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Pulmonary function among flour mill workers: a systematic review and meta-analysis

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Abstract

Background Flour dust, with an inherent allergic nature, increases vulnerability to various respiratory ailments. We systemically reviewed and compared literature-reported pulmonary function parameters to quantify pulmonary dysfunction among individuals with high flour dust exposure (among flour mill workers) and relatively un-exposed groups.

Methods Studies that compared pulmonary function parameters for flour dust exposed and unexposed control groups were systemically searched in PubMed, Scopus and Embase from inception to June 2024. The Newcastle Ottawa scale was used to assess the risk of bias among included studies. With the random effect model, we pooled (along with 95% CI) the mean difference for forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC), the ratio of FEV_1 & FVC, mid-expiratory flow (FEF25-75%), peak expiratory flow rate (PEFR) and other pulmonary function parameters. Cochran-Q test and I^2 statistics were applied to determine heterogeneity.

Results This quantitative synthesis included twenty-two studies involving 2,482 flour dust exposed and 1,925 control participants. The pooled mean difference for FEV_1, FVC, FEV_1/FVC, PEFR and $FEF_{25-75\%}$ were − 0.43 L (-0.57, -0.29; $I^2 = 88.7$), -0.49 L (-0.64, -0.33; $I^2 = 89.3$), -3.5% (-6.49, -0.5; $I^2 = 89.7$), -1.36 L/s (-1.70, -1.03; $I^2 = 90.4$) and − 0.34 L/s (-0.63, -0.06; $I^2 = 77.3$). The pooled odds ratio for obstructive [12.9 (3.41, 49.2); $I^2 = 82.4$)] and restrictive changes [5.11 (0.55, 47.4); $I^2 = 81.6$] were significantly higher among the exposed than controls. As per the bias assessment majority of studies rated with moderate to severe risk of bias.

Conclusion Study observed pulmonary function deficits associated with exposure to flour dust. However, considering the quality of primary studies and higher heterogeneity, high-quality larger studies with longitudinal design are required to affirm the effects of flour dust on lung function.

Keywords Pulmonary function test, Flour dust, Flour mill workers, Respiratory problems

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Introduction

Occupational lung diseases are a major public health concern, considering its magnitude of preventable disease burden [1]. Occupational lung diseases such as silicosis, asbestosis, and anthracosis are continuously investigated and reviewed, while occupational lung diseases due to organic dust exposure receive less attention and are under investigated. Flour, an organic dust, is a finished powder product of milled cereals such as wheat, corn, barley or a combination of multiple cereals [2]. Variable amounts of organic dust are generated and released into the work environment during different industrial processes involving flour such as cleaning, milling, packaging, storage and loading [3]. Flour dust contains several hazardous substances such as silica dust, fungi along with their metabolites, endotoxins, etc. which predisposes workers to different respiratory disease sequelae [4, 5]. As flour dust contains not only organic dust but variable quantities of bio-aerosols, exposure and sensitization of the same as allergens result in short - and long-term health consequences [5, 6].

Exposure to flour dust has been identified as the second most prevalent cause of occupational asthma in the United Kingdom, with an incidence rate of 38.8 per 100,000 individuals [7]. The role of flour dust in the provocation of allergic response was reported in several studies [8, 9]. Studies have linked exposure to flour dust to a significant occurrence of allergies and physical irritations, which manifest as respiratory and non-respiratory symptoms. These symptoms include cough, shortness of breath, wheezing, chest tightness, runny nose, conjunctivitis, etc [9–13].

Realizing the hazardous nature of flour dust, the statutory body American Conference of Governmental Industrial Hygienists (ACGIH(R)) proposed a Threshold Limit Value (TLV(R)) of 0.5 mg/m3 of flour dust with a sensitization notation. With reference to ACGHI(R) value several studies have reported exceeded level of flour dust at workplace [14–17] and studies have reported minimal/no usage of Personal Protective Equipment (PPEs) [18–22], which further raise a serious concern towards preventive/ control measures at workplace.

Research studies consistently indicates alterations in pulmonary function among workers exposed to flour dust in occupational settings, despite the implementation of regulatory standards for flour dust exposure. These studies reveal conflicting reports, wherein few report derangements in pulmonary function [3, 11, 15, 17, 19, 21, 23–28]and few observed no significant changes [29–31]. Additionally, few studies report mixed dust pulmonary fibrosis and restrictive patterns in these flour dust-exposed workers, suggestive of pathogenesis beyond allergic inflammation [11, 32]. There is a necessity to conduct a systematic review of the existing evidence to ascertain the nature of the relationship between exposure to occupational flour dust and alterations in pulmonary function which enables a more comprehensive understanding of the underlying associations and the implementation of appropriate control measures. The current study proposes to systematically review studies investigating changes in pulmonary function parameters among workers occupationally exposed to flour dust compared to controls with no known occupational flour dust exposure.

Methods

Present systematic review and meta-analysis was executed adhering to the updated PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-analysis) guidelines. The protocol for the same was registered at PROSPERO as CRD42023457423 during August 2023. Primary observational studies, either longitudinal or cross-sectional in design, reporting changes in pulmonary function parameters among the flour mill (dust exposed) workers were included. Selective keywords were developed to identify studies reporting pulmonary function changes among adult flour mill workers (aged>18 years of either sex) compared to controls. These keywords were used to search relevant citations from the common biomedical digital repositories, such as Scopus, Embase, and PubMed-Medline. The search included pulmonary function parameters such as forced expiratory volume in first second (FEV_1), vital capacity (VC), forced vital capacity (FVC), ratio of FEV_1 and FVC (FEV_1/FVC), forced expiratory flow between 25% and 75% of vital capacity ($FEF_{25-75\%}$), peak expiratory flow rate (PEFR), maximum voluntary ventilation (MVV) and transfer factor of the lung for carbon monoxide (TL_{CO}). Additionally, the search included studies reporting a prevalence of obstructive and /or restrictive patterns of pulmonary function changes. The choice of keywords to identify relevant studies were designed to ensure maximum precision and sensitivity. The final systematic search (as per Supplementary Table- 1a, 1b& 1c) was performed on June 26, 2024. Lateral search by actively searching from the cross references of the included studies was performed to identify additional studies. Studies without a comparison or control group, those enrolling patients or participants from hospitals, pre-clinical (including in-vitro) studies, and studies reporting only the frequency of respiratory symptoms without the listed pulmonary function parameters were excluded. Additionally, letters to editors, conference abstracts, reviews, commentaries, and methodological papers were excluded.

Screening and reviewing of the studies

Studies identified from the digital repositories were compiled. Abstracts of each study were stringently reviewed

(AV, KU, AS) for their probable inclusion. Full-text articles of the selected abstracts were archived and reviewed (AV, KU). The final list of the studies adhering to inclusion and exclusion criteria was prepared based on mutual consensus among authors (AV, AS, KU).

Data collection, extraction, analysis and management:

A data extraction sheet to extract the desired details to achieve the study objectives was created. The data extraction sheet included basic characteristics of participants (age, sex, geographical region and smoking), outcome parameters such as pulmonary function parameters & patterns of pulmonary function changes (i.e. obstructive/ restrictive/ normal), exposure related parameters (such as duration of exposure, site of workplace exposure, use of PPE and quantitative and / qualitative monitoring of workplace dust) whenever available. Additionally, the sheet incorporated study details such as title, contact details of authors and year of publication. The data from each included study were independently extracted as central tendency (mean/median) and dispersion [standard deviation (SD)/ quartile range/standard error (SE)/ 95% confidence interval (CI)] for continuous variables and frequency of counts for the event occurrences, whenever available (AV, KU). Data was cleaned before initiating the analysis, ensuring consistent and uniform reporting. Data reported in other than standard units are transformed to standard units using appropriate transformations (e.g. conversion litres/minute to i.e. litres/sec) [19, 33–35]. All data was converted to mean and SD using standard transformations for executing pooled meta-analysis [36, 37].

Pooled mean differences (with a 95% confidence interval) between the flour dust exposed and respective control groups for the outcome variables with mean & SD are initially executed using the fixed-effect model. Subsequently, on confirming high heterogeneity, the random-effect model (DerSimonian and Laird model) along with the generic inverse variance was applied to determine the pooled estimate. Similarly, pooled odds' ratio (along with 95% CI) was estimated outcome parameters with count events i.e. obstructive & restrictive pulmonary function changes using generic inverse variance and random effects DerSimonian and Laird model [38].

