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Reduced mid-expiratory flow and inhalational exposure patterns in adults undergoing spirometry – a retrospective case-control study from southeastern Turkey

Emine Tosun[1,A-F] ✉, **Zafer Hasan Ali Sak**[1,A-F]

[1] *Department of Chest Diseases, Harran University Faculty of Medicine, Şanlıurfa, Türkiye*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

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Abstract

Introduction and Objective. Reduced maximal mid-expiratory flow between 25% and 75% of forced vital capacity (MEF25-75) may indicate small-airway impairment, but its relationships with inhalational exposure and symptoms are uncertain. We compared exposure histories, respiratory symptoms and spirometric patterns in adults with reduced MEF25-75 and controls.

Materials and Method. Adult spirometry records (1 January 2023–31 May 2026) were reviewed retrospectively. Reduced MEF25-75 was defined operationally as <70% predicted. The final cohort included 172 adults (100 cases, 72 controls). Propensity-score matching on age, sex, body mass index, smoking and previous respiratory disease yielded 47 matched pairs. Paired tests and false-discovery-rate adjustment were applied.

Results. After matching, broad binary inhalational exposures, including pesticides and bleach/chlorine, did not differ significantly between groups. Post-exposure cough was more frequent among cases (63.8% vs 34.0%; matched odds ratio 3.80, 95% confidence interval 1.37–13.02; p=0.007; q=0.046). Sputum and chest tightness were nominally associated but not significant after adjustment (both q=0.090). Conventional spirometric impairment occurred in 37/47 (78.7%) matched cases versus 6/47 (12.8%) matched controls; 10/47 (21.3%) matched cases had isolated reduced mid-expiratory flow. MEF25-75 correlated with FEV1 (rho=0.862) and FEV1/FVC (rho=0.820).

Conclusions. Reduced MEF25-75 frequently accompanied conventional impairment but occurred in isolation in approximately one-fifth of matched cases. Binary exposure variables were not discriminatory after matching. The <70% cut-off was a study classification rather than a stand-alone diagnostic threshold.

Key words

respiratory function tests, pesticides, occupational exposure, spirometry, disinfectants, environmental exposure, airway obstruction, small airways

INTRODUCTION AND OBJECTIVE

Chronic respiratory disease can be aggravated by occupational and environmental inhalants, including agricultural agents, dusts, fumes and cleaning products [1, 2]. In a region where agricultural work and intensive household or occupational cleaning are common, documenting these exposures is relevant because exposure reduction, ventilation and protective practices may be modifiable, although a retrospective clinical comparison cannot establish causation.

Routine spirometry is interpreted primarily through forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and FEV1/FVC. Maximal mid-expiratory flow between 25% – 75% of FVC (MEF25-75), also reported as forced expiratory flow between 25% – 75% of FVC (FEF25–75), describes flow during the middle half of forced expiration. It has been used as an indicator of possible small-airway impairment, but it is influenced by FVC, age and biological variability. Technical standards favour lower-limit-of-normal (LLN) or z-score interpretation when valid reference equations are available, and MEF25-75 should not be used alone to diagnose small-airway disease [3–6]. For this historical audit, the original operational boundary of 70% predicted was retained for consistent record classification; it was not treated as a diagnostic threshold.

Population data associate reduced mid-expiratory flow with smoking and with less favourable conventional spirometric measures [7]. Structural and longitudinal studies also support the importance of small-airway pathology in obstructive lung disease and suggest that isolated small-airway obstruction may precede later chronic airflow obstruction [8–10]. Pesticide exposure has been associated with respiratory symptoms or impaired lung function, while cleaning products and disinfectants may generate irritant gases, aerosols and secondary pollutants and are associated with work-related airway outcomes [11–16]. Direct clinical comparisons that combine these exposure domains with confounder-balanced mid-expiratory-flow groups remain limited.

✉ Address for correspondence: Emine Tosun, Department of Chest Diseases, Harran University Faculty of Medicine, Şanlıurfa, Türkiye
E-mail: eminedr9591@gmail.com

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OBJECTIVE

The primary aim of the study is to compare inhalational exposure histories and post-exposure respiratory symptoms between adults with MEF25-75 <70% predicted and controls with MEF25-75 >=70% predicted after balancing important measured confounders. Secondary objectives were to compare conventional spirometric indices, quantify isolated versus mixed impairment patterns, and assess associations between MEF25-75 and conventional indices.

