack of contributory role of occupational exposures in a variety of occupational settings. World Health Organisation has suggested that engagement in occupations associated with bronchial asthma and COPD may be taken as surrogate markers for exposure to airborne particulates noxious to

respiratory health²². This is in line with defining occupation specific risks instead of substance specific risk, as most occupational respiratory exposure is a mixture of several noxious substances.

C. Occupational lung cancers

Environmentally and occupationally related lung cancer is in the top 10 causes of cancer mortality in the United States. International Agency for Research on Cancer (IARC) has listed 27 agents as lung carcinogens, including several due to occupational exposures²⁹. The commonest agent implicated in occupational lung cancers is asbestos^{30,31}. Other occupational carcinogens include ionising radiation, chemicals like bis-chloromethyl ether, soot, sulphur mustard, diesel exhausts, etc²⁹.

Occupations classified at risk for respiratory disorders

The most commonly studied occupations for occupational respiratory illnesses are agriculture, mining, manufacturing, construction and transportation. WHO has also suggested engineering and technical, administrative and policy based solutions to address the issue of occupationally related respiratory diseases²².

The hazardous nature of sewage work as an occupation has been discussed in scientific journals for more than half a century, but it has not received comprehensive attention. The International Labour Organisation (2012) had brought out a general hazard sheet on risks associated with waste water treatment work³², but did not emphasise sewage work as a contributor to occupational respiratory diseases.

Sewage work as an occupational respiratory hazard

Sewage management is primarily carried out by sewage workers. Sewage workers are those who enter manholes and closed channels and work in sewage treatment plants as part of their duties²¹. Sewage treatment plants employ technologies like Upflow Anaerobic Sludge Blanket (UASB), Activated Sludge Process (ASP), Fluidized Aerobic Bioreactor, Sedimentation, Trickling Filters, Series of Waste Stabilisation Ponds (WSP), etc.³³ (CPCB, 2005). The mechanical processes like breaking, grinding, pulverising, etc., result in production of "Dusts" which are technically dry particle, biological and non-biological aerosols of sizes less than 1 µm to over 100 µm. Air samples from sewage treatment plants have also been found to have predominantly Gram-negative bacteria^{34,35}. Components of Gram-negative bacteria like Endotoxins and cell wall components have strong inflammatory potential.

The noxious substances that sewage workers get exposed to, through inhalation during the course of their professional duties, include noxious gases (like hydrogen disulfide, methane, ammonia and carbon monoxide), endotoxins and bioaerosols with airborne microorganisms^{36,37}, which get deposited in the airway and alveoli or enter the circulation following absorption^{22,23}.

The noxious substances in sewage are known respiratory irritants which can, on repeated and chronic exposure, adversely impact lung function and cause respiratory diseases like bronchial asthma, toxic pneumonitis and COPD^{34,36,38-47}.

Sewage work has seen incremental growth due to rapid urbanisation and promotion of sewage management systems as the only hygienic method of sewage disposal as well as preferred option for control of infectious diseases with faeco-oral routes of transmission. However, the occupational health hazards of sewage work have not been adequately investigated. Several experimental and epidemiological studies have reported on acute non-specific inflammatory reactions with increased levels of pro-inflammatory cytokines and biomarkers in sputum, broncho-alveolar lavage (BAL), or blood/serum⁴⁸⁻⁵².

Hence, the occupational lung diseases among Sewage workers have not received sufficient scientific attention, despite chronic exposure to noxious biological and chemical particulate matter. Therefore, a systematic investigation is needed to assess lung function in sewage workers and to determine the rates of select lung diseases in sewage workers.

Evidence base for sewage work related respiratory morbidity

A systematic review of literature was conducted using STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) Guidelines⁵³.

An internet based search on Pubmed and Google Scholar was conducted to find scientific literature in English language for sewage work as an occupational hazard. The MeSH terms included "sewage", "waste water", "waste water treatment", "lung diseases", "occupational hazard", "respiratory symptoms", "Pulmonary Diseases", "COPD", "Bronchial Asthma" and "ACOS" in various combinations. The articles were then evaluated for comparable methodology and results for inclusion in systematic review. Thereafter, a systematic review was conducted to determine the current knowledge and evidence base for sewage work as an occupational respiratory hazard.