Heterogeneity, subgroup and sensitivity analyses, leave-one-out-meta-analysis (LOOMA)

Visual inspection of forest plots along with the I-square (I^2) statistics and Cochran-Q test were used to assess heterogeneity among selected studies. The values of $I^2 > 25\%$ and Cochrane-Q < 0.1 were regarded as evidence for heterogeneity among selected studies. To confirm the heterogeneity DerSimonian-laird random effect model was utilised [38]. Where >10 studies were available, the sources of heterogeneity were further explored individually by fitting variables like age and smoking (% of exposed group with smoking behavior) separately in meta-regression [39]. A particular variable was considered as the source heterogeneity when the I^2 drops by 50% or the I^2 statistics turn significant ($p < 0.05$) during meta-regression.

The L'Abbe Plot was used for variables with the binary outcome to visually interpret individual study heterogeneity and effect size against the overall effect size of studies and level of no effect size [40].

Subgroup analysis was performed to identify the effects of the gender (male or female or male & female combined), smoking habit (all non-smoker or mixed group) inclusion of age-sex-height-matched controls and geographical diversity on individual study outcome variables. Subgroup analysis was performed when more than two studies were available in each of the groups. Based on observed changes in mean difference and value of heterogeneity (I^2), it was concluded that whether a particular group influenced the overall results of the group or not. LOOMA was performed for sensitivity analysis. By pooling out the results of all studies while excluding each study sequentially, this analysis quantifies the influence of a particular study on overall results [39]. Further, when >10 studies were available for a particular outcome parameter, the shape (asymmetrical or symmetrical) of the funnel plot, contour enhanced funnel plot along with Egger's test result ($p < 0.001$) was considered to assess source of heterogeneity i.e. due to small size effect and particular type of bias such as publication bias [39, 41, 42].

All statistical analyses were performed with Stata Version 16 [43]. The value of 'p' as <0.05 was regarded as the two-sided statistically significant difference except for sub-group analysis and heterogeneity value of 'p' as <0.10 was considered statistically significant difference.

Assessing the risk of bias

To assess the risk of bias among included studies, the Newcastle Ottawa scale (OHRI-NOS) was independently applied by authors (AV, RB) for each study [44]. Broadly, the OHRI-NOS tool evaluates the risk of bias on three crucial domains: [1] method used for assessing the exposure [2], criteria for selecting & recruiting the participants (exposed- & control- group) and [3] their intergroup comparability. Prior to rating the bias, the criteria to rate the risk of bias was customized to the needs of the current study, based on the recommendations from OHRI-NOS guidelines and mutual consensus by the authors. Details about customised OHRI-NOS SOPs for the current study is shared as supplementary material in Annexure-1.

Certainty of evidence assessment

The certainty of each of the pulmonary function assessment evaluated in this systematic review was assessed using the 'Grading of Recommendations Assessment, Development, and Evaluation' (GRADE) framework [45]. The systematic tool offers a structured and validated methodology for assessing evidence quality, aiding interpretation of the results. The GRADE framework recommends to assess the certainty of evidence for each of the outcome parameter as one of the four levels: High, Moderate, Low, and Very Low, based on criteria such as risk of bias, publication bias, imprecise results, and inconsistency of the included studies. Observational studies generally begin with a Low or Very Low rating, which can be adjusted upwards or downwards depending on the strength, consistency, and robustness of the evidence. By providing a consistent and transparent approach, the GRADE framework facilitates the summarization of findings, thereby improving their interpretability and practical applicability [45].

Results

The systematic search retrieved 5,366 citations from the three major digital repositories & four via lateral search) for the review. On removal of duplicates & screening title abstracts, forty-six articles were identified as suitable for full-text review. Lastly, twenty-two studies were identified for data extraction. Stepwise exclusion of studies, along with reasons, are described in Fig. 1.

Details of the study

Notably, the majority of the studies (fourteen) included only male participants, and a fraction of included studies (ten) were reported to involve only participants with no history of tobacco smoking [3, 14, 18, 20, 22, 26, 27, 33, 46, 47]. The mean age of the participants in the included studies ranged from 27 to 43 years, and the exposed group had a mean occupational exposure of 5–14 years of flour dust exposure. The description of workplace / environmental dust concentration was available for a few studies (ten) and ranged from 1.35 to 12.3 mg/m^3 for total dust and 0.31–7.77 mg/m^3 for respirable dust [14–17, 19, 20, 27, 34, 35, 48]. Additionally, few of these studies reported workplace spores & microbes. Further, personal protective equipment (PPE) usage was rarely described in the included studies and even among those reported, the usage was very low, ranging from 33% - no usage [18–22, 25]. Interestingly, studies were primarily available from the Afro-Asian region (India, Pakistan, Iran, Egypt, Ethiopia, Nigeria, South Africa & Sudan), and a couple (two) from the European region (Croatia and France) and none from Australian or American regions. A detailed description of the included studies is available in Table 1.

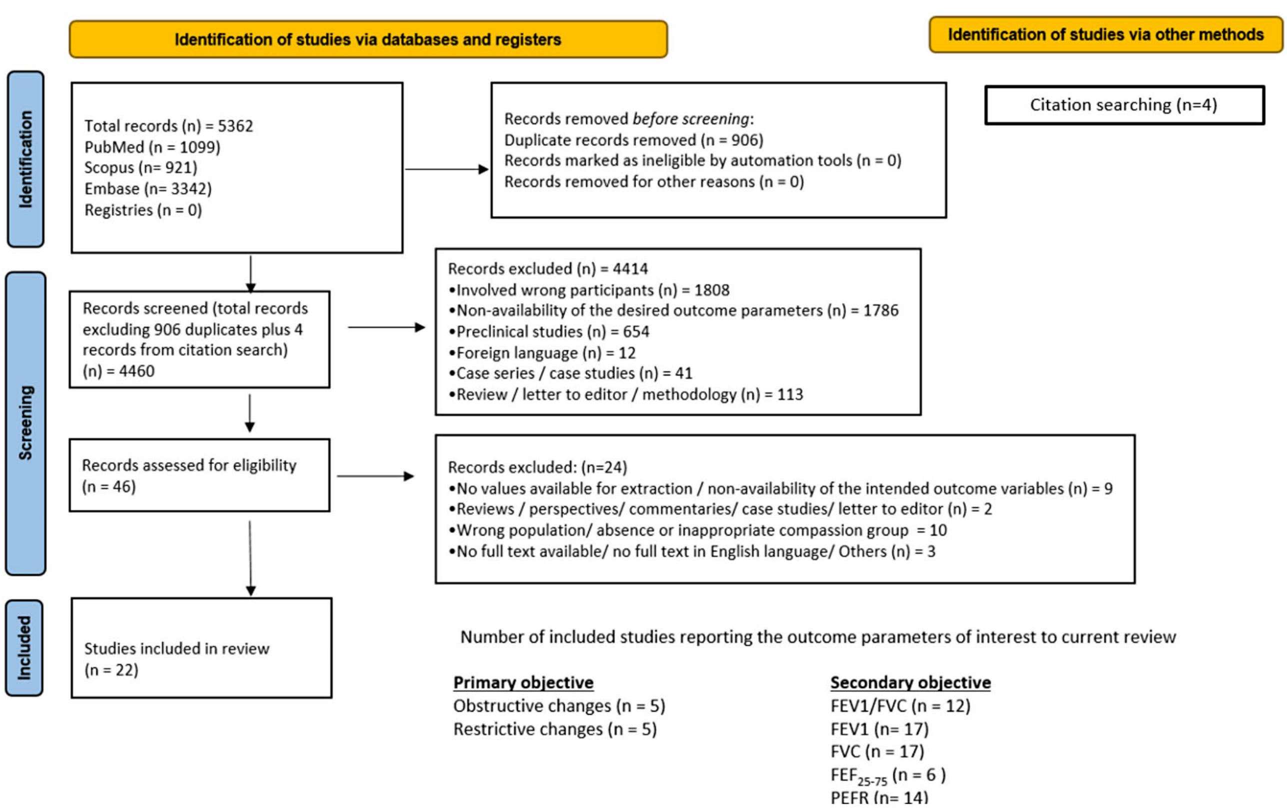

Fig. 1 PRISMA 2020 flow chart. Flow chart describing number of articles/ citations included and excluded at various stage with reasoning