MATERIALS AND METHOD

Study design and setting. This single-centre retrospective case-control study reviewed adult spirometry records from the Department of Chest Diseases, Harran University Faculty of Medicine, Şanlıurfa, southeastern Türkiye, between 1 January 2023 and 31 May 2026.

Participants. Eligible participants were adults evaluated during the study period. Inclusion criteria: (1) age >=18 years; (2) spirometry in the study period; (3) recorded MEF25-75 percent predicted; and (4) sufficient demographic, smoking, exposure and symptom data. Exclusion criteria: (1) acute respiratory infection in the previous 4–6 weeks; (2) lung malignancy or lung resection; (3) marked chest-wall deformity, neuromuscular disease or interstitial lung disease; (4) active or sequelae tuberculosis; (5) technically inadequate spirometry; (6) missing grouping data; or (7) age <18 years. Previous respiratory disease was retained as a measured confounder, not an automatic exclusion.

Data cleaning and dataset locking. Before analysis, records were screened against the eligibility criteria, de-duplicated and harmonised using uniform data-management rules. Group status was assigned from the exact recorded MEF25-75 percent-predicted value: <70% defined a case and >=70% a control. Occupation codes were harmonised, direct identifiers were removed, and values that could not be verified from the source entry were treated as missing. Threshold validation was completed before the de-identified dataset was locked, and before outcome comparisons.

The final analytic cohort comprised 172 unique adults (100 cases and 72 controls). Full record-level cleaning decisions, boundary-value verification and duplicate handling are reported in Supplementary File 1.

Spirometry definitions. Pre-bronchodilator values were analysed. MEF25-75 percent predicted was the grouping variable. A 70% threshold was retained because it was the operational threshold specified in the original study files and analyses and lies within the heterogeneous percent-predicted cut-offs reported in prior studies; the systematic review literature shows no accepted universal cut-off [6]. This threshold was therefore treated as a study classification, not as a diagnostic criterion. LLN and z scores were not consistently available. Conventional variables were FEV1 percent predicted, FVC percent predicted, analytic actual FEV1/FVC and peak expiratory flow rate (PEFR). Large-airway obstruction was defined as actual FEV1/FVC <70%, low FEV1 as <80% predicted and low FVC as <80% predicted. Conventional impairment was defined as FEV1/FVC <70% or FEV1 <80% predicted. Isolated reduced mid-expiratory flow required MEF25-75 <70% with FEV1/FVC >=70% and FEV1 >=80% predicted.

Exposure assessment. Demographic, smoking, work and exposure information was abstracted from clinical records and a standardised exposure form. Exposure variables included indoor and outdoor environments; bleach/chlorine; pesticide or agricultural chemicals; other dust or chemicals; diesel or exhaust; paint; construction dust; organic solvents; use of personal protective equipment (PPE); and protective training. Codes 6 and 7 for occupations were combined as general worker. Because product, dose, frequency, ventilation, mixing practices and cumulative intensity were not consistently recorded, primary agent variables were binary. Post-exposure symptoms included cough, sputum, dyspnoea, wheeze, oral/nasal/throat burning, eye burning or watering, and chest tightness.

Propensity score analysis. Propensity scores for case status were estimated from age, gender, body mass index (BMI), three-level smoking status and previous respiratory disease. These variables were selected because they preceded the recorded spirometry and could confound comparisons of exposures, symptoms and lung function; exposure variables were not included because they were study variables of interest. One-to-one nearest-neighbour matching without replacement was used. Balance was assessed with standardised mean differences (SMDs), with absolute SMD <0.10 considered acceptable. Full model specification, common-support restrictions, caliper and matching diagnostics are provided in Supplementary File 1 [17–19]. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [20].

Statistical analysis. Continuous data are reported as median and inter-quartile range (IQR); categorical data as number and percentage. Analyses of the 172-person cohort were descriptive or sensitivity analyses, whereas matched-pair analyses were the primary confounder-balanced comparisons. Raw groups were compared with the Mann-Whitney U test and chi-square or Fisher exact test. In matched pairs, continuous variables were compared with the Wilcoxon signed-rank test and paired median differences were accompanied by 4,000-sample bootstrap 95% confidence intervals (CIs). Binary variables were compared with exact McNemar tests; matched odds ratios (ORs) and exact 95% CIs were derived from discordant pairs. Benjamini-Hochberg false-discovery-rate q values were calculated separately for exposure and symptom families. Spearman correlations used all available records.