Several international and some national studies have focussed on occupationally related respiratory issues and

illnesses among sewage workers. The literature search revealed 27 studies meeting the search criteria and comparability in methodology and reporting of results. Table I gives the salient findings of each of these studies listed in chronological order. The findings of the systematic review analysed for similarity of constructs studied are as follows.

Respiratory symptomology in sewage workers

The initial studies focussed on self-reported respiratory symptoms exclusively or as part of multi system symptomology.

In 1988 Nethercott *et al* reported that a random sample of 50 sewage workers in Toronto, Canada had a high rate of influenza like symptoms, cough, sore throat, production of sputum and wheezing⁵⁴. Similarly Watt *et al* (1997) also reported that symptoms like sore throat, cough, chest tightness and breathlessness were common in the 26 sewer-men exposed to toxic gas in Aberdeen in Scotland⁵⁵.

Similar studies around the same time in different parts of the world also reported increased rates of respiratory symptoms in this occupational group. Bener *et al* (1998) found significantly high rates of self-reported chronic cough ($p < 0.02$), chronic phlegm ($p < 0.03$), chronic bronchitis ($p < 0.02$), asthma ($p < 0.02$), dyspnoea ($p < 0.001$) and nasal catarrh ($p < 0.001$) in sewage workers in UAE⁵⁶. Similarly, Zuskin *et al* (1990) also reported increased rates of chronic respiratory symptoms in sewage workers in Zagreb, Croatia⁵⁷. However, in another study while 'flu-like symptoms'; 'higher airway symptoms'; 'lower airway symptoms'; were found to be positively associated with working with sewage, but the results were only significant for 'flu-like symptoms' (OR = 5.0; 95% CI = 1.4 - 17.6; $p < 0.05$)⁴¹. The authors also found that practice of simple hygienic measure like daily washing of working clothes was negatively associated with 'flu-like symptoms' (OR = 0.3; 95% CI = 0.1 - 0.6; $p < 0.01$).

A study on respiratory symptoms and airway responsiveness of 34 sewage workers and 35 controls at eight sewage treatment plants in four municipalities in the south of Sweden reported higher nasal irritation and increased airway responsiveness in sewage workers⁴². A similar study was conducted on 149 sewage workers and 138 controls (group matched for age and municipalities) in 11 municipalities in Central Sweden. The authors found that the adjusted odds ratio for self-reported asthma was 5.3 (95% CI: 1.1 - 26) after controlling for age, gender, tobacco use and atopic predisposition. The study also reported that 50% of asthma reporters were on asthma medications⁵⁸.

This was followed by a large scale epidemiological study employing postal survey method to collect multi-system symptom data from 1,453 sewage workers and 839 controls

from 257 municipalities in Sweden. The authors found that sewage workers had increased risk for upper and lower airway symptoms, e.g., breathlessness in a wide range of situations [exposure to gases, fumes, smells (2.4; 95% CI: 1.8 - 3.2), exercise (1.6; 95% CI: 1.2 - 2.0), walking upstairs (1.8; 95% CI: 1.4 - 2.5), walking on plain ground (2.2; 95% CI: 1.3 to 3.9), walking with other persons of similar age (2.6; 95% CI: 1.6 - 4.2), cold weather (1.4; 95% CI: 1.0 - 2.1)]; nose irritation (1.8 95% CI: 1.4 - 2.5), congested nose (2.1; 95% CI: 1.5 - 2.9), cough with phlegm (2.0; 95% CI: 1.4 - 2.9), dry cough (2.8; 95% CI 1.8 - 4.3); wheezing (1.7; 95% CI 1.2 - 2.4), chest tightness during work shift (1.5, 95% CI 1.1 - 2.2), chronic bronchitis (2.8; 95% CI 1.7 - 4.5), toxic pneumonitis (5.4; 95% CI 3.4 - 8.5)³⁹.

In India, Occupational Health and Safety Centre carried out a survey of 200 sewer workers of Brihan Mumbai Corporation in 1988 and found 60% of subjects had shortness of breath and persistent cough^{59,60}. A systematic study of a representative sample of 150 sewage workers in Mumbai also demonstrated that more than half the subjects (52.8%) had respiratory ailments. The sewage workers had high rates of cough (44.3%), breathlessness (39.2%), bronchitis (34.1%) and tightness of chest (32.9%)⁶¹.

A lay epidemiological prospective study on self-reported multi system symptomology of sewage workers (n = 29) over six months in a small town in South India which has open channel sewer carrier system also revealed high rates of cough and cold but no quantitative results were reported⁶².

