CHAPTER-V

DISCUSSION

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In the present study blood parameters such as Hemoglobin, Red Blood Cells and White Blood Cells counts has been observed in control subjects and afflicted with lung disease patients like Asthma, Tuberculosis, Bronchiectasis and Emphysema.

Hemoglobin: - Hemoglobin is a major conjugated protein in the human body consisting of iron porphyrins attach to the protein globin, Hemoglobin possesses the ability to conbine reversibly with oxygen and serves as the oxygen transporter within the blood(Perutz MF; 1978).

Table.16 Showed that Hemoglobin content was declined significantly in tuberculosis patients than the control subjects. But there was no significant difference in other lung disease patients such as Asthma, Bronchiectasis and Emphysema.

Fig.1 Represents the status of the Hemoglobin in control versus clinical blood. The Hemoglobin content for the control subjects was 12.38 g/l, whereas its content in Asthma decreased by 23% in Tuberculosis declined by 46% and in both Bronchiectasis and Emphysema decreased by 26.5% and 33.8% respectively.

In anemia and in some disorders due to bacterial infections, inherited Hemoglobin abnormalities after the interaction of Hemoglobin with oxygen and thereby diminish oxygen transport. The presence of excess of Diphosphoglycerate diminishes the affinity of Hemoglobin for oxygen in the lungs(Michel cc.1984)

From the results obtained in regard to Hemoglobin content of clinical patients afflicted with lung diseases as compared with control

subjects, it is clear that Hemoglobin content gets significantly decreased in Tuberculosis. It seems the Hemoglobin content drops as a result of decrease rate of its synthesis following the infection.

In Asthma and Bronchiectasis Hemoglobin content was marginally decreased. As Hemoglobin level was affected by Po_2(partial pressure of the oxygen) in arterial blood and the respiratory capacity of the lungs is the sole determinant for the Po_2, it appears therefore that in lung disease the respiratory capacity declines in the lung with a concomittant decrease in hemoglobin leval via decreasing Po2.(Bonnett r; 1981).

Due to pulmonary adema in tuberculosis the strecheability of the lungs decrease greatly which may also result in reduced Po2. In lung inflammation the walls of the alveoli are damaged, septal changes are found in the walls of airways and produce larger abnormal airspace, all these pathomorphological changes may again influence the hemoglobin level was found in the present investigation (Zafran N, Heldal E, Pavlovieseta1 1994).

Red Blood Cells: The changes in RBC counts in patients were marginally lower than that in control subjects noted in table 16. There were no correlation between the control and lung disease patients.

RBC play a key role in the transport of oxygen and carbon dioxide between lungs and the tissue. In pathophysiological conditions, individual RBC contain a normal amount of Hemoglobin but there are too few cells. In other disease states, the number of RBC is adequate but the Hemoglobin content of the individual cells is too low(Stephan G Farmer;1991).

Pathologies may also result from abnormal forms of Hemoglobin or from abnormal membrane structure that causes cells to rupture and destroyed. Most of these pathologies result in anemia, a condition in which the blood Hemoglobin content is too low. Because oxygen bonds to Hemoglobin, individuals with anemia cannot transport enough oxygen to the tissues and they become tired and weak (Douglas W; P. Hay; 1993)

During lungs inflammation the tissues become hypoxic because of too little oxygen in the lung inflammation or because failure of delivery of oxygen to tissues. It leads to Hemolytic anemia. These are usually hereditary defects in which the body makes fragile cells and other anemias result from the failure of the bone marrow to make adequate amounts of Hemoglobin (Dean J. Schechter AN; 1978)

In the present study the RBC counts in control was 3.8 mm^3 / litre in Tuberculosis it decline significantly when compared to control by 13.2%. In Asthma and Bronchiectasis it dropped to 8% and in emphysema by 10.5% than the healthy subjects.

White Blood Cells:- In this study it was observed that WBC counts was higher in clinical patients than the control subjects Table-3C showed stastical values of WBC count was elevated in the Tuberculosis patients. The values (in SD ± 726.6). In Asthma it was increased 20%(SD ± 586.2) but in case of Bronchiectasis and Emphysema there was marginal elevation observed in WBC counts.

