A survey about knowledge of exhaled nitric oxide use among Southern Italian pulmonologists and trainees

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To the Editor,

Asthma is a chronic respiratory condition characterized by airway inflammation, bronchoconstriction, and excessive mucus production, leading to recurrent episodes of breathlessness, coughing, and wheezing (1). It affects millions of people worldwide and can significantly impact the quality of life of affected individuals (1). Early and accurate diagnosis, as well as effective management, are crucial in controlling asthma and reducing its long-term effects on patients (1). In recent years, exhaled nitric oxide (FeNO) has emerged as a valuable biomarker in the diagnosis and management of asthma (2). FeNO is a gaseous biomarker that can be measured in the breath. It reflects the activity of the enzyme nitric oxide synthase (NOS) in the airways. Elevated FeNO levels indicate ongoing airway inflammation, particularly in the presence of eosinophils (2).

FeNO levels can be measured using non-invasive, simple, and quick techniques, such as a handheld portable device. The test involves asking the patient to exhale into a mouthpiece, and the FeNO level is measured in parts per billion (ppb) (2). Exhaled FeNO has proven to be a valuable tool in the diagnosis and management of asthma (3). Its non-invasive nature and ability to provide real-time information on airway inflammation make it a promising biomarker. While it is not a standalone diagnostic test, FeNO complements other clinical assessments and helps healthcare providers make informed decisions regarding asthma treatment (3). This testing method is routinely used in respiratory care centers for diagnosing and monitoring

asthmatic patients. As research continues, further insights into the role of FeNO in asthma management will likely contribute to improved patient outcomes and better control of this chronic respiratory condition.

Thus, the purpose of this survey was to assess the knowledge of FeNO testing among our medical trainees and respiratory specialists, within several departments in southern Italy.

Based on a previous study of Ceci Bonello et al (4), the survey consisted of a total of 19 questions with double option (true or false) (see Table 1). It covered various aspects related to FeNO, including general information about FeNO, factors that can influence FeNO levels, and respiratory pathologies which could impact FeNO levels. An official Italian translation from the English version was used for the current investigation. Additionally, demographic data and details regarding the duration of working in the respiratory department were included for specialists and regarding their year of attendance for trainees.

In total, 51 pulmonologists and 43 trainees participated to the survey. All contributors were working in several respiratory department units of southern Italy (Bari, Foggia, Napoli, Catanzaro and Catania). Specialists in respiratory medicine were categorized based on their duration of work in the department, with a cutoff set at <5 years (n. 21 out of 51) and ≥5 years (n. 30 out of 51), whereas trainees were divided into their years of attendance in the postgraduate school of respiratory medicine (in detail: n.11 were attending the first year, n. 14 the second year, n. 10 the third year and n. 7 the fourth year). This division aimed to assess any statistical significance in the knowledge of FeNO

Table 1. The proposed survey with 19 items and their correct answers (translated from the Italian version).

No.	Question	Answer
1	Nitric oxide is generated within the lungs.	True
2	Prior to commencing asthma treatment, FeNO testing is necessary.	False
3	Utilizing FeNO is highly recommended for monitoring airway inflammation in patients with eosinophilic asthma.	True
4	FeNO testing is employed for asthma cases that are non-eosinophilic in nature.	False
5	FeNO testing is utilized to evaluate the potential response to anti-inflammatory agents, particularly inhaled corticosteroids.	True
6	A negative test result rules out an asthma diagnosis.	False
7	A FeNO level greater than 40 ppb in adults indicates a positive test outcome.	True
8	FeNO level below 25 ppb suggests a lower likelihood of eosinophilic inflammation and corticosteroid responsiveness.	True
9	A significantly elevated FeNO level (>50 ppb) can aid in identifying poor adherence in asthma patients with apparently "controlled" asthma.	True
10	Low FeNO levels are commonly observed in males and individuals of tall stature.	False
11	Diets high in nitrates may lead to increased FeNO levels.	True
12	Patients with active rhinovirus infection may exhibit reduced FeNO levels.	False
13	FeNO levels may be lower in patients recently treated with inhaled or oral corticosteroids.	True
14	Cystic fibrosis is associated with decreased FeNO levels.	True
15	Smoking impacts FeNO levels.	True
16	Pulmonary hypertension is linked to elevated FeNO levels.	False
17	Atopic non-eosinophilic bronchitis is characterized by high FeNO levels.	False
18	High FeNO levels are observed during COPD exacerbations.	True
19	FeNO testing can be employed in post-COVID follow-up.	False

testing between specialists and trainees and among the aforementioned subgroups.

To ensure anonymity, the questionnaire was kept anonymous, and participants were instructed to place their completed questionnaires in a closed box. The investigator was present during the questionnaire completion to prevent participants from searching for correct answers. After completing the questionnaire, participants were provided with an information booklet about FeNO, containing answers to all the questions. The collected results were successively compiled and analyzed. All participants signed an informed consent to participate.

