Characterization of some biochemical parameters in respiratory system diseases

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Abstract. This review article presents a general investigation about respiratory diseases starting with definition and classification also we are focus on the parameters which are useful to diagnose this disease, finally the treatment methods of all respiratory diseases were mentioned in. There are two common types of respiratory disease were expressed in detail with the define by physiological and biochemical causes of each diseases or illness. Chemical tests, biological investigations, and imagining techniques are three ways to diagnose the infection of respiratory system with multiple abilities to recognize between different diseases by all the diagnosis methods. Treatment of all types of respiratory diseases achieved by the elimination of inflammation by special drugs or by last therapeutic option the Lung transplant. Finally, we concluded there are several types of respiratory diseases differ from each other by many considerations and the diagnosis of respiratory diseases can be doing by biochemical and biological tests also we find the treatment of all types of respiratory diseases achieved by the elimination of inflammation or transplant the lung.

1. Introduction

Lung is the primary organ of the respiratory process in human body and the most important organ in respiratory system which consist of nasal and oral cavity, pharynx, larynx (upper airway), trachea and lung (lower airway). It consists of right and left sides; the right lung has three parts and the left lung has two parts, after trachea there is two big airways tubes known the bronchi inter into both lungs. Bronchi gradually form a more generations and gradually decreasing in diameter, continued to the end of lungs the bronchi finally form a structure called the alveoli or air sacs[1].

Through the respiratory cycle, the mainly of consumed oxygen and forms the carbon dioxide and water as byproducts [2]. Oxygen arrives the alveoli then moves from into the capillaries through their tinnny walls. The capillaries are carry out oxygenated blood to the blood circulation that supplies other tissues. Carbon dioxide and water are released from the blood to the lungs and respired [3].
Respiratory diseases can be subdivided according to its risk into two types chronic and acute or according to the region of infection into upper respiratory system diseases and lower tract diseases commonly called as pulmonary diseases and lung disease referer infection at the lung especially [4]

1.1 Chronic respiratory diseases (CRDs)

Are chronic diseases of the lung and the airways. It involves many chronic respiratory illnesses such as asthma, obstructive pulmonary disease COPD, Cystic Fibrosis (CF), occupational lung diseases, interstitial lung disease and others[5]. We are focuses mainly on asthma, CF and COPD, which are major public health problems.

1.1.1 Asthma

Asthma is a chronic lung disease caused by inflammation of the lung’s airways lead to obstruction and a rigidity of the muscles. Some grade of airway blocking is often existing in those with asthma, but more severe conditions can occur due to exposure to a variety of causes. smoke, dust, pollen, exercise, cold air and many others [6]. shortness of breath and wheezing are more complications of asthma and a patients feels like they cannot breathe but its consider a rare cause to death [7].

Figure 1. The normal and asthmatic lungs and airways.[6]

Chemically Intracellular adhesion molecule-1(CAM-1), a one of the immunoglobulin superfamily adhesion molecules that normally facilitates adhesion between leukocytes and endothelial cells after injury, has been associated in the pathogenesis of asthma. Increased ICAM-1 expression is observed in the respiratory tract of
individuals with asthma. This may help an inappropriately big number of immune cells to migrate there, stimulating chronic inflammation [8].

1.1.2 Obstructive pulmonary disease

Obstructive or Restrictive pulmonary disease is a disorder that includes as a result of environmental exposure to poisonous chemicals or to many infection. Term that refers to two diseases, emphysema and chronic bronchitis. COPD term is used because each diseases are characterized by obstruction to airway that interferes with normal breathing and the two frequently co-exist [9]. The tissues between the bronchioles and alveoli are fixed, fibro vascular and areolar. In the restrictive lung diseases, also this interstitial tissue comes suddenly scarified, and as it does, the alveolar air spaces become compacted[10].

1.1.3 Bronchitis

In the bronchitis the airways also become blocked because the mucus synthesized more than usual. While in Emphysema formed the walls between the alveoli lead to lose their flexibility. The alveoli become rigid and weakened, creating irreversible holes in the tissues of the lungs[11]. The lungs will have more difficulty moving air out and in, also the exchange of oxygen and carbon dioxide with the blood may be decreased. Smoking, environmental effect and genetic factors give high chance to get COPD[12].

