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Editorial

Estimating Prevalence of Chronic Obstructive Pulmonary Disease: From Questionnaires to Spirometry

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality all over the world and is the commonest disease causally linked with cigarette smoking. It has a long and silent phase of few or no symptoms and then, in a large proportion of population, progresses at varying rates causing increasing dyspnoea, limitation of activities and major disability eventually rendering the patients, respiratory cripples. The major pathology of COPD resides in the small airways, a bronchiolitis characterised by inflammation of the lining mucosa with luminal secretions and remodelling along with parenchymal destruction leading to a loss of support to the smaller airways. This latter process is called "emphysema". The respiratory bronchioles are the first site to be affected.[1] These pathological changes are usually quite advanced before causing airflow limitation and hyperinflation, and resultant symptoms of dyspnoea and disability. There is also, in addition, an associated large airway involvement with hypertrophy of the mucous glands and hyperplasia of goblet cells leading to symptoms of cough and mucous hypersecretion, an entity clinically described as "chronic bronchitis".

The present treatment for COPD is largely unsatisfactory. Apart from quitting smoking and oxygen therapy in terminal stages, other treatments are only symptomatic and supportive and do not alter the natural history of COPD. Clearly, the burden of the disease on the individual, family, society and the state is tremendous. It is a tragic irony that the disease is largely preventable, a fact that is a prominent part of the current definitions.[2,3]

Unlike other leading causes of disability and mortality, the projections for COPD for the next few decades are ominous. Already among the leading causes of morbidity worldwide, COPD is slated to become the third leading cause of death by the year 2020, moving up from the current 5th rank.[4,5] Thus, being a major public health issue, an epidemiological assessment of its magnitude and causative factors has become a thrust area of research in COPD. While newer concepts take root in our understanding of pathogenesis, heterogeneity and therapeutics of COPD, the epidemiological approach to the study of the disease in populations has also evolved rapidly.

Several guidelines on management of COPD are there, but the GOLD guidelines are the most cited and followed.[2] According to these, a clinical diagnosis of COPD should be considered in a patient above 40 years of age presenting with symptoms of chronic and progressive cough, breathlessness and/or a history of exposure to risk factors for the disease. On spirometry, a post-bronchodilator ratio of forced expiratory volume in one second to forced vital capacity (FEV_1/FVC) less than 0.70 confirms airflow limitation that is not fully reversible.[2] Due to sheer numbers, majority of the patients receive treatment at primary and secondary levels of healthcare all over the world. Lack of awareness, incorrect diagnostic practices, and lack of training and facilities for spirometry are some of the reasons why the management of COPD at these levels of healthcare is below the standards envisaged by the current guidelines. The patients often under-perceive the degree of the altered pathophysiology or adapt to functional loss by reducing activities of daily living to avoid symptoms or ignore these as part of an aging process. Thus, it remains grossly under-diagnosed in the community.[6,7] It can hardly be disputed that the identified cases of COPD in India represent only the tip of the iceberg formed by the undiagnosed cases.

An accurate assessment of the magnitude of the problem and the burden due to it requires reliable estimates of prevalence. This input is also vital for policy decisions, resource allocation and prioritisation, and for the development of control programmes. The starting point for determination of prevalence of a disease is the definition. Whereas a clinical diagnosis of COPD is fairly straightforward in a symptomatic patient, identification of the disease in epidemiological studies has been a complex and debatable issue. Definitions of COPD used in population studies have been so widely different and changing from time to time that it is very difficult to quantify prevalence, to evaluate its change over time, and to compare different regions within the same country as well as different countries. Surprisingly, while most pulmonary clinicians will diagnose a patient with a nearly similar approach, agreement eludes the epidemiologists. In the absence of a consensus on how to measure the prevalence, any comparisons between studies lose their meaning. In studies over the last few decades from several countries including India,[8-10] estimates of self-reported or physician-diagnosed disease, and estimates obtained from standardised and validated respiratory symptoms questionnaires, with or without some measure of lung function (peak flow rate or spirometry), have been used to determine the prevalence of COPD. More recently, the physiological definitions using spirometry to document airways obstruction have become the standard worldwide.[11-13] The result of differing definitions is a very wide variation in the reported prevalence, from less than 1% to as high as 15% or more. Methodological

differences contribute as much or perhaps even more to these differences than those due to population and risk factors.