Data analysis was performed by SPSS version 16.0. Continuous variables were expressed as mean±standard deviation, or median (interquartile range) for non-parametrical variables. Whereas categorical variables were expressed as frequency and percentage. The comparison of test scores among groups was assessed by Mann-Whitney U test. For all cases, a $p<0.05$ was considered as significant.

A total number of 94 surveys were collected (51 specialists, 43 trainees). Participant demographics and test scores are shown in Table 2. There were differences among the groups in terms of age (45.2±16.7 for specialists vs 28.5±9.3 for trainees, $p<0.01$) and gender (percentage of females 44% for specialists vs 65% for trainees, $p<0.05$). The median score was 14 for both pulmonologists and trainees (IQ 25-75: 13-16 and 12-15, respectively, p=ns). When exploring single questions, significant differences between the two groups were found in 4 out of 19 items (number 2, 15, 16 and 17; $p<0.05$ for all). No significant differences in terms of age of experience (<5 years/>5 years) were detected in the group of specialists. Among trainees, those attending the first year had lower scores compared to the

Table 2. Participant demographics and test scores for pulmonologists and trainees.

Parameter	Pulmonologists	Trainees	p
Number	51	43	/
Mean Age (yrs±SD)	45.2±16.7	28.5±9.3	<0.01
Females (%)	44	65	<0.05
Median score	14 (13-16)	14 (2-15)	ns
Item 1 (% correct)	92.7	92.3	ns
Item 2 (% correct)	56.1	69.2	<0.05
Item 3 (% correct)	92.6	92.3	ns
Item 4 (% correct)	68.3	76.9	ns
Item 5 (% correct)	95.1	84.6	ns
Item 6 (% correct)	92.7	100.0	ns
Item 7 (% correct)	92.6	92.3	ns
Item 8 (% correct)	78.1	84.6	ns
Item 9 (% correct)	90.2	84.6	ns
Item 10 (% correct)	80.4	76.9	ns
Item 11 (% correct)	53.7	53.8	ns
Item 12 (% correct)	53.6	47.1	ns
Item 13 (% correct)	95.1	92.3	ns
Item 14 (% correct)	58.5	46.1	ns
Item 15 (% correct)	60.9	46.2	<0.05
Item 16 (% correct)	70.7	53.8	<0.05
Item 17 (% correct)	73.1	53.9	<0.05
Item 18 (% correct)	60.9	69.2	ns
Item 19 (% correct)	60.9	61.5	ns

second, third and fourth year (p=0.05, 0.01 and 0.05, respectively).

The results of our study showed an adequate knowledge about the use of FeNO concerning the diagnosis and management of asthma among specialist and trainees of respiratory medicine in southern Italy. As expected, first year trainees had overall less knowledge regarding FeNO.

The current findings extend and are coherent to those previously collected by Maltese pulmonologists (4), both indicating sufficient knowledge of FeNO among specialists and trainees.

When examining single questions of the survey, participants displayed a good understanding of the use of FeNO measurement for treatment response assessment and monitoring, as well as they generally demonstrated correct responses regarding correct cut-off values.

FeNO levels can be influenced by various external factors and other respiratory conditions, as mentioned in BTS guidelines (5). For example, smoking can reduce FeNO levels, although it remains higher in smokers with asthma compared to non-asthmatic smokers (6). Surprisingly, nearly 50% of participants were not aware of this important issue.

Our study has two important limitations, firstly the small sample size, although five large university hospitals of Southern Italy were involved. Recently, Italy had experienced issues related to the lack of pulmonology wards or beds, especially during peak periods such as flu seasons or when dealing with respiratory outbreaks. These shortages can be attributed to various factors, including a higher demand for healthcare services than the available capacity, financial constraints, and infrastructure limitations. Furthermore, the distribution of healthcare resources may not always align with the demand in specific regions or areas. There can be disparities between northern and southern areas, with more specialized medical facilities concentrated in northern cities, leading to challenges in accessing pulmonology care in certain regions. Further studies should also extend the above observation to other respiratory centers throughout the Italian territory.

Secondly, despite previously used (4), the survey was not validated. Undoubtedly, the absence of a validated questionnaire highlights the necessity for future larger research endeavors to prioritize the validation of these important tools to ensure the reliability and credibility of results.

In conclusion, this survey aimed to assess the knowledge and interpretation of FeNO among respiratory care-oriented professionals, with the intention of contributing to continuous medical education and postgraduate learning. The results indicate that pulmonologists and trainees of respiratory diseases in southern Italian departments generally possess. However, there is room for improvement in understanding the application and interpretation of FeNO in relation to other respiratory conditions and comorbidities. Conducting further audits, studies, and educational meetings among the departments is recommended to enhance clinical expertise and optimize patient management.

Conflicts of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Ethic Committee: Due to the nature of the study, there was no need to require a formal approval by the ethics committee.

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