Table 1 Description of all studies included in the present systematic review

Citation (study site/country)	Outcome parameters assessed	Sample size (n) & age reported as mean (SD) years	Male (%); history of tobacco smoking (%)	anthropometry details as Mean(SD)	Exposure details of flour mill workers
El Karim MA et al. [15] (Sudan)	FEV1*, FEV1/FVC, FVC*	Exposed: 100, aged 34 (8.6); Control: 30, aged 34.7 (8.8)	100% male participants in both groups; 34% & 40% of them with smoking history among exposed and controls respectively.	Height (cm): Exposed – 165.9 (8.1) Control – 164.7 (7.7)	Exposure duration 10 (6.2) years; Total dust ranged between 1.35–3.57 mg/m^3 and respirable dust ranged between 0.31–0.85 mg/m^3 at different venues of the flour mill, the study confirmed the dust levels exceeded that of ACGIH recommended threshold limit values (TLV) by factor 3.7. There is no description of the PPE usage
Demeke D et al. [18] (Ethiopia)	FEV1*, FEV1/FVC, FVC*, FEF25-75%*, PEFR*,Prevalence of obstructive & restrictive changes	54 participants per group; exposed: 27.37 (6.71) years, controls: 28 (5.33) years	Included only non-smoking male participants	Height (cm): Exposed – 166 (7) Control – 168 (5)	Exposure duration ranged 1–12 years; No description of the workplace/ environmental dust concentration, 33.3% of workers using PPEs
Gholami A et al. [16] (Iran)	FEV1*, FEV1/FVC*, FVC* & PEFR*	Exposed: 176, aged 35.2 (8.6); Control: 110, aged 35.5 (8.5)	100% male participants in both groups; 22.1% & 23.6% of them with smoking history among exposed and controls respectively.	Height (cm): Exposed – 171.6 (8.6) Control – 170.7 (6.2)	Exposure duration 11 (8) years; The total dust (45.66 ± 4.2 mg/m^3) included the inhalable dust of ≥ 5 μ diameter (33.26 ± 3.47 mg/m^3) and respirable dust of < 5 μ in diameter (12.4 ± 2.4 mg/m^3) is measured at various locations of flour mill. The TLV of dust exposure exceeds that recommended by ACGIH and the National (Iran) Technical Committee of Health Professionals. There is no description of the PPE usage
Ibekwe RU et al. [49] (Nigeria)	FEV1, FEV1/FVC, FVC, PEFR*,Prevalence of obstructive & restrictive changes	200 participants per group; exposed: 39.8 (10.05) years, controls: 39.9 (9.94) years	100% male participants in both groups; 10% & 17.2% of them with smoking history among exposed and controls respectively.	Not provided	Exposure duration 10 (2) years; No description of the workplace/ environmental dust concentration, No description of the PPE usage
Ijadunola KT et al. [19] (Nigeria)	FEV1*, FEV1/FVC*, FVC, PEFR*,Prevalence of obstructive & restrictive changes	Exposed: 91, aged 34.3 (8.8); Control:121, aged 36.1 (9.6)	100% male participants in both groups; 17.5% & 9.9% of them with smoking history among exposed and controls respectively.	Height (cm): Exposed – 171.1 (12.5) Control – 171.6 (5.6)	Exposure duration 5.6 (3.9) years; The total suspended particulate of dust - TSP (< 4 μ in diameter) concentration ranged between 0.6–4.7 mg/m^3, exceeding the Federal Environmental Protection Agency [FEPA, 1991] standards of 0.25 mg/m^3. Majority of workers did not use any form of PPE at the workplace
Iyogun K et al. [20] (Nigeria)	FEV1*, PEFR*	72 participants per group; exposed: 34.6 (10.8) years, controls: 32.7 (9.2) years	Included only non-smoking male participants	Height (cm): Exposed – 165.9 (8.1) Control – 164.7 (7.7)	More than 85% workers with job duration > 5 years; The PM_{10} levels ranged between 212.7–1711.2 μg/m^3 during the morning hours and 418.6–2299.6 μg/m^3 during postnoon hours, exceeding the WHO's 24 hour 50μg/m3 limit. The $PM_{2.5}$ levels ranged between 103.4–2226.5 μg/m^3 during the morning hours and 368.6–3755.2 μg/m^3 during postnoon hours, exceeding the WHO's 24 hour 25μg/m^3. PPE usage is reported among < 5% of exposed workers
Raj Kapoor et al. [50] (India)	FEV1/FVC, FVC, FEF25-75%, PEFR*,MVV & TLCO	25 exposed and 50 control participants with age ranging across 19–50 years	Exposed: all male participants, 60% smokers; Control: 50% male and all participants were non- smoking	Not mentioned	Maximum exposure duration 10.29 (6.62) years, respectively; No description of workplace/ environmental dust concentration or the PPE usage among workers
Lagiso ZA et al. [21] (Ethiopia)	FEV1*, FEV1/FVC*, FVC*	Exposed: 196, aged 32.1 (9.99); Control: 210, aged 31.28 (7.87)	Exposed: 80.1% male, 19.9% smokers; Control: 76.7% male, 1.9% smokers	Height (cm): Exposed – 167 (7) Control – 169 (7)	About 70% workers were exposed for > 6 years; No description of workplace/ environmental dust concentration, PPE were not usage by workers

Table 1 (continued)

Citation (study site/country)	Outcome parameters assessed	Sample size (n) & age reported as mean (SD) years	Male (%); history of tobacco smoking (%)	anthropometry details as Mean(SD)	Exposure details of flour mill workers
Meo SA et al. [33] (Pakistan)	FEV1*, FEV1/FVC, FVC*, FEF25-75%, PEFR*, MVV*	46 participants per group; exposed: 34.97 (1.9) years, controls: 35.08 (1.8) years	Included only non-smoking male participants	Height (cm): Exposed – 168.2 (SEM- 0.8) Control – 167.3 (SEM-0.9)	Exposed duration 6.3 (0.4) years; No description of the workplace/ environmental dust concentration, PPE were not usage by workers
Mohammadien HA et al. [25] (Egypt)	FEV1/FVC*	200 participants per group; exposed: 38.8 (11.2) years, controls: 40.5(9.6)	100% male participants in both groups; 75% & 30% of them with smoking history among exposed and controls respectively.	Height (cm): Exposed – 169.3 (SEM-0.7) Control – 168.2 (SEM-0.8)	48% of the workers were exposed to > 10 years, while the remaining 52% of them were exposed to ≤ 10 years of duration; No description of the workplace/ environmental dust concentration, No description of the PPE usage
Patel NS et al. [22] (India)	FEV1*, FEV1/FVC*, FVC*	60 participants per group; Age*: exposed: 42.15 (7.86) years, controls: 33.77 (9.38) years	Included only non-smoking male participants	Height (cm): Exposed – 167.5 (5.9) Control – 165.8 (8.7)	Included exposed participants with > 2 years of exposure; No description of the workplace/ environmental dust concentration, PPE were not usage by workers
Relkar-Joshi R et al. [47] (India)	Prevalence of obstructive & restrictive changes	75 participants per group; exposed: 33.31 (7.75) years, controls: 33.28 (8.39) years	All participant were non-smoking, no description of the sex of participants	Not mentioned	Exposed duration 12.2 (5.9) years; No description of the workplace/ environmental dust concentration, No description of the PPE usage
Taytard A et al. [48] (France)	FEV1*, FVC, PEFR	63 participants per group, with age ranging between 19–50 years	All participants were male participants and 51% of them with smoking history	Not mentioned	44% of the workers are exposed to ≤ 5 years of exposure, while the remaining 56% workers were exposed to > 5 years; global dust (organic & inorganic) levels ranged 2.3–124.8 mg/m^3. Qualitative assessment confirmed the presence of pencillium and cladosporium. No description of the PPE usage
Wagh ND et al. [27] (India)	FEV1*,FVC*, PEFR*, MVV, TLCO	Exposed: 59, aged 41 (9); Control: 54, aged 43 (13)	All participant were non-smoking, no description of the sex of participants	Height (cm): Exposed – 159 (5) Control – 161 (8)	About 75% workers were exposed for > 3 years; Total PM10 dust ranged 430–814 µg/m^3. No description of the PPE usage.
Yach D et al. [28] (South Africa)	FEV1, FVC, FEF25-75%	Exposed: 582, aged 36.9 (12.9); Control:153, aged 36.1 (13.7)	No description of the sex of the participants; Exposed: 67.3% smokers; Control: 68.6% smokers	Height (cm): Exposed – 170.7 (8) Control – 171.9 (7.2)	Exposed duration 7.1 (8.1) years; No description of the workplace/ environmental dust concentration, No description of the PPE usage
Zamani A et al. [17] (Iran)	FEV1*, FEV1/FVC*, FVC*, PEFR*	67 exposed & 53 control group participants, with no description of age	100% male participants in both groups; 19.4% & 20.7% of them with smoking history among exposed and controls respectively.	BMI(kg/m^2): Exposed: 56% normal, 40% obese, 4% underweight Control: 60% normal, 38% obese, 2% under weight	65.7% workers were exposed to < 10 years and the remaining 34.3% were exposure to ≥ 10 years; The study reported total and respirable dust levels as 11.06 ± 8.73 and 7.77 ± 8.35 mg/m^3 respectively, with the ACGIH threshold limit recommendation being 10 & 0.5 mg/m^3 respectively. Level of respirable flour dust exceeds in 45% samples as per ACGIH criteria. No description of the PPE usage