A long asymptomatic phase, and the well known fact of underdiagnosis of COPD by physicians means that its prevalence in the community will be underestimated if physician-diagnosed or self-reported disease is measured.[14] Historically, respiratory symptom questionnaires have been popular and used extensively. These respiratory questionnaires have relied largely on the response to the question on the occurrence of chronic cough with phlegm, for three months in a year for two years – a positive response identifying chronic bronchitis. Although the terms chronic bronchitis and emphysema are no longer used to define COPD, the concept that COPD represents a variable mix of the two elements has been firmly entrenched in the minds of clinicians for decades. Emphysema and airways obstruction do not lend themselves to detection by questionnaires. Therefore, patients responding positively to the question for chronic bronchitis are usually labelled as having COPD in these studies.[8-10] Yet, chronic bronchitis only signifies chronic mucous hypersecretion, a large airways phenomenon. As we understand COPD today, it is debatable whether a simple chronic bronchitis qualifies to be a part of the COPD spectrum unless airways obstruction is also present. The concept that smoking caused chronic mucous hypersecretion and that later led to airways obstruction following recurrent infections was called the "British hypothesis" but was discarded following the demonstration by Fletcher and Thinker[15] that only a proportion of smokers developed COPD and that was independent of the presence of chronic bronchitis. In a landmark paper, Fletcher and Peto[16] later followed up 1136 patients for eight years with regular spirometry to study the natural history of chronic airflow limitation and concluded that chronic hypersecretion (i.e., chronic bronchitis) and chronic airflow limitation (i.e., COPD) are largely independent phenomena, though both causally linked to smoking. The distinction between chronic bronchitis and COPD was further clarified by Hogg *et al*[17] who provided pathological evidence that cough and sputum production that defines chronic bronchitis is independent of the disease process in the small airways that is responsible for airways obstruction in patients with COPD. Using the data of the three surveys in the Copenhagen City Heart study, Vestbro and Lange have shown that subjects in GOLD stage 0 with symptoms of chronic bronchitis did not have a greater risk of developing COPD as compared to a smoking cohort without symptoms after 15 years observation.[18] Due to lack of evidence that chronic bronchitis progressed to COPD, the "at risk" stage 0 that corresponded to chronic mucous hypersecretion was removed from the original GOLD classification when it was updated.[19] While simple chronic bronchitis continues to be recognised as an important smoking-related disease, it is a distinct entity, separate from COPD. The current opinion was recently summarised in a review.[20] Therefore, there is little justification to continue the use the prevalence of chronic bronchitis as a surrogate for the prevalence of COPD. By quantifying chronic bronchitis, we may be only estimating the prevalence of another smoking-related disease that is pathologically and physiologically a different disease from COPD.

Besides the conceptual differences between chronic bronchitis and COPD, there are other risks of errors. As a substantial proportion of patients with chronic bronchitis do not have airflow limitation, using the chronic bronchitis criteria to define COPD will overestimate the latter. On the other hand, prevalence of chronic bronchitis is even more likely to underestimate the true prevalence of COPD because a large proportion of patients have few symptoms or are virtually asymptomatic even in the presence of airflow limitation.[7,11-13] The discordance between symptoms, physician diagnosis and spirometry was found to be glaring in the National Health and Nutrition Examination Survey III (NHANES III).[21] Respiratory symptoms did not correlate with the presence or degree of airways obstruction. Thus, prevalence estimates using the questionnaires carry a risk of both overestimation and underestimation and do not reflect prevalence of true COPD defined physiologically. Almost all the studies carried out in India, including a recent multicentric study, have relied on questionnaires and have reported prevalence as defined by the chronic bronchitis criteria.[10,22]

The defining characteristic of COPD is airflow limitation, and therefore, physiological diagnosis has become the standard to define COPD in epidemiological studies.[11-13] Irrespective of the presence of symptoms, a post-bronchodilator FEV_1/FVC ratio of less than 0.7 as recommended by GOLD is the most often used criteria to define COPD. The continued debate over the correctness of a fixed cut-off notwithstanding, this is the commonest definition used in epidemiological studies now. The PLATINO study[11] has described the epidemiology of COPD in Latin American countries. The BOLD study[12] has spread out to several countries across continents making country-to-country comparisons possible. The estimates using spirometric criteria are typically higher than those reported in questionnaire-based studies as asymptomatic patients are also detected. The 12-site results reported in 2007 in the BOLD study gave a prevalence of 10.1% with a wide variation (SE 4.8%). In a separate study in China,[13] in a sample of 20,000 plus, the prevalence was found to be 8.2% (males 12.4%, females 5.1%). Have we reached a perfect definition and criteria for COPD?

The use of spirometry and the wide application of the GOLD criteria is not without controversies and debate. Spirometry requires careful selection and maintenance of equipment, trained personnel and a very stringent quality control. Administration of a bronchodilator adds to the problems in a field study. These pose practical difficulties in resource-poor countries. Use of spirometry also assumes that other causes of airflow limitation are few and will not significantly affect the prevalence of COPD, an assumption that may not hold true in low and moderate income countries such as India with a high burden of post-tubercular sequaelae. The other major issue in the use of spirometry is the criteria itself. Numerous studies have shown that the fixed, GOLD-defined ratio of FEV_1/FVC overestimates airflow limitation in the older subjects compared to use of the criteria of lower limits of normal (LLN) below the 5th percentile values.[8,9] In a study from New Zealand,[23] the prevalence based on LLN criteria was 9.0% while it was 14.2% by the GOLD criteria in the 40 years+ population, an increase of 50% with the latter. The BOLD study[12] has caused further confusion by presenting data of GOLD stage II or higher. This can itself have a major influence on results. Finally, use of post-bronchodilator values results in substantially lower estimates of prevalence.[24]

One can expect that all future studies on epidemiology of COPD in resource-rich countries will use quality-assured spirometry as the diagnostic tool. However, countries with limited resources, including India, will continue to use a questionnaire based approach for COPD, except for local or regional small-scale studies. A way out is to attempt to improve the predictive ability of questionnaires for airways obstruction by additional questions. This remains a daunting task. True differences in prevalence will thus be overshadowed by methodological differences unless a consensus on what defines COPD for epidemiological purposes emerges.

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