Not all studies have reported significantly higher respiratory morbidity in sewage workers. Khuder *et al* (1998) reported no significant difference in self-reported respiratory symptoms between 150 waste water treatment workers and 54 controls in a retrospective epidemiological study in USA⁶³.

Similarly, in India, an employer instituted health survey study by Brihan Mumbai Corporation study in 1994 found that only 0.9% of 678 sewer staff had respiratory complaints⁵⁹.

Pulmonary function test studies

Only a few studies have employed spirometry as an objective marker of respiratory compromise and assessment of airborne endotoxins as a marker of noxious respiratory effect of sewage work.

Rylander *et al* (1999) in a study on 34 sewage workers and 35 controls employed in eight sewage treatment plants in four municipalities in the south of Sweden found no differences between the groups on spirometry, despite having significantly more cases of nasal irritation and airway

responsiveness in sewage workers group⁴², (Rylander *et al*, 1999).

Zuskin *et al* (1993) reported obstructive pattern in smaller airways on pulmonary function test in 74 sewage workers, close channel workers and drainage workers in Croatia³⁷.

In a study of 68 sewage workers in USA in 1995, Richardson *et al* found that those exposed to Hydrogen sulphide had reduced lung function (decreased FEV1/FVC: -3.1, SE 1.4) after taking into account age, height, race and comorbid nicotine use⁶⁴.

Similarly, Bener *et al* (1998) reported significantly lower FVC, FEV1, FEV1/FVC, PEF 25:75 and PEFr (p < 0.05) in his study on sewage workers in UAE⁵⁶.

Heldal *et al* (2010) also found lower FEV1/FVC ratio in sewage workers as compared to controls. They also reported an association between exposure to endotoxin-containing dust and respiratory symptoms like airway irritation and cough among sewage workers⁶⁵.

The Mumbai sewage worker study also reported predominantly obstructive pattern on Pulmonary Function Test in nearly half the subjects, though restrictive pattern was also seen in about one-fifth of subjects. In those having obstructive pattern, 35.44% had moderate obstruction while 22.7% had severe obstruction⁶¹.

An Egyptian study on 43 waste water workers and 43 controls also found a significantly lower FEV1 (percentage of predicted) and PEF (percentage of predicted), suggestive of obstruction in waste water treatment plant workers in comparison to controls⁶⁶.

In a study on sewage workers in Aligarh in 2014, Shadab *et al* also found significant reduction in Peak Expiratory Flow Rate (PEFR), Forced Expiratory Volume in first divond (FEV1) and FEV1/FVC percent ratio (<80%) and Forced Expiratory Flow at 25% - 75% of volume as percentage of Vital Capacity (FEF 25% - 75%) as compared to controls indicating an obstructive pattern⁶⁷.

However, a prospective cohort study of garbage workers and waste water workers with annual evaluation over 5 years in Switzerland showed only a modest healthy worker effect with those leaving the occupation reporting a significantly higher rate of respiratory symptoms like dyspnoea on exertion and FEV1 pred. Amongst those who continued their profession, there was a significant difference in FEV1 slope or FEV1/FVC between garbage workers, waste water workers and controls⁶⁸.

Nevertheless, Cyprowski *et al* (2015) found that even low levels of endotoxin exposure resulted in significant decline in FEV1, despite taking into account confounders like inhalable dust and smoking⁶⁹.

Table I: Brief description of studies on respiratory morbidity in sewage workers.