A robust multivariable logistic regression was used as a sensitivity analysis in the full dataset and included age, gender, BMI, current and former smoking, previous respiratory disease, exposure duration, bleach/chlorine exposure and pesticide exposure. Robust HC3 standard errors, ORs and 95% CIs were reported. Variance-inflation factors were <=3.19, and quadratic-term checks did not suggest material non-linearity for age, BMI or exposure duration. Analyses used available data without imputation: PEFR was missing for one participant, MEF25-75 L/s for two and environment for one. A sensitivity calculation, rather than conventional post-hoc power, showed that 47 pairs

Table 1. Characteristics and covariate balance before and after propensity-score matching

Variable	Cases (n=100)	Controls (n=72)	SMD before	Matched cases (n=47)	Matched controls (n=47)	SMD after
Age, years	49.5 (37.5-61.2)	42.0 (32.8-47.0)	0.513	42.0 (30.5-49.5)	41.0 (32.5-47.0)	-0.095
BMI, kg/m2	27.2 (25.2-30.0)	28.5 (25.9-31.1)	-0.199	27.7 (25.8-30.2)	27.8 (25.9-29.9)	0.034
Exposure duration, years	14.0 (9.0-20.0)	15.0 (10.0-20.0)	0.005	10.0 (4.0-19.0)	15.0 (10.0-20.0)	-0.304
Female gender	48 (48.0)	29 (40.3)	0.156	23 (48.9)	22 (46.8)	0.043
Current smoker	32 (32.0)	21 (29.2)	0.061	15 (31.9)	15 (31.9)	0.000
Former smoker	20 (20.0)	2 (2.8)	0.542	2 (4.3)	2 (4.3)	0.000
Never smoker	48 (48.0)	49 (68.1)	-0.406	30 (63.8)	30 (63.8)	0.000
Previous respiratory disease	57 (57.0)	15 (20.8)	0.742	14 (29.8)	13 (27.7)	0.047
Indoor exposure	55 (55.0)	40 (56.3)	-0.027	27 (57.4)	27 (58.7)	-0.025
Outdoor exposure	52 (52.0)	31 (43.7)	0.167	23 (48.9)	19 (41.3)	0.153
Bleach/chlorine exposure	44 (44.0)	34 (47.2)	-0.065	19 (40.4)	24 (51.1)	-0.214
Pesticide/agricultural chemical exposure	43 (43.0)	24 (33.3)	0.199	17 (36.2)	17 (36.2)	0.000
Other dust/chemical exposure	13 (13.0)	10 (13.9)	-0.026	7 (14.9)	4 (8.5)	0.199
Diesel/exhaust exposure	8 (8.0)	3 (4.2)	0.160	6 (12.8)	1 (2.1)	0.405
Multiple particle/chemical exposures	8 (8.0)	3 (4.2)	0.160	2 (4.3)	2 (4.3)	0.000
No personal protective equipment use	92 (92.0)	66 (91.7)	0.012	41 (87.2)	43 (91.5)	-0.138
No protective training	98 (98.0)	67 (93.1)	0.239	45 (95.7)	45 (95.7)	0.000

Values are median (IQR) or n (%). SMD, standardised mean difference. The propensity-score variables specified for the revision analysis were age, sex, BMI, three-level smoking status and previous respiratory disease. Exposure variables are shown descriptively and were not matching covariates. Percentages use available non-missing denominators

provided 80% power at two-sided alpha=0.05 to detect an approximately 0.42-standard-deviation paired difference; the unmatched design could detect approximately 0.43. These values describe precision limits and are not evidence that null findings prove no association.

RESULTS

Participant flow. The final analytic population comprised 172 adults (100 cases and 72 controls), and propensity-score matching yielded 47 case-control pairs (94 participants) (Fig. 1). Before matching, cases were older than controls [49.5 (37.5–61.2) vs 42.0 (32.8–47.0) years; SMD=0.513], and former smoking and previous respiratory disease were substantially imbalanced (SMDs=0.542 and 0.742, respectively) (Tab. 1).