Table 1 (continued)

Citation (study site/country)	Outcome parameters assessed	Sample size (n) & age reported as mean (SD) years	Male (%); history of tobacco smoking (%)	anthropometry details as Mean(SD)	Exposure details of flour mill workers
Zodpe SP et al. [34] (India)	PEFR*	286 participants per group, with no description of age	100% male participants in both groups; 72% & 91% of them with smoking history among exposed and controls respectively.	Not mentioned	Exposed duration 7.4 (2.1) years; No description of the workplace/ environmental dust concentration, No description of the PPE usage
Zuskin E et al. [33] (Croatia)	FEV1, FVC	Participants: Exposed: 53 Control: 40 Age: Exposed: 33(4) Control:31(4)	Exposed: 0% male, 13% smokers; Control: 0% male, 6% smokers	Height (cm): Exposed: mean 167; Control: mean 156 SD not available	Exposed duration 14 (range 1–22) years; The total dust and respirable dust fraction ranged from 2.4–17.1 mg/m^3 and 0.5–2.7 mg/m^3 respectively. The levels are higher than the National (Croatia) federal standards for organic dust i.e. 3 mg/m^3 and 1 mg/m^3 for total dust and respirable dust levels. No description of the PPE usage
Pande P et al. [46] (India)	FEV1*, FEV1/FVC*, FVC*, FEF25-75%*, PEFR*,TLCO*, VC*	100 participants per group, with no description of age	All participant were non-smoking, no description of the sex of participants	Not mentioned	No description of workplace/ environmental dust concentration or the PPE usage among workers
Dhillon SK et al. [26] (India)	FEV1*, FVC*, FEF25-75%*, PEFR*, MVV	50 participants per group: exposed: 34.56 (8.5), controls: 35.23 (8.51)	All participant were non-smoking, no description of the sex of participants	Height (cm): Exposed – 168.3(6.5) Control – 164.3 (6.5)	No description of workplace/ environmental dust concentration or the PPE usage among workers
Bhageri HM et al. [14] (Iran)	FEV1, FEV1/FVC*, FVC*, PEFR*	Exposed: 35, aged 40.41 (10.57); Control: 20 aged, 39.4 (12.49)	All participant were non-smoking, no description of the sex of participants	Height (cm): Exposed – 172.1(5.9) Control – 174.9 (7.4)	Exposed duration 12.1 (9.7) years; the average total and respirable dust at the workplace 8.06 ± 2.58 mg/m^3 and 5.09 ± 2.31 mg/m^3 respectively. Workplace exposure for both total and respirable dust exceeds ACGIH recommended level. No description of the PPE usage
Melo CA et al. [3] (India)	Prevalence of obstructive & restrictive changes	40 participants per group; with exposed 28.5 years & controls 27.75 years of age	Included only non-smoking male participants	Height (cm): Exposed: mean 162.8; Control: mean 173 SD not available	No description of duration of exposure or the workplace/ environmental dust concentration, PPE were used by 17.5% workers

*indicates statistically significant difference ($p < 0.05$) between the two groups

PPE: Personal protective equipment

Risk of bias assessment

Potential risks of biases at various levels of primary studies that could have influenced the results of the current review were assessed using OHRI-NOS [44]. The rating of biases at participant selection & recruitment, exposure assessment and outcomes were determined for each study is described in Table 2. Briefly, the included studies failed to define the participants (exposed & control group), the steps in the selection and exclusion of participants, demonstrate the comparability between the two [2] groups and identify and record the factors that could potentially influence pulmonary function.

A large proportion of studies have failed to adequately address the comparability of the control group, such as enrolling the comparison group from the same workplace or failing to control for factors like age, gender, sociodemographic profile, and anthropometric parameters. About 2/3rd (64%) of the included studies failed to report/characterize the workplace dust/spore / microbial exposure, thereby carrying a high risk of bias under the "measurement of exposure". While the remaining one-third (36%) of studies describing these workplace exposure levels have cross-sectionally assessed and generalized for the entire work duration [14–17, 19, 20, 27, 48]. Further, only two studies Zamani A. et al. (2019) & Zodpe SP et al. [34] described the response and rejection rate, thereby carrying a high risk of bias under the "non-response rate" [17, 34]. Notably, the majority of studies adhered to similar methods in both groups for assessing the outcome parameters, thereby being rated as having a "low" risk of bias for the "Ascertainment method similarities" domain. Lastly, about two-thirds (2/3rd) of the

Table 2 Newcastle-Ottawa scale for risk of bias assessment for included studies

Study	Case definition	Case representativeness	Control selection	Control definition	Group comparability	Exposure ascertainment	Ascertainment method similarities	Non-Response rate	Total ^
El Karim MA et al. [15]	-	-	-	-	*	*	*	-	3
Demeke D et al. [18]	-	-	-	-	*	-	*	-	2
Gholami A et al. [16]	-	-	-	-	*	*	*	-	3
Ibekwe RU et al. [49]	*	*	-	-	*	-	*	-	4
Ijadunola KT et al. [19]	*	*	*	-	*	*	*	-	6
Iyogun K et al. [20]	-	-	-	-	-	*	-	-	1
Raj Kapoor et al. [50]	*	-	-	*	-	-	-	-	2
Lagiso ZA et al. [21]	-	-	-	-	*	-	*	-	2
Meo SA et al. [33]	-	-	-	-	-	-	*	-	1
Mohammadien HA et al. [25]	-	-	-	-	*	-	*	-	2
Patel NS et al. [21]	*	-	-	*	-	-	*	-	3
Relkar-Joshi R et al. [47]	-	-	-	-	-	-	-	-	0
Taytard A et al. [48]	*	*	-	-	-	*	*	-	4
Wagh ND et al. [27]	-	-	-	-	-	*	-	-	2
Yach D et al. [28]	-	-	-	-	-	-	*	-	1
Zamani A et al. [17]	*	-	*	-	-	*	*	*	5
Zodpe SP et al. [34]	*	*	-	-	-	-	-	*	4
Zuskin E et al. [33]	-	-	-	-	-	-	*	-	1
Pande P et al. [46]	*	*	-	*	-	-	*	-	4
Dhillon SK et al. [26]	*	-	*	-	-	-	*	-	3
Bhageri HM et al. [14]	*	*	-	-	-	*	*	-	4
Melo CA et al. [3]	*	*	-	-	-	-	*	-	3
Percentage	54.5%	31.8%	13.6%	13.6%	31.8%	36.3%	77.2%	9%	

included studies (n=15) carried a "high" risk of bias in five of the eight assessed domains of OHRI-NOS.

Certainty of evidence

The certainty of evidence for the relationship between occupational flour dust exposure and pulmonary function injury is rated as very low according to the GRADE assessment. A detailed evidence profile and summary of findings are presented in Supplementary Table 2. The overall certainty of evidence across the majority of outcome indicators was rated as very low, primarily due to significant concerns related to bias. Serious risks of bias, including potential publication bias and other systematic biases, were identified through comprehensive assessments using the Newcastle-Ottawa Scale (NOS), funnel plots, and contour-enhanced funnel plots. Furthermore, the evidence was further downgraded owing to narrow estimates of mean differences juxtaposed with wide 95% confidence intervals, highlighting substantial inconsistencies and imprecision in the findings. These limitations reflect variability in study methodologies and outcomes, undermining the reliability of the observed associations.