S No.	Study (Year)	Population	Study Design	Assessments	Outcomes
1.	Nethercott <i>et al</i> (1988) ⁵⁴	Random sample of 50 sewage workers using a heat treatment method for processing sewage sludge in Toronto, Canada	Observational study	Self-reported respiratory symptoms questionnaire	High rate of influenza like symptoms, cough, sore throat, production of sputum and wheezing. Decreased FVC and FEV1
2.	Zuskin <i>et al</i> (1990) ⁵⁷	70 sewage workers in Zagreb, Croatia and similar controls	Observational study	Self-reported respiratory symptoms questionnaire	Increased rates of chronic respiratory symptoms significant only for chest tightness ($p < 0.01$)
3.	Zuskin <i>et al</i> (1993) ³⁷	74 sewage workers, (26 close channel workers, 31 drainage workers, 17 other sewage workers) in Croatia	Case control study	Self-reported respiratory symptoms questionnaire and Spirometry	Higher rates of chronic respiratory symptoms in closed channel workers: chronic cough, chronic phlegm, chronic bronchitis and chest tightness Obstructive pattern in smaller airways on PFT
4.	Friis <i>et al</i> (1993) ⁷³	711 employees at 17 Swedish sewage plants employed for at least for 1 year during the years 1965 - 86	Retrospective cohort study	Analysis of Swedish Cancer Register records along with collation of information on duration of employment and nature of exposure as per task performed: laboratory work, work in the sewage processing plant, sludge pipe flushing or exhaustion, and work at sewage pump stations.	No significant increase in respiratory cancers of trachea, bronchi and lung at 1 year, 10, and 20 years induction latency periods
5.	Brihan Mumbai Corporation (1994) ⁵⁹	678 sewer staff	Employer instituted health survey study	Multisystem Health Survey	Respiratory complaints: 0.9%
6.	Occupational Health and Safety Centre (1994) ⁶⁰	200 sewer workers from Main Sewerage Department of Brihan Mumbai Corporation, Mumbai, India	Observational study	Multi system health survey	Shortness of breath and persistent cough: 60%
7.	Richardson <i>et al</i> (1995) ⁶⁴	68 sewage workers exposed to Hydrogen Sulphide and 60 water treatment workers in USA	Case control study	Clinical evaluation, Spirometry	Significantly reduced mean FEV1/FVC
8.	Watt <i>et al</i> (1997) ⁵⁵	26 sewer-men exposed to toxic gas leak in Aberdeen (Scotland)	Observational study	Clinical examination, PFT	Sore throat, cough, chest tightness and breathlessness in 14 (53.84%) workers
9.	Bener <i>et al</i> , (1998) ⁵⁶	144 sewage workers and 149 manual workers in UAE	Case control study	Physician administered questionnaire, Clinical examination and Spirometry	High rates of self-reported respiratory symptoms Significantly lower FVC, FEV1, FEV1/FVC, PEF 25:75 and PEFR ($p < 0.05$)
10.	Khuder <i>et al</i> (1998) ⁶³	150 waste water treatment workers and 54 controls in USA	Retrospective epidemiological study	Self-reported retrospective recall of multi system symptom questionnaire for past 12 months	No significant differences in respiratory symptoms
11.	Rylander (1999) ⁴²	34 sewage workers and 35 controls eight sewage treatment plants in four municipalities in the south of Sweden	Case control study	Questionnaire, spirometry and airway responsiveness; Measurements of airborne endotoxin at different workplaces	Higher nose irritation and increased airway responsiveness in sewage workers No differences between the groups on spirometry
12.	Friis <i>et al</i> (1999) ⁵⁸	149 sewage workers, 138 controls (group matched for age and municipalities) in 11 municipalities in Central Sweden	Case control study	Self administered questionnaire for multi-systemic symptoms over previous two years	High adjusted OR for self-reported asthma in sewage workers (after controlling for age, gender, tobacco use and history of atopy. 50% of asthma reporters on asthma medications
13.	Douwes <i>et al</i> , 2001 ⁴¹	147 sewage treatment workers	Observational study	Self-administered questionnaire for multi-systemic symptoms.	Low personal endotoxin exposure (< 10 Endotoxin Units/m ³). 'flu-like symptoms'; 'higher airway symptoms'; 'lower airway