Propensity score balance. After matching, all pre-specified covariates achieved acceptable balance (absolute SMD <0.10) (Fig. 2 and Suppl. File 1). The matched sample was therefore used for the primary comparisons of exposures, symptoms and spirometric outcomes; estimates from the full cohort are presented for context and sensitivity assessment.

Inhalational exposures and symptoms. In the matched analysis, pesticide exposure was identical in both groups [17/47 (36.2%); matched OR 1.00, 95% CI 0.39–2.54], and no statistically significant differences were detected for indoor, outdoor, bleach/chlorine, other dust/chemical, multiple exposure, PPE non-use or lack of training (all q>=0.56) (Tab. 2). Diesel/exhaust exposure showed five discordant case-positive pairs and no control-positive discordant pair, but the exact result was imprecise (p=0.063; q=0.563). Full-cohort estimates are shown in Table 2 for context and were not the basis for confounder-balanced inference.

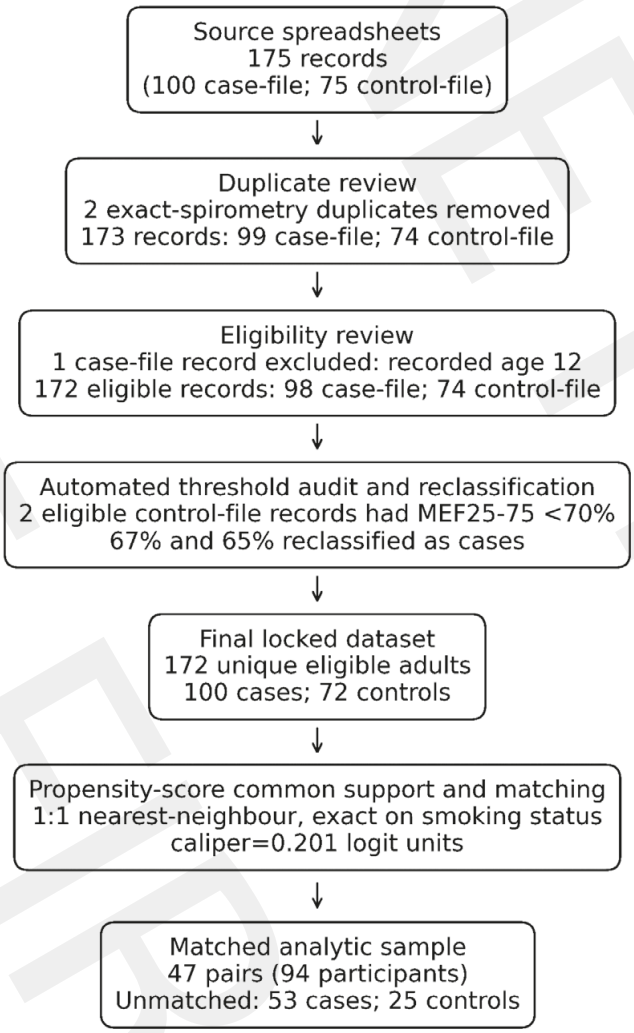


Figure 1. Participant flow, data cleaning, and propensity-score matching

Table 2. Inhalational exposure variables before and after matching

Variable	Raw cases	Raw controls	Raw OR (95% CI)	Raw p	Matched cases	Matched controls	Matched OR (95% CI)	Matched p	Matched q
Indoor exposure	55 (55.0)	40 (56.3)	0.95 (0.51–1.75)	0.862	27 (58.7)	27 (58.7)	1.00 (0.37–2.68)	1.000	1.000
Outdoor exposure	52 (52.0)	31 (43.7)	1.40 (0.76–2.58)	0.282	22 (47.8)	19 (41.3)	1.43 (0.49–4.42)	0.629	1.000
Bleach/chlorine exposure	44 (44.0)	34 (47.2)	0.88 (0.48–1.61)	0.675	19 (40.4)	24 (51.1)	0.62 (0.22–1.60)	0.383	1.000
Pesticide/agricultural chemical exposure	43 (43.0)	24 (33.3)	1.51 (0.80–2.83)	0.200	17 (36.2)	17 (36.2)	1.00 (0.39–2.54)	1.000	1.000
Other dust/chemical exposure	13 (13.0)	10 (13.9)	0.93 (0.38–2.25)	0.866	7 (14.9)	4 (8.5)	2.00 (0.43–12.36)	0.508	1.000
Diesel/exhaust exposure	8 (8.0)	3 (4.2)	2.00 (0.51–7.82)	0.363	6 (12.8)	1 (2.1)	infinite (0.92-infinite)	0.063	0.563
Multiple exposures (>=2 agents)	8 (8.0)	3 (4.2)	2.00 (0.51–7.82)	0.363	2 (4.3)	2 (4.3)	1.00 (0.01–78.50)	1.000	1.000
No PPE use	92 (92.0)	66 (91.7)	1.05 (0.35–3.16)	0.937	41 (87.2)	43 (91.5)	0.60 (0.09–3.08)	0.727	1.000
No protective training	98 (98.0)	67 (93.1)	3.66 (0.69–19.41)	0.131	45 (95.7)	45 (95.7)	1.00 (0.07–13.80)	1.000	1.000

