Exhaled Breath Analysis in Tuberculosis Case Detection: The New Horizon

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Editorial

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Sixty years ago, Nobel Prize winner Linus Pauling proposed the concept that human breath is a complex and dynamic gaseous mixture of more than 200 different endogenous volatile organic compounds (VOCs) that are continually being released in different quantities within the internal environment during health and disease. The researchers estimate that more than a thousand chemicals produced in different organ-systems as metabolic end products come out every minute through the respiratory tract. Volatile organic compounds and other products of oxidative stress are a big chunk among these exhaled breath elements[1].
Scientists are on the lookout for cost-effective, non-invasive diagnostic tests using exhaled breath to provide critical information in real time, which may have various advantages over fluid and image-based testing. The author himself is working in a team of researchers in India to find out potential usefulness of exhaled breath analysis by porphyrin based sensor array with the highly sensitive and specific and good positive and negative predictive values as well as simple, rapid, inexpensive and non-invasive viable method of diagnosis.
Researchers have used various methods like Isotopic ratio mass spectrometer, Ultraviolet absorbance spectrometer, Gas chromatography/Mass spectroscopy, Polymerase Chain Reaction (PCR) amplification, Immunosensor, Bio-optical technology, Colorimetric sensor array etc. to detect volatile organic compounds in different communicable and non-communicable diseases. Breath tests that assay products of mycobacterial metabolism (exhaled antigen 85, mycobacterial urease activity, and detection by trained rats of disease-specific odor in sputum) have promise as early biomarkers to assess the efficacy of treatment when the breath tests results rapidly became negative. Exhaled nitric oxide (eNO) levels were analyzed by validated handheld analyser on culture-confirmed TB cases. To date, eNO measurement has had limited evidence in direct diagnosis, but it still has potential for further development and evaluation as a cost-effective replacement of chest roentgenogram in screening algorithms of active pulmonary TB. Investigators at United States analyzed breath volatile organic compounds in high-risk patients of active pulmonary TB using gas chromatography/mass spectroscopy and were able to identify biomarkers with a Monte Carlo analysis of time-slice alveolar gradients. Breath biomarkers were also identified for active pulmonary tuberculosis, comprising

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oxidative stress products and volatile metabolites, when sputum culture, microscopy, and chest radiography were either all positive or all negative with greater accuracy in symptomatic high-risk subjects[2-5].

A biotechnology company in Fort Lee, New Jersey, is testing a point-of-care breath test for rapid identification of biomarkers of active pulmonary TB cases in developing countries that will probably be able to detect compounds in the breath in concentrations of parts per trillion. Although the viability of breath analysis to detect TB was established, current practice includes the use of GC/MS gas chromatography/mass spectrometry for diagnostic purposes which is quite expensive and has slow turnaround times[6].Workers in this field also have also been able to identify other compounds in the exhaled breath of patients suffering from pulmonary TB, namely Monomethylated alkanes, like dimethylcyclohexane, methylheptane, methylcyclododecane, and tetramethylbenzene[7-9].

From the standpoint of clinical epidemiology, we have to assess the potential usefulness of exhaled breath analysis in early diagnosis, prompt treatment and prognosis of active pulmonary TB cases. Furthermore, there is a need of standardization of investigations with similar patho-physiological conditions to reach our goal of a futuristic model of non-invasive diagnostic procedure by fixing the VOCs of pulmonary TB with pattern recognition to help reach a new screening algorithm. Further studies have to be undertaken to determine the diagnostic sensitivity, specificity and predictive value to obviate the potential bias in multicenter trials when compared to standardized microbiological and clinical indicators of disease which could even extend to comparison with the 'gold standard' of sputum culture.

Numerous confounding factors hinder the progress in exhaled breath research to formulate any standardized procedure. They range from how the breath is collected to the complicated factors of gaseous exchange in the respiratory tract with the products coming out from the gastrointestinal system. It has also been noted that the physiological parameters of cardiovascular, pulmonary or other organ-systems are intimately influenced by the physico-chemical properties of the exhaled breath analytes[1].

To be of use at the primary health care levels, we have to improve the portability, simplicity of use and speed of the test device as a tool to aid early identification of infectious cases. We would also need to standardize the protocols to demarcate healthy from cases with and without risk correlates and co-morbid confounding morbidities.

To sum up, the extensive use of prompt, non-invasive, and low-cost breath diagnosis has opened up several promising avenues for further research in the diagnostic process of tuberculosis globally[10]. There is a worldwide movement towards inexpensive assessment tools and rapid point-of-care diagnostic methods of different diseases. Success in non-invasive clinical diagnosis will have a far reaching impact in the development of the self-administered instruments for diagnosis and prognosis.

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