			Measurement of endotoxin at two treatment plants	symptoms'; positively associated with working with sewage, but only significant for 'flu-like symptoms' (OR = 5.0; 95% CI = 1.4 - 17.6; p < 0.05) Use of daily washed working clothes negatively associated with 'flu-like symptoms' (OR = 0.3; 95% CI = 0.1 - 0.6; p < 0.01).	
14.	Thorn <i>et al</i> (2002) ³⁹	1,453 sewage workers, 839 controls from 257 municipalities in Sweden	Case control study	Nationwide postal survey for multi system symptoms	Increased risk for upper and lower airway symptoms: breathlessness in a wide range of situations; nose irritation, congested nose, cough with phlegm, dry cough; wheezing, chest tightness during work shift, chronic bronchitis, toxic pneumonitis High rates for respiratory symptoms in workers in pump stations or filter units and sludge handling units
15.	Krajewski <i>et al</i> (2004) ⁷⁰	99 sewage workers employed in different sewage operations: mechanical treatment (n = 24), biological treatment (n = 14), sewage sludge treatment (n = 26), operation control (n = 35)	Observational study	Self Reported Likert Styled Questionnaire	High rates of respiratory symptoms in sewage workers irrespective of operational station
16.	Smit <i>et al</i> (2005) ⁷⁵	468 employees from 67 sewage treatment plants in Australia	Cross-sectional study	Self reported symptom questionnaire Personal endotoxin exposure detection over 8 hours in three different periods over a year	Endotoxin exposure - of 27 (0.6 to 2093) endotoxin units (EU)/m ³ Three clusters of correlated symptoms: "lower respiratory and skin symptoms," "flu like and systemic symptoms," and "upper respiratory symptoms." On factor analysis. More prevalent symptoms in workers exposed high endotoxin levels (more than 50 EU/m ³) Significant dose response relationship for "lower respiratory and skin symptoms" and "flu like and systemic symptoms." (P < 0.05).
17.	Wild <i>et al</i> (2006) ⁷⁴	All Sewage workers in Paris from 1970	Propective cohort study	Mortality records from 1970 to 1999	High mortality due to Lung Cancer (SMR= 1.47) associated with duration of occupational exposure and unrelated to smoking prevalence
18.	Heldal <i>et al</i> (2010) ⁶⁵	19 workers handling dry sludge, 25 other sewage workers from 8 different municipal sewage plants in Norway and 36 controls	Case control study	Self-administered questionnaire for multi-systemic symptoms, before and after shift Spirometry, acoustic rhinometry; nitric oxide estimation in exhaled air, Serum CRP, Personal filter air sample estimation for inhalable dust, total bacterial cells and fungal spores and endotoxins	High rates of airway related symptoms (p = 0.04), nasal irritation (p < 0.01) and cough (p = 0.03) Lower FEV1/FVC ratio (p = 0.001) and FVC% of predicted (p = 0.01) among sewage workers, and lowest in workers handling dry sludge. Association between exposure to endotoxin-containing dust and respiratory symptoms like airway irritation and cough
19.	Giri <i>et al</i> (2010) ⁶¹	150 sewage workers employed in the Main Sewerage Department from a randomly selected division of Greater Mumbai, India	Observational study	Semi structured interview schedule for multi systemic morbidity, clinical examination and Pulmonary Function Tests	Respiratory ailments: 52.8%; cough: 44.3%; breathlessness: 39.2%; bronchitis: 34.1%; tightness of chest: 32.9% Obstructive pattern on PFT (48.1%: Moderate obstruction 35.44%; Severe Obstruction: 22.7%) and restrictive pattern (20.2%) Decline in pulmonary functions associated with duration of service as a sewage worker (p < 0.05)