ORs are unadjusted in the raw sample and discordant-pair ORs after matching. Exact p values are from McNemar tests. q values are Benjamini-Hochberg false-discovery-rate adjusted within the matched exposure family. Matched percentages and tests use pairwise-complete data; one matched control had a missing environment code, so indoor and outdoor comparisons used 46 complete pairs. An infinite estimate reflects zero discordant control-positive pairs; its confidence interval and exact p value convey the imprecision. PPE, personal protective equipment

Cough was more frequent in matched cases than controls [30/47 (63.8%) vs 16/47 (34.0%); matched OR 3.80, 95% CI 1.37–13.02; exact p=0.007; q=0.046] (Tab. 3). Sputum [34.0% vs 12.8%; OR 3.50, 95% CI 1.10–14.60; p=0.031] and chest tightness [23.4% vs 6.4%; OR 5.00, 95% CI 1.07–46.93; p=0.039] were nominally different, but neither retained statistical significance after false-discovery-rate adjustment (both q=0.090). Dyspnoea, wheeze and irritant symptoms were not statistically different after matching.

Spirometry and pattern distribution. In the matched analysis, cases had lower FEV1, FVC, analytic actual FEV1/FVC, PEFR and measured MEF25-75 L/s (Tab. 4). Median paired differences were -24.0 percentage points for FEV1 predicted (95% CI -30.0 to -18.0), -10.0 for FVC predicted (-19.0 to -3.0), -12.7 for actual FEV1/FVC (-14.8 to -10.1), -78.2 for PEFR (-159.7 to -54.0), and -1.9 L/s for measured MEF25-75 (-2.3 to -1.5); all paired p values were <=0.001. Conventional impairment was present in 37/47 (78.7%) matched cases and 6/47 (12.8%) matched controls. Isolated reduced mid-expiratory flow occurred in 10/47 (21.3%) matched cases (Fig. 3). Because MEF25-75 percent predicted defined group membership, its between-group contrast and the isolated-flow pattern were reported descriptively without hypothesis tests.

Correlations and sensitivity analysis. MEF25-75 percent predicted correlated with FEV1 predicted (rho=0.862, 95% CI 0.818–0.896), analytic actual FEV1/FVC (rho=0.820, 95% CI 0.764–0.863), PEFR (rho=0.664, 95% CI 0.571–0.741) and FVC predicted (rho=0.538, 95% CI 0.423–0.637); all p<0.001 (Tab. 5). In the robust full-sample sensitivity model, pesticide exposure was not associated with case status (OR 1.26, 95% CI 0.46–3.48; p=0.650). Bleach/chlorine exposure had an inverse estimate (OR 0.27, 95% CI 0.07–0.95; p=0.042), but this isolated estimate was not considered causal because