Pulmonary function parameters

Forced expiratory volume in the first second (FEV$_1$)

Thirteen of the seventeen included studies reporting FEV$_1$ observed significantly lower FEV$_1$ among flour dust exposed group as compared to control [14–22, 26–28, 33, 35, 46, 48, 49]. Pooling primary data exhibited significantly lower FEV$_1$ [pooled mean difference −0.43 L (-0.57 to -0.29)] among the exposed group in comparison to the control group with high heterogeneity I^2=88.77% (Fig. 2). The LOOMA indicated that no single study had a significant impact on the overall pooled estimate. (Supplementary Fig. 1). Asymmetry of the funnel plot along with Egger's test (p<0.001) result is suggestive of probable publication bias (Supplementary Fig. 2). In continuation, the counter enhanced funnel plot identified asymmetrical distribution of studies under the areas of statistically significant and non-significance suggestive of additional biases (Supplementary Fig. 3). Subgroup analysis to investigate the impact of study region, involvement of male-only participants or non-smoking participants on FEV$_1$ neither identified the sources of heterogeneity nor altered the direction of pooled effect. However, subgroup analysis by involvement of age-sex-height matched comparators revealed a drop in heterogeneity (I^2=60.42%) suggesting the possible source of heterogeneity (supplementary Fig. 4).

Forced vital capacity (FVC)

FVC changes between the groups were available for seventeen studies [14–19, 21, 22, 26–28, 33, 35, 46, 48–50]. All studies observed lower FVC among the exposed group, while the majority (n=11) of the studies reported statistical significance [14–18, 21, 22, 26–28, 33, 46]. The exposed group exhibited a significant decline in FVC [Mean difference was −0.49 L (-0.64 to -0.33), I^2=89.37%] compared to the control group (Fig. 3). The LOOMA indicated that no single study had a significant impact on the overall pooled FVC estimate (Supplementary Fig. 5).

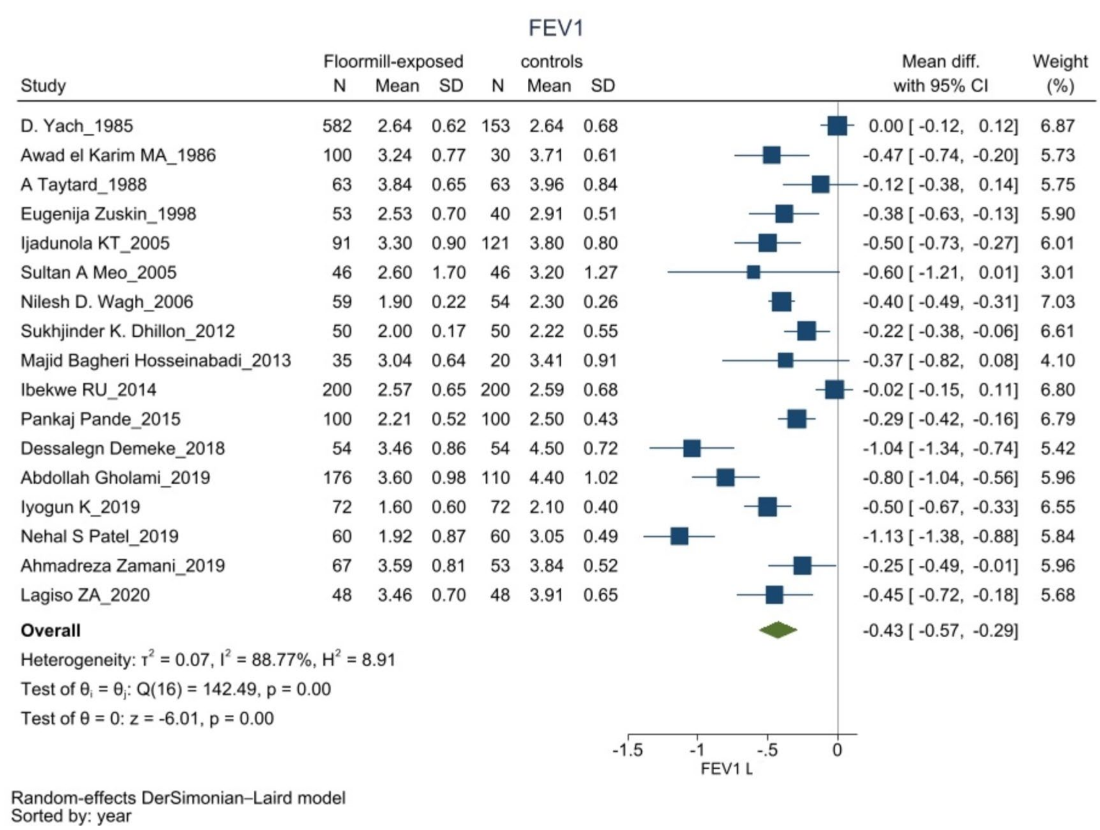

Fig. 2 Forest plot for forced expiratory volume in first second (FEV1). Group differences for FEV1 between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower FEV1 (−0.43 L with 95% CI, -0.57 to -0.29) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2=88.7%)

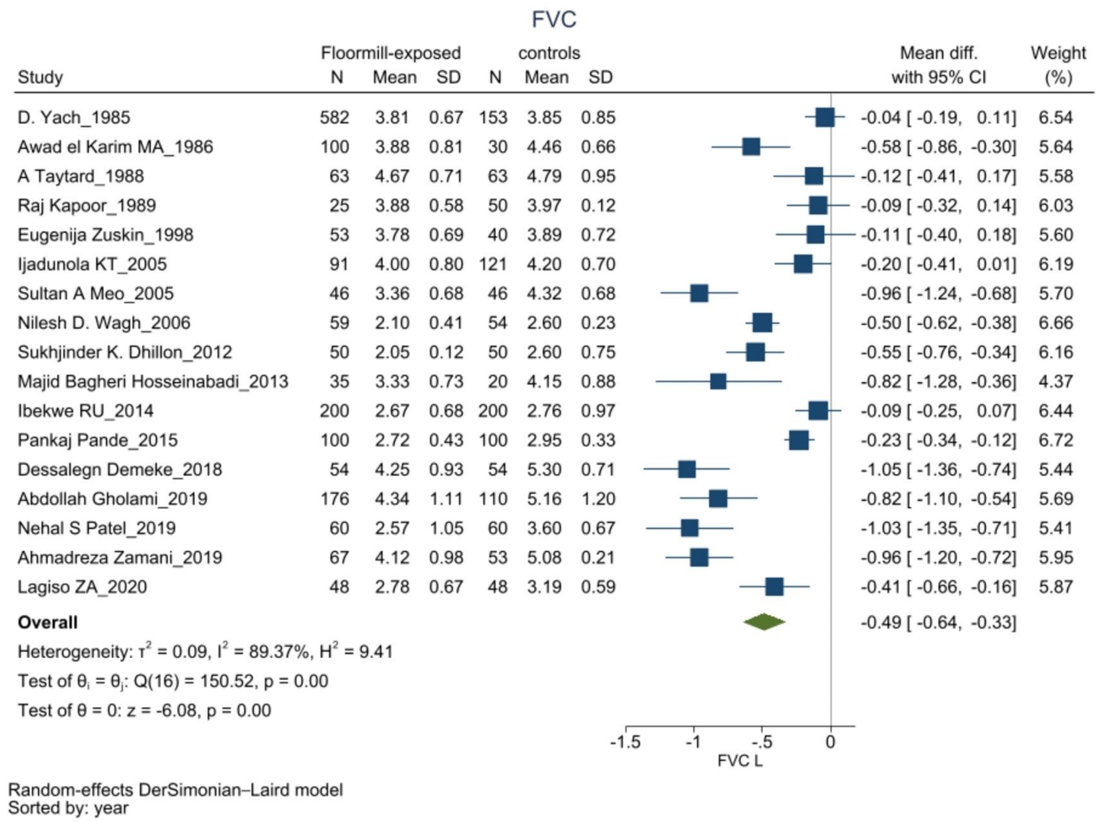

Fig. 3 Forest plot for forced vital capacity (FVC). Group differences for FVC between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower FVC (−0.49 L with 95% CI, -0.64 to -0.33) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2=89.3%)

The asymmetrical funnel plot and Egger's test result ($p<0.001$) are suggestive of the probable publication bias (Supplementary Fig. 6). The absence of studies in the areas of statistically significant and non-significant zones on counter-enhanced forest plots is suggestive of additional biases (Supplementary Fig. 7). Subgroup analysis to investigate the impact of study region, involvement of male-only participants, involvement of age-sex-height matched comparators or non-smoking participants on FVC neither identified the sources of heterogeneity nor altered the direction of pooled effect. (Supplementary Fig. 8).