20.	Daneshzadeh Tabrizi <i>et al</i> (2010) ⁷⁷	316 wastewater workers, 67 garbage collectors, and 395 control subjects in Switzerland		ELISA estimation of Surface Protein D (SP-D) Assessment of exposure to bioaerosols by interview-based indicators and by preliminary endotoxin measurements using the Limulus amoebocyte lysate assay.	Wastewater workers had higher endotoxin exposure and increase in SP-D concentration on multiple linear regression considering smoking, glomerular function, lung diseases, obesity, and other confounders
21.	Al Batanony <i>et al</i> , (2011) ⁶⁶	43 workers at Berket Al-Sabih WWTPs in Egypt and 43 controls	Case control	Physician administered multisystem symptom questionnaire, Post-work shift Spirometry, resting ECG echocardiography for those with ECG abnormalities. Estimation of sulf- haemoglobin, as an indicator of H ₂ S exposure Other investigations	Lower FEV1 (percentage of predicted) and PEF (percentage of predicted) suggestive of obstructive pattern in waste water treatment plant workers in comparison to controls.
22.	Tschopp <i>et al</i> (2011) ⁶⁸	247 waste water workers, 52 garbage workers, 304 controls from canton of Zurich in Switzerland	Prospective cohort study over 5 years	Baseline and 4 annual follow-up physician administered questionnaire, Spirometry and Serum investigations for CC 16 and SP-A	Modest healthy worker effect those quitting: higher rate of respiratory symptoms like dyspnoea on exertion and FEV1 pred. Those continuing with sewage work: difference in FEV1 slope or FEV1/FVC between garbage workers, waste water workers and controls. No difference for duration of exposure, exposure to raw sewage and splashes
23.	Heldal <i>et al</i> , (2013) ⁷⁶	44 workers from 8 sewage treatment plants in Sweden and 38 controls	Case control study	Assessment of Microbial aerosol from personal inhalable samplers including bacterial concentration and endotoxin assay along with estimation of Pneumoproteins (Clara cell protein: CC16, and Surfactant proteins A and D: SP-A, SP-D) in post work shift blood samples	Lower mean CC16 compared to controls (4.9 ng/ml; 6.4 ng/ml, p < 0.01) in sewage workers No significant difference in SP-D and SP-A. Exposure to bacteria positively associated with CC16 (p < 0.05) and SP-D (p < 0.05)
24.	Shadab <i>et al</i> (2013) ⁷⁸	62 sewage workers (32 non-smokers and 30 smokers) and 60 control subjects (30 smokers and 30 non-smokers) in Aligarh, India	Case control study	Clinical examination, Spirometry	Significant reduction PEFR, FEV1 and FEV1/FVC% FEF 25% - 75% in sewage workers indicating an obstructive pattern
25.	Shadab <i>et al</i> (2014) ⁶⁷	62 sewage workers (32 non-smokers and 30 smokers) and 60 control subjects (30 smokers and 30 non-smokers) in Aligarh, India	Case control study	Serum Malondialdehyde (MDA)	Increased Serum MDA (p < 0.05)
26.	Cyprowski <i>et al</i> (2015) ⁶⁹	78 Sewage Treatment Plant workers in Central Poland in different operations (mechanical treatment: 9, biological treatment workers: 14, sewage sludge treatment: 14, Operations control: 28 and administration: 14)	Observational study	Endotoxin assessment for air borne dust and Spirometry	Even low levels of endotoxin exposure resulted in significant decline in FEV1 (p = 0.044) despite taking into account confounders like inhalable dust and smoking.
27.	Rangamani <i>et al</i> , (2015) ⁶²	29 sewage workers (M:F = 18:11) in Chitradurga, Karnataka, India	Prospective observational study over 6 months	Four rounds of self-reported symptom survey over 6 months using questionnaire	High rates of cough and cold

Abbreviations: PEFR: Peak Expiratory Flow Rate; FEV1: Forced Expiratory Volume in first second; FVC: Forced Vital Capacity; FEV1/FVC %: FEV1/FVC percent ratio; FEF 25%-75%: Forced Expiratory Flow at 25% - 75% of volume as percentage of Vital Capacity; OR: Odds Ratio; CC 16: Club Cell Secretory Protein 16; SP-A & SP-D: Surfactant proteins A and D; H₂S: Hydrogen Sulphide; SMR: Standardised Mortality Rate.

Impact of nature of sewage work

Studies have also been conducted on the impact of nature of sewage work on respiratory morbidity.

Zuskin *et al* (1993) also found that amongst 74 sewage workers, close channel workers and drainage workers had significantly higher rates of chronic respiratory symptoms like chronic cough (41.9% vs. 14.3%), chronic phlegm (38.7% vs. 14.3%), chronic bronchitis (32.3% vs. 8.6%) and chest tightness (29.0% vs. 0%) as compared to other sewage workers³⁷.

Thorn *et al* (2002) also reported high rates of respiratory symptoms in those working in pump stations or filter units and sludge handling units in their large scale epidemiological study with case control design on nearly 1,500 sewage workers and nearly 850 controls from 257 municipalities in Sweden³⁹.

A Norwegian study on 19 workers handling dry sludge and 25 other sewage workers from 8 different municipal sewage plants 36 controls also found lower FEV1/FVC ratio ($p = 0.001$) and FVC% of predicted ($p = 0.01$) among sewage workers with the lowest levels in workers handling dry sludge in before and after shift spirometry. This study also conducted personal filter air sample estimation for inhalable dust, total bacterial cells and fungal spores and endotoxins. They were also able establish a direct association between exposure to endotoxin-containing dust and respiratory symptoms like airway irritation and cough⁶⁵.

However, a Polish study, conducted to determine the hazardous nature of different sewage processing related operations, found no impact of employment in different sewage operations on respiratory symptoms. The study was conducted on 99 sewage workers engaged in operations like mechanical treatment ($n = 24$), biological treatment ($n = 14$), sewage sludge treatment ($n = 26$) and operation control ($n = 35$) at the largest sewage treatment facility in Poland. The authors reported that though the rates of various respiratory symptoms [nasal irritation (26%), allergic rhinitis (25%) productive and non-productive cough (9%; 17%), dyspnoea (9%), chest tightness (9%), wheezing (4%) and flu like symptoms (18%)] were high in all sewage workers, there was no differential impact of employment in different sewage operations⁷⁰.