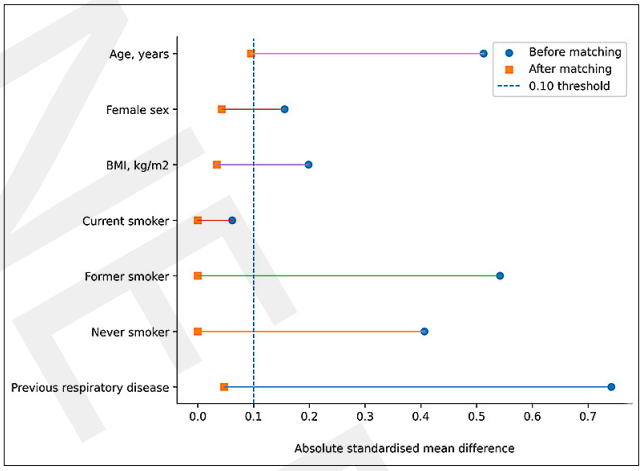


Figure 2. Covariate balance before and after matching

Table 3. Post-exposure respiratory symptoms before and after matching

Variable	Raw cases	Raw controls	Raw OR (95% CI)	Raw p	Matched cases	Matched controls	Matched OR (95% CI)	Matched p	Matched q
Cough	68 (68.0)	28 (38.9)	3.34 (1.77–6.29)	<0.001	30 (63.8)	16 (34.0)	3.80 (1.37–13.02)	0.007	0.046
Sputum	42 (42.0)	8 (11.1)	5.79 (2.51–13.36)	<0.001	16 (34.0)	6 (12.8)	3.50 (1.10–14.60)	0.031	0.090
Dyspnea	73 (73.0)	42 (58.3)	1.93 (1.01–3.68)	0.044	35 (74.5)	25 (53.2)	2.43 (0.96–6.93)	0.064	0.112
Wheeze	21 (21.0)	10 (13.9)	1.65 (0.72–3.75)	0.231	8 (17.0)	8 (17.0)	1.00 (0.30–3.34)	1.000	1.000
Oral/nasal/throat burning	49 (49.0)	36 (50.0)	0.96 (0.52–1.76)	0.897	23 (48.9)	26 (55.3)	0.77 (0.30–1.90)	0.678	0.791
Eye burning/watering	60 (60.0)	36 (50.0)	1.50 (0.81–2.76)	0.193	30 (63.8)	27 (57.4)	1.30 (0.53–3.31)	0.678	0.791
Chest tightness	23 (23.0)	4 (5.6)	5.08 (1.67–15.42)	0.002	11 (23.4)	3 (6.4)	5.00 (1.07–46.93)	0.039	0.090

Matched p values are exact McNemar tests. q values are Benjamini-Hochberg adjusted within the matched symptom family. Nominal p<0.05 with q>=0.05 is described as a nominal signal rather than a multiplicity-adjusted finding

Table 4. Spirometric variables and impairment patterns before and after matching

Parameter/pattern	Raw cases	Raw controls	Raw p	Matched cases	Matched controls	Paired median difference (95% bootstrap CI)	Matched p
FEV1, % predicted	68.0 (54.0–79.2)	93.0 (86.0–101.5)	<0.001	68.0 (62.5–80.0)	93.0 (86.0–103.0)	-24.0 (-30.0 to -18.0)	<0.001
FVC, % predicted	80.5 (68.8–92.0)	91.0 (82.8–106.0)	<0.001	82.0 (73.0–92.5)	91.0 (85.0–105.5)	-10.0 (-19.0 to -3.0)	0.001
Analytic actual FEV1/FVC, %	69.6 (62.9–75.4)	83.9 (81.3–86.9)	<0.001	71.3 (66.9–77.9)	84.2 (81.2–86.4)	-12.7 (-14.8 to -10.1)	<0.001
PEFR	236.0 (182.7–341.5)	381.9 (293.5–490.1)	<0.001	291.0 (204.2–365.0)	395.8 (289.9–505.8)	-78.2 (-159.7 to -54.0)	<0.001
FEF25–75, % predicted	39.0 (24.0–52.0)	84.0 (78.0–101.0)	Not tested (group-defining)	44.0 (36.5–56.5)	84.0 (79.0–96.5)	-47.0 (-53.0 to -33.0)	Not tested (group-defining)
FEF25–75, L/s	1.4 (0.8–2.0)	3.5 (3.0–4.3)	<0.001	1.8 (1.3–2.2)	3.5 (3.2–4.1)	-1.9 (-2.3 to -1.5)	<0.001
Large-airway obstruction (FEV1/FVC <70%)	51 (51.0)	0 (0.0)	<0.001	19 (40.4)	0 (0.0)	infinite (4.67-infinite)	<0.001
FEV1 <80% predicted	75 (75.0)	8 (11.1)	<0.001	34 (72.3)	6 (12.8)	29.00 (4.81–1184.44)	<0.001
FVC <80% predicted	48 (48.0)	10 (13.9)	<0.001	19 (40.4)	8 (17.0)	2.83 (1.07–8.78)	0.035
Conventional impairment	81 (81.0)	8 (11.1)	<0.001	37 (78.7)	6 (12.8)	32.00 (5.35–1302.93)	<0.001
Isolated reduced mid-expiratory flow	19 (19.0)	0 (0.0)	Not tested (structurally linked)	10 (21.3)	0 (0.0)	Matched OR not estimable/ structurally defined	Not tested (structurally linked)