Ratio between FEV_1 and FVC (FEV_1/FVC)

The group differences for FEV_1/FVC was available from thirteen [13] included studies [14–19, 21, 22, 25, 33, 46, 49, 50]. About 2/3rd [9] of these observed lower FEV_1/FVC (%) among the exposed group as compared to the control group and five [5] of them with statistical significance. As per Fig. 4, the forest plot revealed a trend of lower FEV_1/FVC [i.e mean difference of -3.5% (-6.49 to -0.5)] among the exposed as compared to the control group with high heterogeneity (I^2=89.7%). Notably, Bhageri et al. (2013) reported conflicting higher values among the exposed group in the table while describing lower values among the exposed group in the manuscript result text. Hence, Bhageri et al. (2013) was excluded from further FEV_1/FVC analysis. The LOOMA indicated that no single study (after excluding Bhageri et al. 2013) had a significant impact on the overall pooled FEV_1/FVC estimate. (Supplementary Fig. 9). Relative asymmetry of the funnel plot with Egger's value ($p<0.001$) suggests a high likelihood of publication bias (Supplementary Fig. 10). Further, the paucity of studies on areas of statistically significant and non-significant suggests additional biases (Supplementary Fig. 11). Subgroup analysis to investigate the impact of study region, involvement of male-only participants, participants, involvement of age-sex-height matched comparators or non-smoking participants on FEV_1/FVC neither identified the sources of heterogeneity nor altered the direction of pooled effect. (Supplementary Fig. 12).

Peak expiratory flow rate (PEFR)

Fourteen [14] studies compared PEFR values between the exposed and control group [14, 16–20, 26, 27, 33, 34, 46, 48–50]. All studies reported lower PEFR among the exposed group than the control group, with all but

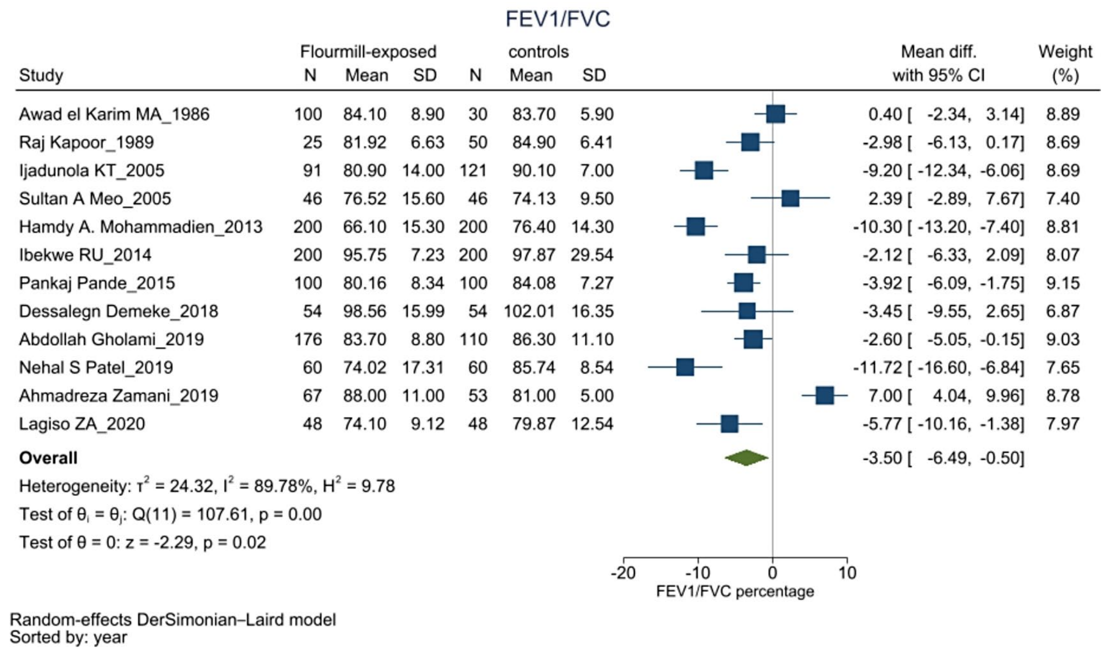

Fig. 4 Forest plot for FEV1/FVC. Group differences for FEV1/FVC between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower FEV1/FVC (−3.5% with 95% CI, -6.49 to -0.5) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2=89.7%)

Taytard A et al. (1988) identifying statistical significance. Overall, the control group exhibited significantly lower pooled mean difference in PEFR [-1.36 L/s (-1.70, -1.03) L/s] compared to the control group with high heterogeneity (I^2=90.4%) (Fig. 5). The LOOMA indicated that no single study had a significant impact on the overall pooled PEFR estimate. (Supplementary Fig. 13). An asymmetrical layout of the funnel plot accompanied by Egger's test result as $p<0.001$ indicates a higher risk of publication bias (Supplementary Fig. 14). Subgroup analysis to investigate the impact of the study region, involvement of male-only participants, involvement of age-sex-height matched comparators or non-smoking participants on PEFR neither identified the sources of heterogeneity nor altered the direction of pooled effect (Supplementary Fig. 15).

Forced expiratory flow from 25 to 75% of the FVC ($FEF_{25\text{-}75\%}$)

About quarter [6] of the included studies reported $FEF_{25\text{-}75\%}$ values [18, 26, 28, 33, 46, 50]. Exposed group of all studies but Dhillon et al. (2012) observed lower $FEF_{25\text{-}75\%}$ values as compared to the control group, with two of these studies (Pande P et al. 2015 & Demeke D et al. 2018) observing statistical significance. Overall pooled analysis revealed a trend of 0.34 L/s (-0.63 to -0.06), lower $FEF_{25\text{-}75\%}$ among the exposed group as compared to the control with high heterogeneity (I^2=77.3) (Fig. 6). The LOOMA indicated that no single study had a significant impact on the overall pooled $FEF_{25\text{-}75\%}$ estimate (Supplementary Fig. 16). In view of the limited number of studies, additional analyses such as funnel plots, subgroups and meta-regression weren't taken.

Maximum voluntary ventilation(MVV)

Three [3] studies reporting MVV changes, observed lower levels among the exposed group as compared to the control group [26, 33, 50]. Pooled analysis between the exposed and control groups identified significantly lower MVV among the exposed group with a mean difference of -17.43 L/min (95% CI -27.82 to -7.05) and unacceptable heterogeneity levels (I^2=57.2% (Fig. 7).

Obstructive changes

Five [5] studies reported the number of participants with (frequency of) pulmonary function suggestive of obstructive changes [3, 18, 19, 47, 49]. All observed higher odds of obstructive changes among exposed, with three [3] of them observing statistically significant results. Forest plots revealed significantly higher odds of obstructive changes among the exposed group with pooled OR of 12.96 (3.41–49.24; I^2=82.39%) as compared to the control group (Fig. 8). The LOOMA indicated that no single study had a significant impact on the overall pooled OR for obstructive changes. (Supplementary Fig. 17). Further, L'Abbe Plot analysis revealed that the majority of the studies lay away from the effect-size line, indicating high heterogeneity among the studies, congruent with the I^2 (82.39%) heterogeneity test (Supplementary Fig. 18). In view of the limited number of studies, additional analyses