Similarly, Tschopp *et al* (2011) also reported no difference in pulmonary function test with respect to exposure variables like category of exposure, exposure to raw sewage and exposure to splashes⁶⁸.

Impact of duration of exposure to sewage work

Giri *et al* (2010) investigated the impact of duration of exposure to sewage work as an occupational respiratory

hazard. They discovered that the decline in pulmonary functions was associated with duration of service as a sewage worker ($p < 0.05$) which is a surrogate marker for duration of occupational exposure⁶¹.

On the other hand, Tschopp *et al* (2011) reported no significant difference in pulmonary function test with respect to duration of exposure to raw sewage and splashes. However, this study had a modest health worker effect as stated earlier which can account for such findings⁶⁸.

Impact of comorbid nicotine use

Nicotine use is a common confounding factor in respiratory diseases. Shadab *et al* (2014) controlled for the confounding effect of smoking in their study design by having equal proportion of smokers and non smokers in sewage worker group (32 non-smokers and 30 smokers) and control group subjects (30 smokers and 30 non-smokers). They found obstructive pattern on pulmonary function tests which could be attributed to occupational exposure to harmful dust, gases and bio-aerosols in sewage workers⁶⁷.

Similarly, Cyprowski *et al* (2015) also established an independent impact of even low levels of endotoxin exposure resulting in significant decline in FEV1 ($p = 0.044$) after taking into account confounders like smoking and inhalable dust⁶⁹.

Cancer and Sewage work

Several studies have explored the incidence and prevalence of cancers in sewage workers primarily through retrospective review of cancer registry and mortality registry and also prospective cohort studies. While several studies found significantly higher rates of cancer and cancer related mortality^{71,72}, the studies on respiratory cancers *per se* are equivocal. While Friis *et al* found no significant increase in respiratory cancers, Wild *et al* found that lung cancer did contribute to excessive mortality in sewage workers (Standardised mortality rate = 1.47) (SMR = 1.47, 68 cases)^{73,74}. Wild *et al* (2006) also found that the excessive mortality associated with lung cancer in sewage workers was also independent of smoking status⁷⁴.

Studies on possible pathophysiological mechanisms and biomarkers

The exposure routes of intake and transmission of noxious sewage substances are oral intake from splashes, contaminated foodstuffs, hand to mouth contact; penetration through skin or mucous membranes through injuries or breach in personal protective equipment and through inhalation. Of these, the primary route of respiratory exposure is through inhalation as the processing of sewage

in Sewage Treatment Plants results in production of aerosols. Sewage Treatment Plants also employ mechanical processes like breaking, grinding, pulverizing etc. resulting in production of "Dusts" which are technically dry particle biological and non-biological aerosols of sizes less than 1 µm to over 100 µm. These noxious agents may either get deposited in the airway and alveoli or enter the circulation following absorption²².

Air samples from sewage treatment plants have also been found to have predominantly Gram-negative bacteria^{34,35}. Components of Gram-negative bacteria like Endotoxins and cell wall components have strong inflammatory potential. Several experimental and epidemiological studies have reported on acute non-specific inflammatory reactions with increased levels of pro-inflammatory cytokines and biomarkers in sputum, broncho-alveolar lavage (BAL), or blood/serum⁴⁸⁻⁵².

These noxious substances in sewage are known to be respiratory irritants. Repeated and chronic exposure to such toxic substances can have adverse effects on the respiratory system resulting in airway irritation and pulmonary diseases like bronchial asthma and toxic pneumonitis^{38-40,42}. Repeated episodes of toxic pneumonitis in chronically exposed sewage workers may result in irreversible reduced pulmonary functions and may contribute to the development of chronic obstructive pulmonary disease⁴⁴⁻⁴⁷.

In order to establish the causative role of occupational exposure to sewage work and associated respiratory symptoms and findings on pulmonary function tests, different researchers attempted to identify the mediating agent which could explain the pathophysiological mechanisms.