Continuous values are median (IQR); paired differences are case minus control with bootstrap 95% CIs. Binary matched estimates are discordant-pair ORs. MEF25–75 percent predicted defined group status, so its between-group contrast and the isolated-flow pattern are structurally linked to the study classification; hypothesis tests were therefore not performed for those two rows.

Table 5. Correlations and robust multivariable sensitivity model

Panel A variable	n	Spearman rho (95% CI)	p
FEV1, % predicted	172	0.862 (0.818-0.896)	<0.001
FVC, % predicted	172	0.538 (0.423-0.637)	<0.001
Analytic actual FEV1/FVC	172	0.820 (0.764-0.863)	<0.001
PEFR	171	0.664 (0.571-0.741)	<0.001
Panel B. Robust multivariable logistic regression for case status			
Variable		OR (95% CI)	p
Age, per year		1.04 (1.01-1.07)	0.011
Female gender		5.72 (1.77-18.48)	0.004
BMI, per kg/m^2		0.95 (0.88-1.02)	0.129
Current smoking vs never		1.69 (0.73-3.90)	0.218
Former smoking vs never		15.94 (2.44-104.18)	0.004
Previous respiratory disease		4.66 (2.08-10.43)	<0.001
Exposure duration, per year		0.94 (0.90-0.99)	0.013
Bleach/chlorine exposure		0.27 (0.07-0.95)	0.042
Pesticide exposure		1.26 (0.46-3.48)	0.650

Panel B used a full-sample binomial model with HC3 robust standard errors. The model was a sensitivity analysis; individual estimates were not treated as causal and were not multiplicity-adjusted.

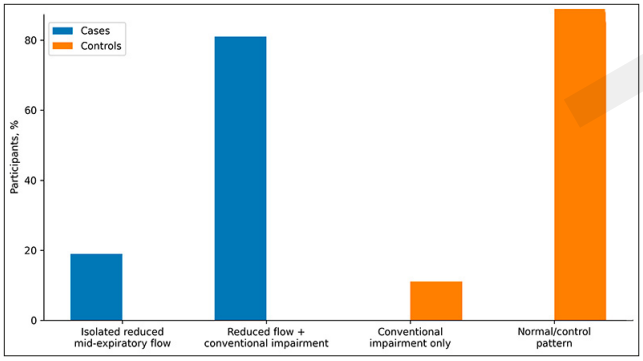


Figure 3. Distribution of mutually exclusive spirometric patterns (100 cases and 72 controls)

exposure was binary, residual confounding was plausible and multiple model terms were examined. Older age, female gender, former smoking and previous respiratory disease were associated with case status; the former-smoking CI was wide, indicating sparse-data imprecision.

DISCUSSION

Propensity-score matching was necessary because the initial groups differed substantially in age, smoking history and previous respiratory disease, each of which can influence respiratory symptoms and spirometric performance. The 47 matched pairs represented participants with

overlapping measured baseline profiles. Accordingly, the matched analyses were treated as the primary comparisons, while full-cohort estimates were used for description and sensitivity assessment. After matching, none of the broad binary inhalational exposure variables clearly distinguished reduced-MEF25-75 cases from controls. This finding applies to the matched overlap population and does not eliminate residual confounding or support a causal interpretation.