A proteolytic enzyme α1-antiproteinase (antitrypsin), which inhibits an enzyme known as elastase in the lung. It is one of the many weapons used by these cells to kill or damage invading pathogens and also causes COPD[13]. However, once the pathogen has been killed, elastase activity must be inhibited and this is achieved by release of α1-antitrypsin. Unfortunately, one effect of which is to decrease their ability to secrete α1-antitrypsin the free radicals in tobacco smoke cause chronic damage to the cells in the lung, so that elastase is not inhibited. This results in further damage to the lung. The process is, therefore, a vicious circle, which eventually results in emphysema and COPD a chronic inflammation of the airways [14].
1.1.4 Cystic Fibrosis (CF)

This illness is an autosomal disease that caused by a mutation on chromosome 7, which involves a gene that encodes a transmembrane chloride channel [9]. In sweat ducts, more of chloride is secreted, but in lung tissues chloride does not emerge from the epithelial lining cells into the lumen, and also sodium is retained as well, the result is a dried airways. This airways misses its mucinous wet layer, and ciliary action is reduced [10]. In cystic fibrosis, all secretions of exocrine are damaged, involving those of salivary glands. Affected children may require artificial saliva measures to keep the mucosa comfortable and moist [6].

1.2 Acute diseases

Acute Respiratory disease is a disorder in which the lungs suffer severe extensive injury, interfering with their ability to take up oxygen. It characterized by shortness and rapid of breathing such as Influenza, Pneumonia, Tuberculosis and Lung Cancer.

1.2.1 Influenza

Influenza is a type of acute respiratory diseases which produced by infection with viruses, the typical features of influenza include sever onset of fever and respiratory symptoms such as cough almost nonproductive, coryza and sore throat, as well as muscle aches, headache, and fatigue. The clinical severity of infection can ranged from asymptomatic illness to primary viral pneumonia and death [9].

Influenza viruses divided into four types; A, B, C, and D. influenza A virus subtypes influenza A (H3N2) and A (H1N1), Influenza B viruses are not divided, type C Influenza viruses were not associated with several disease, pandemics or epidemic while influenza D viruses primarily affect of cattle and are not known to infect or cause illness in human [3].

1.2.2 Pneumonia
In pneumonia, a group of fibrosing lesions develop from long exposure to inspired chemical materials, such as beryllium, coal dust (anthracosis), silica and asbestos. Assured infections with bacteria and viruses lead to interstitial pneumonitis, whereby the interstitial spaces were edematous and inflamed and heal by the fibrosis. In pneumonia the lung relies on defense by macrophages, and phagocytosis by macrophages depends upon glutamine [8].

1.2.3 Tuberculosis TB

A disease which is usually caused by bacteria of the Mycobacterium tuberculosis complexes, one of first diseases known to affect individual human and from a major cause of death in the worldwide. An proved more than one billion persons, third of the world’s population, were infected with the Tuberculosis. Problem arises when sputum smear result was repeatedly negative for acid fast bacilli [15]. Tuberculosis was spread by aerosol spread in close contact with infected subject or individuals[2]. The infection occurs at two stages primary infection the periphery of the lung tissue, and via lymphatics, a Hilary lymph node grow into infected and then enlarged with granulomas. The secondary infection occurs in the face intact T-cell response and a positive tuberculin skin test resulting. Reinfection or reactivation of the tubercle bacillus[16].

Mycobacterium phagocytosed by macrophages to be incorporated within the phagosome. With ‘normal’ bacteria, the phagosomes fuses with the lysosomes to form the phagolysosome, in which the bacteria are killed. However the mycobacteria prevent fusion of the phagosome with the lysosome and hence avoid death. [13].

![Figure 3. Tuberculosis](image)

1.2.4 Lung Cancer

Lung cancer is a long common disease with an increasing trend and is a fatal and important cancer a 5 year survival rate of only thirteen percentage after the time of characterized. There are two types of lung cancer as
shown below and this type of lung cancer is defined according to the type of cells in the lung tissue and
Unfortunately, lung cancer is takes a long time until appear the symptoms, therefore is diagnosed in progressive
stages in most cases [16], the types are :

1 - small cell carcinoma SCC This type is the more common type of lung cancer and has fast growth and
metastasis rate, and extents to other organs easily also it arises in the larger airways bronchi and strongly
associated with smoking.