Some researchers measured airborne endotoxin at different workplaces in sewage treatment facility^{42,69}. An Australian study found more prevalent respiratory symptoms and a significant dose response relationship between "lower respiratory and skin symptoms" and "flu like and systemic symptoms" and endotoxin exposure levels ($P < 0.05$)⁷⁵.

Other researchers have conducted estimation of nitric oxide estimation in exhaled air, estimation of inhalable dust, total bacterial cells and fungal spores and endotoxins in personal filter air samples with determination of the association between exposure to endotoxin-containing dust and respiratory symptoms like airway irritation and cough and estimation of microbial aerosol including bacterial concentration and endotoxin assay from personal inhalable samplers^{65,76}.

Sulf-haemoglobin, as an indicator of H₂S exposure has also

been explored as a surrogate marker for exposure to sewage associated respiratory hazards⁶⁶.

Surfactant protein D is considered a biomarker of bioaerosol/endotoxin induced inflammatory damage to lung blood barrier as this results in increased permeability and leakage of SP-D (which is a lung specific protein) into the blood stream. A Swiss study determined that not only the sewage workers had higher endotoxin exposure, but they also had increase in SP-D concentration on multiple linear regression considering smoking, glomerular function, lung diseases, obesity, and other confounders. This provided preliminary evidence of possible pathogenic mechanisms triggered by endotoxins in bioaerosols associated with sewage⁷⁷.

Another study explored estimation of multiple pneumo-proteins (Club Cell Secretory Protein (Clara cell protein)-CC16, and Surfactant proteins A and D: SP-A, SP-D) in post-work shift blood samples. The findings were slightly different. The result showed lower mean CC16 compared to controls (4.9 ng/ml; 6.4 ng/ml, $p < 0.01$) in sewage workers with no significant difference in SP-D and SP-A. Exposure to bacteria was also determined to be positively associated with CC16 ($p < 0.05$) and SP-D ($p < 0.05$) after adjusting for possible confounders^{68,76}.

Oxidative stress has also been explored as a possible pathophysiological pathway in the noxious effect of sewage work on pulmonary function. Malondialdehyde (MDA) has been investigated as a surrogate marker for oxidative stress in sewage workers and found to be significantly increased⁷⁸.

However, there is no consistent biological marker of exposure to sewage work which can help us understand the pathophysiological mechanisms of respiratory morbidity due to exposure to sewage work.

Limitations in existing literature

The available scientific literature fails to establish unequivocally sewage treatment work as an occupational respiratory hazard as all the studies had some methodological issues including lack of controls, use of self-reported questionnaires and lack of clinical assessment. Some researchers studied a wide range of multisystem morbidities like eye, skin, gastrointestinal, etc., while others focussed on assessing only self-reported respiratory symptoms^{57,61}.

No study focussed on identifying various pulmonary diseases as per standard diagnostic guidelines. While some studies assessed pulmonary functions without taking into account confounders like smoking, exposure to biomass fuel, selection/survivor effects, definition of occupational exposure, etc.^{37,67}, no study investigated the association

between clinically diagnosed pulmonary diseases and investigations like pulmonary function tests, High Resolution Computerised Tomography of Chest (HRCT Chest), etc.

Further, no study has been conducted on the risk of pulmonary infections like tuberculosis in sewage workers. In addition, no study has been carried-out on the rates of lung cancers in sewage workers and the possible carcinogen exposures thereof.

Hence, these lacunae in scientific literature pose a challenge in attributing respiratory symptoms and diseases unequivocally to occupational exposure as a sewage worker³⁶. In other words, these studies failed to establish unequivocally sewage treatment work as an occupational respiratory hazard.

Conclusion

With rapid urbanisation there has been incremental growth of sewage management systems as the only hygienic method of sewage disposal to control infectious diseases with faeco-oral routes of transmission. In India, all metropolitan cities and smaller cities and towns (with more than 50,000 population) have extensive sewage networks (CPCB). However, the rapid expansion of sewage system globally and also in India has occurred without sufficient investigation into the hazard faced by the sewage workers. Several studies have been conducted on sewage workers worldwide with largely consistent finding. However, these studies on sewage workers have methodological limitations and have been unable to unequivocally the sewage treatment work as an occupational respiratory hazard.

Further, systematic studies are required to address gaps in scientific knowledge about sewage work as an occupational respiratory hazard. It is only after establishing evidence on the basis of systematic research, that sewage work can be accorded hazardous occupation status and specific prevention and mitigation strategies can be implemented for ensuring respiratory health of sewage workers.

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