Airway obstruction is physiologically heterogeneous and may involve both central and peripheral airways. Narrowing or loss of small conducting airways, airway-wall remodelling, luminal secretions and premature airway closure can reduce flow during the middle portion of forced expiration and, as the disease becomes more extensive, lower FEV1 and FEV1/FVC. Pathological and micro-computed-tomography studies have documented small-airway narrowing and loss in chronic obstructive pulmonary disease, including mild-to-moderate disease [8,9]. This provides a plausible explanation for the matched finding that reduced MEF25-75 commonly coexisted with lower conventional indices, and that 37/47 matched cases met the study definition of conventional impairment. Nevertheless, 10/47 matched cases had preserved FEV1 and FEV1/FVC.

Population studies have associated small-airway indices with smoking [7] and occupational exposure categories [2], and longitudinal data suggest that isolated small-airway obstruction can precede later chronic airflow obstruction [10]. These studies support possible early peripheral-airway involvement in some individuals, but they do not make MEF25-75 a stand-alone diagnostic test. MEF25-75 depends on FVC and the forced-expiratory manoeuvre and shows substantial biological and technical variability [3–6]. The 70% predicted boundary was therefore retained only as the historical study classification; values close to it require cautious interpretation.

In the current study, lack of statistically significant matched differences for pesticides, bleach/chlorine or indoor exposure differs from reports linking occupational or environmental exposures with respiratory symptoms, small-airway obstruction or chronic obstructive pulmonary disease [2,11–16]. Several features may explain this difference: the present cohort was clinically selected; exposures were generally recorded as binary variables; intensity, frequency, chemical class, application method, product mixing and ventilation were unavailable; and exposure prevalence was high in both groups. In addition, matching intentionally balanced smoking and previous respiratory disease, reducing confounding but also restricting inference to 94 participants with comparable measured profiles. The confidence intervals remain compatible with clinically relevant effects, particularly for uncommon exposures.

Cough remained more frequent in matched cases after false-discovery-rate adjustment, whereas sputum and chest tightness were nominal signals with wide confidence intervals and dyspnoea, wheeze and irritant symptoms were not statistically distinguishable. Cough may accompany airway irritation, mucus hypersecretion or underlying obstructive disease, but the retrospective records do not establish which mechanism predominated. These findings support symptom-aware interpretation and further evaluation of the complete flow-volume curve, and should not be used to infer that reduced MEF25-75 caused the symptoms.

Strengths and limitations of the study. Strengths include consistent application of the grouping rule before analysis, transparent separation of the 172-person full cohort from the 94-person matched sample, matching on major measured confounders, post-matching balance assessment, paired effect estimates with confidence intervals, false-discovery-rate adjustment and a full-cohort sensitivity model. Detailed data-verification and matching procedures are supplied in Supplementary File 1.

Limitations include the single-centre retrospective design, clinically selected population, pre-bronchodilator spirometry, fixed percent-predicted thresholds, unavailable LLN/z scores and incomplete device/reference-equation metadata. The case definition makes the MEF25-75 contrast structural, and historical source fields could not be externally verified in every record. Exposures and symptoms were record-derived; dose, timing and product-specific information were unavailable. Former smoking was sparse among controls, matching reduced the analysis to 47 pairs, and residual confounding remains possible. Null results indicate that no statistically significant association was detected, not that an association is absent.

CONCLUSIONS

In adults undergoing spirometry, broad binary inhalational exposure variables did not differ significantly between confounder-balanced reduced-MEF25-75 cases and controls. Cough remained more frequent, and reduced MEF25-75 commonly coexisted with poorer conventional spirometric indices, although approximately one-fifth of cases had preserved FEV1 and FEV1/FVC. MEF25-75 <70% predicted should be understood as an operational research classification and possible marker of small-airway impairment, not a stand-alone diagnosis. Prospective studies using LLN/z scores, post-bronchodilator testing and quantitative exposure assessment are needed.

Declarations

Ethics statement. The study was approved by the Harran University Clinical Research Ethics Committee on 30 June 2025 (session 12; decision HRÜ/25.12.43).

Informed consent statement. The study used anonymised retrospective records. Individual informed consent was waived or not required under the approved file-review protocol.

Data availability. The de-identified analytic dataset and reproducible code may be shared with the journal for peer review and, subject to institutional and ethics approval, made available by the corresponding author on reasonable request.

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Conflict of interest. The authors declare no conflict of interest.

Author contributions. Both authors contributed to study conception, data interpretation, critical revision and final approval.

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