2 - non-small cell carcinoma NSCC: There are many types of this cancer squamous-cell carcinoma, large-cell
carcinoma and adenocarcinoma.

![Main types of Lung Cancer](https://index-china.com, 2020)

**Figure 4.** Small and non-small cell lung cancer. (https://index-china.com, 2020)

Survival frequency of patients with any type of this cancer is important signs in disease assessment and
control of treatment methods. Many researchers seeking with this point; recently reported a range survival time
of 6.5 months for patient individuals. [9].

1.3 Interstitial lung disease (ILD)
ILD are define a varied range of the lung disorders, which are an important cause of mortality and morbidity in
all of age groups. ILDs may be made-up of as those with a known etiology commonly due to occupational and
environmental exposures and those with an unknown etiology, including idiopathic pulmonary fibrosis (IPF),
sarcoidosis and ILD associated with connective tissues diseases[6].
This project addressed on the respiratory diseases reviewed their types, causes, diagnose and treatment. we
focus on the biochemistry of all above diseases to investigate and establish the biochemical markers of
respiratory disease and the best one uses to diagnose this illnesses especially at the lung and lower respiratory
system.
2. Biomarker and diagnose

Respiratory diseases can be diagnosed by several parameters including biochemical tests, physical imaging and biological tests. Chemical tests including measure of some molecules such as enzymes, proteins, minerals and other factors. Imaging techniques provide important information about respiratory tract like size and form of lung and other organs in respiratory system. Culture for many types of bacteria like tubercle bacilli and test of flu viruses are helpful to diagnose several respiratory diseases.

Patients with this disease characteristically suffer from a dry cough that are acute and shortness of breath. These symptoms or signs are almost attributed to deconditioning or aging, take a time to diagnosis. The rate of progress of these symptoms are typically not fast but varies with the type of disease and can irregularly simulate pneumonia in its acuity. The Spirometry is a common test used to know how well the lungs work by assessing how much air exhale and inhale. Spirometry is used to diagnose COPD, asthma, and other disorders that affect breathing [17].

Many researchers uses the proteins as parameters to diagnose respiratory diseases, C. Hermans et.al [Hermans and Bernard, 2014] estimate the Lung Epithelium proteins as biomarker the found it in normal distribution in healthy individuals and. In several disorders, these proteins changes either to a loss of integrity of the bronchoalveolar–blood barrier or to changes in secretion into the respiratory tract, and also they are proved the decreasing of proteins from the lung into the circulation system appears to be governed by a number of effectors.

Jose V. et.al.[10] studied on the toxicant molecules at lung and they are proved that the respiratory tract is repeatedly exposed to raised concentrations of these molecules and consider the main target for toxicity and also they proved the prolonged exposure to a unlimited variety of chemicals may result in acute or delayed injury to cells of the respiratory tract. Recently estimated the levels of molecular biomarker to consider evidence to detect the earlier lung cancer, they concluded application of biomarkers to helping the early detection of both types of lung cancer has the potential to improve the ability to select patients for lung cancer fellowship, and to help with the characterization of uncertain lung nodules. Also they are proved related considerations and have been suggesting standards to use when determining whether a molecular biomarker for the early diagnose of lung cancer is ready for clinical use.

Enzymes has more range in researches to use as parameters, Doris B. et al., [13] estimate Enzyme Activities and Isozyme at lung tumors patients the measure in surgical biopsy the activity for six enzymes. The tumors revealed significant deviations with respect to the malate dehydrogenase MDH and lactate dehydrogenase LDH. The adenylate kinase and alpha glycerophosphate dehydrogenase activities of the tumors while about one-tenth and one-fourth, respectively, of those of non-neoplastic adult lung. These lower activities obvious also in normal fetal lung were accompanied by 3- to 5-fold increases in the LDH, MDH, kinase hexokinase, and pyruvate activities of the tumors. M. Zalewska et.al investigate on the antioxidant enzymes at NSCLC, they have proved significant change in the activity of antioxidant enzymes were observed throughout the process of carcinogenesis. Tumor cells always have a low Super Oxide Dismutase (SOD) activity, usually low
Cu/Zn SOD activity, and almost always decreased catalase activity compared with those of the analogous normal tissues. The activities of Glutathione SH-related enzymes were significant clinically high in lung cancer tissues, irrespective of the histological type of lung cancer, which could possibly be the way by which tumor cells protect themselves against increased oxidative stress.