In this study mentioned that patients exposed to air pollutant because of their occupation which initiate a pulmonary inflammatory response. WBC play a key role in defending the body against foreign invaders such as parasites, bacteria and viruses.

Pulmonary inflammation elevates macrophages in the lungs particles are cleaved from the gas exchange region of the lungs by alveolar. Macrophages by AMS (Alveolar macrophages) also release inflammatory mediators and growth factors involve in the development of pulmonary fibrosis (Knowlesetal 1990).

A key component of lung inflammatory response to either air borne pollutant or tobacco particles is an activation of alveolar macrophages and recruitment of polymorphonuclear leukocytes into branchoalveolar (Castranova 2000). This branchoalveolar population of cells, consisting of alveolar macrophages and leukocytes, it has been shown to release a number of inflammatory mediators it leads the elevation of WBC level (B. Lackford etal 1994).

In Asthma patients exposed to air borne particles, which play an important role in the defense against pathogens and appears to be involved in the tissue damaged associated with inflammatory process. (Talenti etal 1992; Gastonetal 1994)

In patients with asthma, eosinophils are present increased numbers in blood (Schatzeta 1982) various marker of eosinophil activation have been shown to correlate significantly with the severity of asthma or with the degree of airway responsivenesi (Wardlaw etal 1988; Bousquet etal 1990).

Polymorphonuclear leukocytes play a fundamental role in the primary host defense against bacterial pathogens and elevate in the patients affected with Tuberculosis (Alowsy etal 2001) Table 3C showed in Tuberculosis patients WBC count was elevated. The rationale being that smoking, age and exposure to oxidants have been reported to induce

changes in the blood concentration of mediators of inflammation which might be elevated polymorphonuclear leukocytes. (Bugajski etal 1999)

Excess recruitment of activated neutrophils to the lung to envisage a mechanism that can lead to destructive lung disease. This situation could arise for a variety of reasons including continued recruitment, excess release of chemotactic factors, increase cell adhesion, increased sensitivity to chemoattractants increase activation and increased enzyme content. (Stockley etal; 1988), the secretions from patients with Bronchiectasis contains chemotactic factors causes the elevation of WBC count in patients. (Currie etal 1987)

Blood glucose:- Blood glucose serves as an important source of energy for vital activities by serving the tissues as a major metabolic fuel.(Mc. Gilvery; 1979).

Comparative account of blood glucose of normal and clinical patients afflicted with lung diseases were shown in Table 17. The level of blood glucose in Emphysema was elevated than control subjects but remaining lung patients showed only marginal changes in levels of these parameter was noted.

Information required to prove the elevation of blood glucose in Emphysema patients is unavailable. But probably it might be elevated due to age effect. In the present study, all the patients Emphysema were about 60 years of age because of aging the insulin secretion by pancreas might be reduced than the normal secretion i.e. 50 units / day in those genetic subjects.

Diminished action of insulin either by the absolute depletion of β - cells in pancreatic islets or by the insulin resistant state is also potentiated

by the disturbances in the regulation of intrinsic prooxidant, antioxidant homeostasis regulated by the mitochondria, Mitochondrial electrons flux becomes uncoupled from ATP synthesis during hyper glycemia (Anderson 1999).

Reduced respiration with resultant decrements in ATP production in mitochondria and the depletion of muscle glycogen stores with excersice may lead to increased glucose transporter in order to balance high demands for glucose during an aerobic matabolism (Borghouts and Keizer; 2000).

In Emphysema patient's glucose level was slightly elevated by 8% then the control subjects (Table 17). The value of blood glucose was declined in Tuberculosis by 11.3%. In Asthma and Bronchiectasis patients, also slightly decreased than the control values.

During the lung inflammation, patients affected with hypoxic condition, substantially enhance glucose uptake in muscle, was reported by several authors and reviewed by (Ismail - Beigi 1993). Both hypoxic and inhibitors of oxidative phosphorylation activate glucose transports and via cis - acting sequences (Elbert etal 1995).

Serum protein:- The serum proteins act to transport metals hormones, nutritive materials, buffers and clotting factors. Almost all proteins are synthesized in the liver, the main exception being immunoglobulins which are manufactured throughout the body in plasma cells of the immune system.