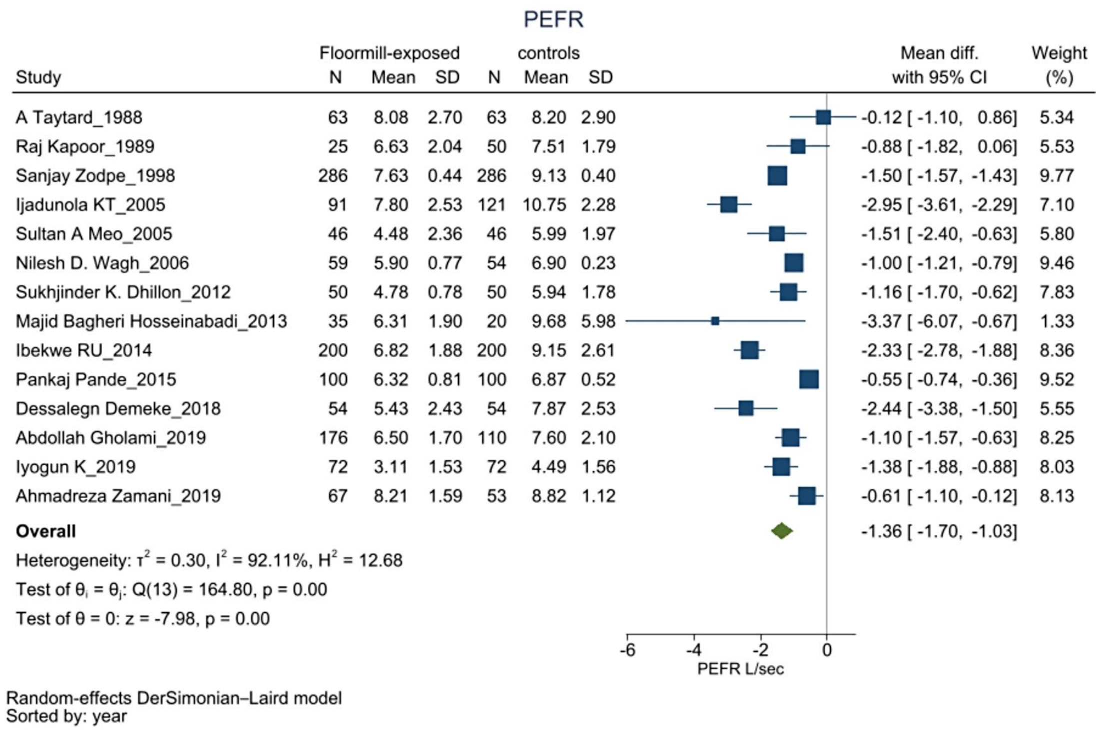

Fig. 5 Forest plot for PEFR. Group differences for PEFR between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower PEFR (−1.36 L/s with 95% CI, -1.70 to -1.03) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2=90.4%)

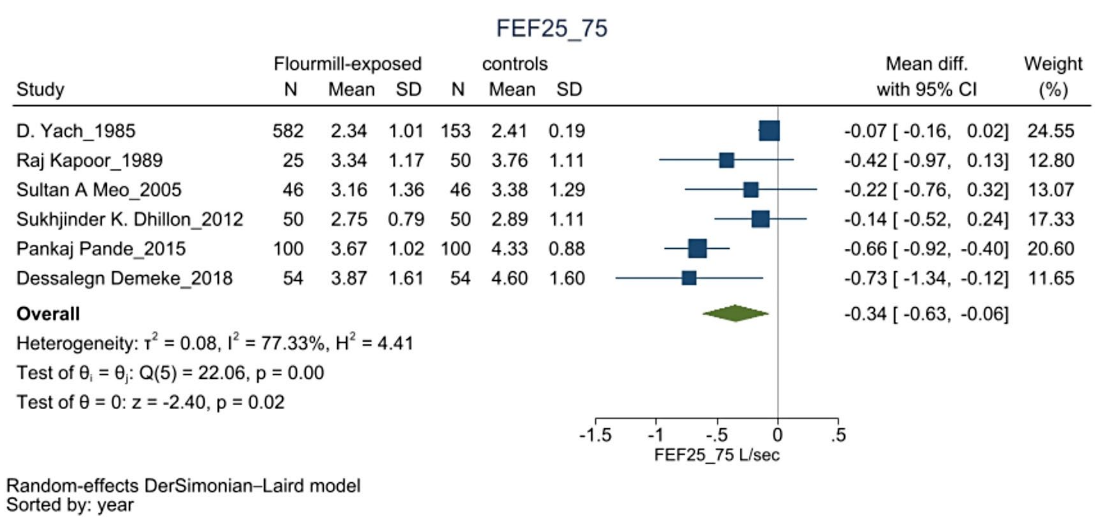

Fig. 6 Forest plot for $FEF_{25-75\%}$. Group differences for $FEF_{25-75\%}$ between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower $FEF_{25-75\%}$ (−0.34 L/s with 95% CI, -0.63 to -0.06) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2=77.3%)

such as funnel plots, sub-groups and meta-regression weren't taken.

Restrictive changes

Five [5] studies reported the number of participants with (frequency of) pulmonary function suggestive of restrictive changes [3, 18, 19, 47, 49]. Three [3] of these observed no restrictive changes in the control group, therefore reporting higher odds of restrictive changes among the exposed. The forest plot revealed a trend of higher odds of restrictive changes among the exposed group with pooled OR of 5.11 (0.55–47.38; I^2=81.62%) as compared to the control group (Fig. 9). In view of the

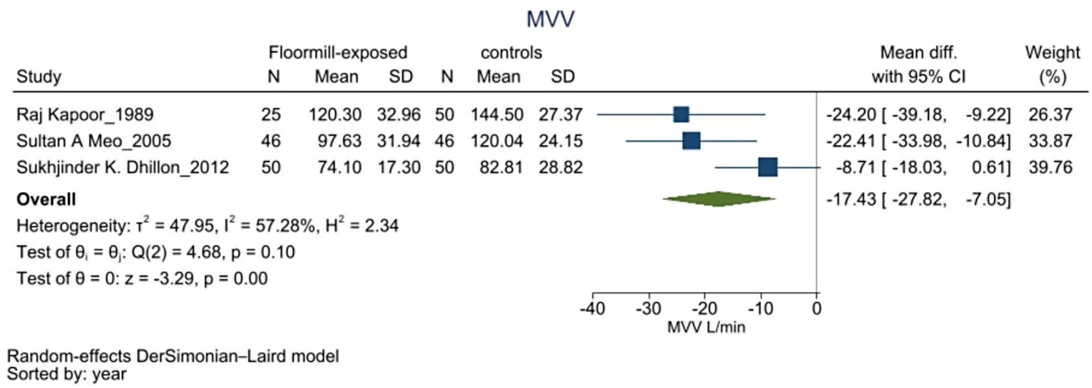

Fig. 7 Forest plot for MVV. Group differences for MVV between flour dust exposed and unexposed group. Forest plot demonstrates significantly lower MVV (– 17.43 L/min with 95% CI, -27.82 to -7.05) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2 = 57.3%)

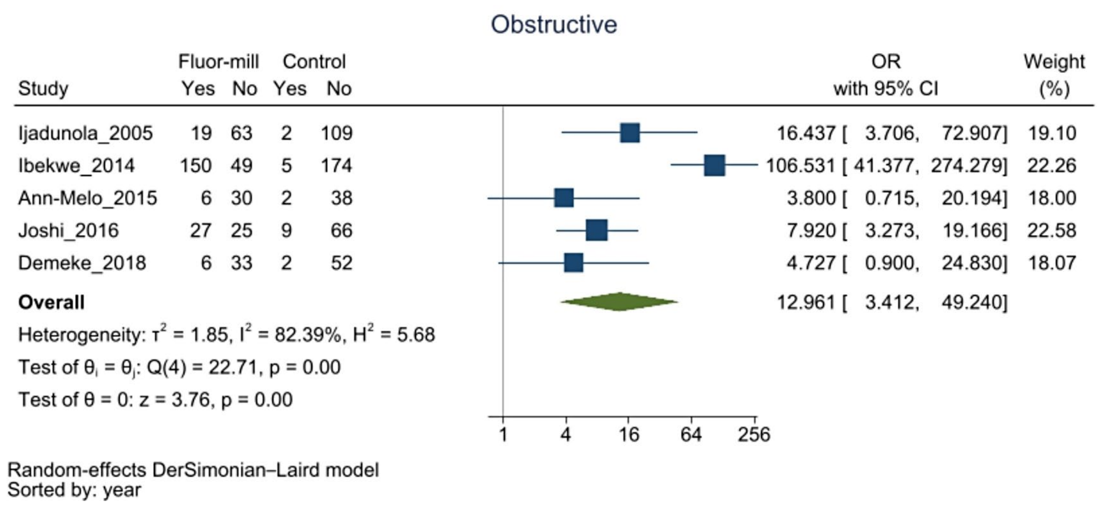

Fig. 8 Forest plot for obstructive pattern changes. Odd's for obstructive changes among flour dust exposed group in comparison to un exposed group. Forest plot demonstrates significantly higher odd's of obstructive changes (12.96 with 95% CI, 3.41 to 49.24) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high (I^2 = 82.39%)

limited number of studies, additional analyses such as funnel plots, sub-groups and meta-regression weren't taken.

Other additional pulmonary function parameters

Few studies additionally reported vital capacity (VC) and transfer capacity of the lung, using the carbon monoxide uptake model (TLco). The study Pande P et al. (2015) reported TLco and VC, while the study by Rajkapoor et al. (1989) reported TLco alone [46, 50]. The mean TLco of the exposed group (27.54±6.08 & 24.80±2.73 ml/min/mmHg, respectively) are significantly lower than the control group (30.49±4.13 & 37.15±4.78 ml/min/mmHg, respectively). The lone study reporting VC observed significantly (p<0.01) lower VC among the exposed group (i.e. 3.18±0.4 L) as compared to the control (i.e. group 3.42±0.36 L).