Glutathione and related enzyme activity are estimated also by J. Carmichael et.al. [19] at thirty patent with lung cancer lines they found the lower levels were noticed in cell lines derived from SCLC specimens compared to non-small cell lines had no significantly differences were detected between cell lines derived from the previously untreated patients, compared with those derived from patients who had received chemotherapy.

Serum Enzymes including phosphohexose isomerase, lactic-acid dehydrogenase LDH, glutamic oxaloacetic transaminase GOT and alkaline phosphatase AP in Patients with carcinoma of lung have been studied by M. H. Gault et.al. [20] they conclude Normal values occurred often at the time of the first test and quite commonly during the last month of life; sometimes there was an increase in activity only shortly before death, particularly of AP and GOT. With several exceptions, extent of tumor growth, hepatic involvement and loss of tumor-cell differentiation appeared to relate to increased activity of LDH and PHI; values for these two enzymes correlated closely. Significantly elevated values of any of these four enzymes (unrelated to chemotherapy) most often occurred late in the disease and strongly suggested the presence of metastases, usually extensive. Increased AP activity occurred in some cases without demonstrable hepatic or bone metastases, but, overall, elevation became more marked with increasing liver and bone involvement. GOT activity was seldom increased; it was normal in some cases with hepatic metastases, and elevated in some without. Activity of LDH and PHI, and to a lesser extent of GOT and AP, frequently increased when 5-fluorouracil or vinblastine sulfate was administered; activity returned rapidly to pre-therapy values. Analysis of results using the highest value obtained for enzyme activity during each patient's illness gives a false impression of the diagnostic value of enzyme determinations; this was particularly evident for GOT and AP.

Adenosine deaminase ADA estimated by Sanjay V. et.al [12]. Patients of pulmonary tuberculosis proved significantly elevated ranges of serum ADA level had been observed in presence of disorders of more than one month duration. There was no significant relationship between sputum status and serum ADA levels. It was raised significantly in both negative cases as well as sputum positive.

Biological parameters used by Jose. et.al. [10] Tracheal aspirate culture showed a predominance of gram-negative bacteria with Pseudomonas aeruginosa (11/17), Kiebsiella pneumonia ( 11/17) and Escherichia coli (8/17) predominating. Staphyllococcus aureus (5/17) was the major gram-positive microorganism isolated. Candida albicans was present in five infants. The distribution of gram-negative microorganisms was similar in those infants who died to those who survived and provide there was a good correlation between the microorganisms isolated on the tracheal culture and at autopsy from the lungs. Leonard R. et.al [21] trying with the rapid diagnostic test for respiratory virus, they conclude the test kit affords a rapid, easily performed means for detecting virus in the absence of a fully equipped virology diagnostic laboratory or when such a facility is not readily available. From the data, they provided 66 of 137 (48%) specimens were positive for Respiratory Virus.
Hyde et.al. [9] use the X-Ray to measure total number and mean size of alveoli in mammalian lung and they conclude severe abnormalities were demonstrated on all the chest roentgenograms. Hyperinflation was a constant feature and this was the only abnormality in four infants at the onset of their illness. Right upper lobe atelectasis was seen in 11 out of the 17 infants.

3. Treatment

The central and major aims of treatment are suppress of inflammatory component and to stop exposure to the causal agent of the disease alveolitis, and also to treat the other future complications. The first objective is only possible when the etiology of the disease is known. The elimination of the alveolitis is the only therapeutic treatment for an idiopathic respiratory disease, since no anti fibrotic drugs of recognized efficacy are currently available the drugs used are corticosteroids and immunosuppressant’s [22].

Lung transplant was the last one from therapeutic options for the lung disease that progress to cause lung failure and fibrosis. Transplant applicants must fulfill the general criteria for eligibility that apply at any sort of the lung transplant and must not present contraindications[23]. NSCC was often treated with surgery, while SCC usually responds better to chemotherapy and radiotherapy. The treatments for these different chronic respiratory diseases share similarities[21].

4. Conclusion

There are several types of respiratory diseases differ from each other by many considerations, according to causes it varies into genetic disorder or acquired since it may be caused by chemical disorder like asthma, COPD and CF or biological effect such as bacterium; tuber cellulosic and viral infection; influenza. Respiratory diseases also differ by the damaged region may be happen in the trachea, alveoli; COPD or lung; lung cancer. In addition to obvious classification the main classification is chronic like asthma, CF and COPD and acute diseases like Influenza, Pneumonia, Tuberculosis and Lung Cancer.

Diagnosis of respiratory diseases can be did by biochemical tests measure of some molecules such as enzymes, proteins, minerals and other factors, physical imaging, imagining techniques and biological tests, culture for many types of bacteria and test of flu viruses are helpful to diagnose several respiratory diseases. Treatment of all types of respiratory diseases achieved by the elimination of inflammation by special drugs or by last therapeutic option the Lung transplant.

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5. References

[1] Inhibitors T K 2018 Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted 321–46

[2] Speizer F E, Horton S, Batt J and Slutsky A S 2001 Chapter 35 Respiratory Diseases of Adults 681–94

[3] Tierney D F 1974 Lung Metabolism and Biochemistry Annu. Rev. Physiol. 36 209–31

[4] American Lung Association 2010 State of Lung Disease Communities 106

[5] Delhi N 2018 WHO Package of Essential NCD Interventions (PEN)

[6] OSUMC 2016 Types of Lung Disease. The Ohio State University Wexner Medical Center.

[7] Eversole L R 2019 Oral medicine ch.5 Respiratory Diseases p.42–53.

[8] Crowley J, Po E, Celi P and Muscatello G 2013 Systemic and respiratory oxidative stress in the pathogenesis and diagnosis of Rhodococcus equi pneumonia 45 20–5

[9] Hyde D M, Tyler N K, Putney L F, Singh P and Gundersen H J G 2004 Total Number and Mean Size of Alveoli in Mammalian Lung Estimated Using Fractionator Sampling and Unbiased Estimates of the Euler Characteristic of Alveolar Openings Anat. Rec. - Part A Discov. Mol. Cell. Evol. Biol. 277 216–26

[10] Castell V, Donato M T and Jose M 2005 Article in press experimental and toxicologic Metabolism and bioactivation of toxicants in the lung. The in vitro cellular approach

[11] Ward J and McDonald C 2010 Interstitial lung disease: An approach to diagnosis and management Aust. Fam. Physician 39 106–10

[12] Varma S and Toppo A 2015 Estimation of serum adenosine deaminase level in patients of pulmonary tuberculosis in a tertiary care hospital in Chhattisgarh. International Journal of Research in Health Sciences. 3 451-456.

[13] Balinsky D, Greengard O, Cayanis E and Head J F 1984 Enzyme Activities and Isozyme Patterns in Human Lung Tumors I 44 1058–62

[14] Escobar J A and Reyes A 1976 Etiology of Respiratory Tract Infections in Children in 57

[15] Nasarre P, Potiron V, Drabkin H and Roche J 2010 Guidance molecules in lung cancer Cell Adhes. Migr. 4 130–45
[16] Abazari M, Gholamnejad M and Roshanaei G 2015 Estimation of Survival Rates in Patients with Lung Cancer in West Azerbaijan, the Northwest of Iran 9–13

[17] Lloyd-still J D and Shwachman H 2020 Severe Respiratory in Infants With Cystic Fibrosis 53

[18] Hermans C and Bernard 1999 A State of the Art Lung Epithelium – specific Proteins Characteristics and Potential Applications as Markers. American Journal of Respiratory and Critical Care Medicine 159 646-658.

[19] Carmichaeli J, Mitchell J B, Friedman N, Gazdar A F and Russo A 1988 Glutathione and related activity in human lung cell lines 437–40

[20] Dehydrogenase L and Isomerase P 1967 Serum Enzymes in Patients with Carcinoma of Lung: 96

[21] Lipson M, Barone R, Harkness S H, Krilov R, Kaplan H and Abbott R S V 2020 Evaluation of a Rapid Diagnostic Potential Test for Respiratory for Bedside Diagnosis Syncytial Virus 93

[22] Xaubet A, Ancochea J, Blanquer R, Montero C, Morell F, Rodríguez Becerra E, Sueiro A and Villena V 2003 Diagnosis and Treatment of Diffuse Interstitial Lung Diseases Arch. Bronconeumol. 39 580–600

[23] Hughes J M B 2009 Interpreting pulmonary function tests Breathe 102–10