Discussion

The present work systematically reviewed the studies reporting the performance of pulmonary function parameters among the occupationally exposed flour dust workers as compared to the control group (un-exposed to flour dust). Pooled results indicate a significant decline in all pulmonary functions among flour dust-exposed workers relative to the control group with the decline being more pronounced in subgroup analyses limited to studies with anthropometry-matched comparators. Furthermore, the reduced pulmonary functions in the exposed group qualified for clinical patterns of pulmonary dysfunction, such as obstructive and / or restrictive types. Consequently, exposure to flour dust not only diminishes pulmonary function but also increases the risk of developing clinical pulmonary dysfunction. Notably, all of the available primary studies are cross-sectional in nature, with high levels of heterogeneity and carry a significant

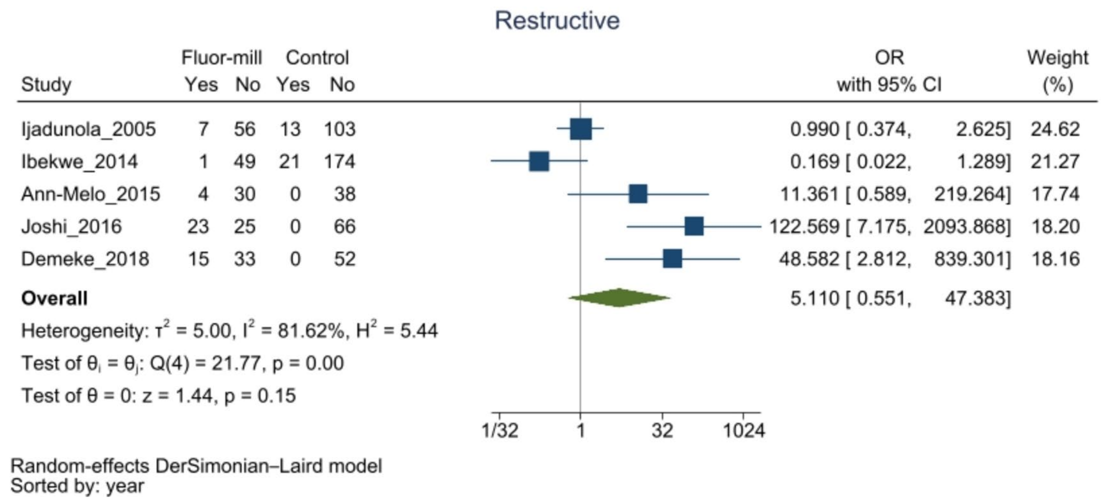

Fig. 9 Forest plot for restrictive pattern changes. Odd's for restrictive changes among flour dust exposed group in comparison to un exposed group. Forest plot demonstrates significantly higher odd's of restrictive changes (5.11 with 95% CI, 0.55 to 47.38) among flour dust exposed individuals. However, the heterogeneity among the studies were unacceptably high ($I^2 = 81.6\%$)

risk of bias in terms of their case definition (for exposed & un-exposed group), participant recruitment, matching and exposure assessment, which results in subpar quality of evidence and lower certainty of evidence.

In the hierarchy of control measures aimed at preventing or mitigating occupational hazards, the reduction of dust in the workplace through administrative and engineering controls is of paramount importance [51]. Numerous strategies exist to manage dust levels in the workplace, ensuring compliance with established statutory limits. The current review noted only a fraction (nine) of studies reported total dust and respirable dust concentrations at the workplaces, and all of them observed dust levels higher than the recommended statutory levels [14–17, 19, 20, 27, 48]. Further, the usage of personal protective equipment (PPE), although is the last resort to prevent/reduce exposure to occupational hazard, is scarcely reported [3, 18–22, 33]. The evidence from the existing studies indicates that workplaces involving flour dust have not succeeded in ensuring a safe and healthy environment for flour mill workers.

The exposed group exhibited a pooled estimate of ~ 500 ml lower lung volume (FEV_1 & FVC) as compared to the control group. Reduction in the FEV_1/FVC and FEF25-75% parameters suggest aberrations in both larger and smaller airways. Additionally, the rate of airflow through the airway (PEFR & MVV) is reduced among the exposed group as compared to the control group. Considering the reduced lung volume and rate of airflow through the airways, the exposed group experienced both obstructive and restrictive patterns of pulmonary aberrations and few studies confirm the clinical pulmonary dysfunction among the exposed group. In alignment with the aggregated findings, a limited number of primary studies indicated a heightened occurrence of respiratory symptoms, including cough, phlegm, and dyspnea. Nevertheless, due to the lack of standardized symptom reporting, it was not possible to estimate the pooled odds or frequency of these symptoms.

Smoking is a known risk for pulmonary dysfunction, leading to aberrations in the pulmonary function parameters. The pooled observations remained consistent in the sub-group analysis of studies that involved participants with no previous history of smoking. Thereby suggesting the impaired pulmonary function is beyond smoking behavior and attributed to exposure to flour dust. In view of the limitations in the availability of primary studies, the influence of duration of exposure and dust levels on impaired pulmonary function could not be evaluated.

The pathogenesis for development of pulmonary dysfunction associated with flour dust is characterized by the induction of a hypersensitivity reaction and the activation of an inflammatory response resulting from physical irritation [52, 53]. Earlier studies have reported varied pulmonary pathologies involving bronchi, interstitial parenchyma and alveoli due to flour dust exposure [54, 55]. Consistent with the literature, the current systematic review reiterates the hazardous role of flour dust on pulmonary function.

Earlier studies investigating occupational flour dust exposure are cross-sectional and report both long-term and acute pulmonary illnesses such as allergic rhinitis, asthma, febrile reaction, chronic bronchitis, lung fibrosis and allergic alveolitis [56, 57]. However, in view of the lack of longitudinal studies, the reversibility of pulmonary conditions associated with long-term flour dust exposure is unknown.

The present study is perhaps the earliest to acknowledge and quantify pulmonary aberrations due to occupational flour dust exposure by systematically reviewing the current literature. The observations, although derived from subpar primary evidence derived from three bibliographic data bases (PubMed, Embase & Scopus), high heterogeneity, involvement of anthropometric un-controlled comparators, high risk of biases and lower certainty of evidence, confirm the pulmonary derangements due to occupational flour dust exposure. Longitudinal studies are essential, incorporating industrial hygiene assessments and comprehensive respiratory evaluations, to elucidate the relationship between occupational exposure to flour dust and pulmonary dysfunction, as well as the potential for reversibility following the cessation of exposure. Primary studies confirm the inadequate implementation of control measures to reduce or prevent occupational hazards associated with flour dust. This is reflected in dust levels exceeding the recommended limits set by statutory bodies and the infrequent use of personal protective equipment (PPE). Given the significant association between exposure to flour dust and respiratory impairment, it is essential to implement workplace interventions, particularly through engineering controls, to minimize flour dust emissions during industrial activities. Furthermore, it is crucial to emphasize the use of personal protective equipment (PPE) during work. Regular industrial hygiene assessments for measuring flour dust levels, along with periodic medical examinations, should be standard practice to evaluate the effectiveness of implemented workplace interventions.

Conclusion

The present systematic review suggested a significant association between occupational flour dust exposure and pulmonary dysfunction. Although the evidence is derived from subpar primary literature and lower certainty of evidence, considering the depth of seriousness of health hazards, the results recommend necessary actions from stakeholders for effective regulation of dust control measures and prevent pulmonary dysfunction. In future interventional longitudinal studies, besides qualitative and quantitative estimation of flour dust and pulmonary function, it is essential to understand the reversibility of the flour dust-related lung function derangements.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-21286-6.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Author contributions

Conceptualization (AV, KU, AS, BS, RB), screening for articles (AV, KU, AS), Proposal Design (AV, AS), data extraction (KU, AV), data analysis (RB, BS), statistical analysis (RB, AV), manuscript writing (AV, AS, BS), editing of final version of manuscript(AV, KU), approval of final version (AV, KU, AS, BS, RB).

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Data availability

All data relevant to the study are included in the article or uploaded as Supplementary Information. In addition, the datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Human ethics and consent to participate

Not applicable. This study is based solely on a review of the existing literature and does not involve any primary data collection from humans or animals. Therefore, ethical approval and consent to participate declarations are not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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