This result did not find significant changes between control and clinical patients, the values of serum protein in tuberculosis patients was decreased by 15.8% and in Emphysema patients by 10.4% then the

control subjects similar to the study (Baggiolini etal 1988) also found that the decline of serum protein during airway inflammation, lungs inflammation brings serum protein and cells to the cite of damage. The inflammatory reaction is mediated by a variety of mediators derived from plasma enzyme system. The specific and non specific immune system or the invading pathogens themselves. Several groups of mediators exist inflammatory mediators released by cells can bring about changes in the functioning of the target cells likewise protein mobilized towards the cells activation (Bray 1986. Hamilton and Adam 1987, Korchak 1988).

Enzymes:- Profile of some key Enzymes activity was shown in Table 18. Enzymatic profile was also found to be changed in studied pulmonary diseases. So it can be used as the important diagnostic tool for them.

Serum enzymology provides aid in making the diagnosis, monitoring the course and demonstrating subclinical evidence of disease. Diseases that are characterized by distinctly abnormal values of one or more enzymes can be readily distinguished from clinically similar states in which abnormal values for the respective enzymes do not occur(Wilkinson J; etal 1970).

The diagnostic application of serum enzyme assays is based on the accumulated clinical experience and experimental data that permit formulation of factors that lead to abnormal enzyme levels and correlation of particular serum enzymes with the nature of the pathology process and the organ involved. The enzymatic assessment serves to epitomize most of the foregoing material (Granner DK; Hargrove JL; 1983).

In the present study the investigated enzymes were aminotransferases (SGOT, SGPT), acid phosphatase and lactate dehydrogenase.

Aminotransferases:- The serum enzymes investigated are the two important transaminases such as Glutamate oxalo Aminotransferase (SGOT) and Glutamate Alanine Aminotransferase (SGPT); these values are shown in Table-18 and status of SGOT and SGPT can be seen in figure 6 and 7 respectively. SGOT values were elevated by 23% in Bronchiectasis patients but in the remaining lung patients the values were not significantly different when compared to controls. Whereas the SGPT decline in clinical serum. The stastical values of SGOT and SGPT were shown in the Tables 11-A to 14A and 11B to 14B. Control subjects of SGOT and SGPT values were (SD ± 1.94) and (SD ±4.58). In Asthma SGOT values were (± 3.27), Tuberculosis (± 3.58), Bronchiectasis (± 19.12) and in Emphysema (± 2.71) whereas the SGPT values in Asthma (± 2.25), in Tuberculosis (± 1.94), in Bronchiectasis (± 15.13) and in Emphysema it was (± 2.63).

Aminotransferase enzymes are felt to play a minor role in cytoplasmic tyrosine catabolism under normal conditions (Stoner E; 1984). Its main functions in overall metabolism are to provide the catalytic function in the fed state, whereby nitrogen derived from branched chain amino acid oxidation can be denoted to pyruvate and returned to the liver for fixation and the catalytic function in fasting, whereby 3-carbon units derived from muscle protein breakdown to amino acids can be aminated, directed to the liver for gluconeogenesis (Ahlborg G; Felig P; 1974).

In the present study showed that in Bronchiectasis patients SGOT slightly elevated than control serum due to the chronic inflammation of the bronchial wall causes destruction of the musculoelastic tissue, recurrent massive hemoptysis, cystic fibrosis causes myocardial infarction as per noted in introduction, which may leads to increase transaminase in clinical serum.

Acid Phosphatase:- Serum Acid Phosphatase activity of the clinical and control subjects has been shown in the Table-18 and Figure 8 express its status in clinical serum. It revealed that Acid Phosphatase activity of the clinical serum were high than the control. In asthma it was elevated by 22%, by 27% in Tuberculosis, in Bronchiectasis it was shown higher by 42% and in Emphysema Acid Phosphatase was slightly increased by 16.4%.

Schins (in 1997) reported that changers in blood antioxidant status in persons with occupational respiratory diseases, including elevated antioxidant enzymes in the erythrocytes of patients, elevated catalase in patients with higher dust exposures and moer severe pneumoconiosis (Nadif etal 1998).

Those changes may reflect a loss of bodies ability to maintain a homeostatic balance between oxidant production and antioxidant defenses in lungs patients (Englen etal 1990). The elevated level might be due to inflamation correspond to the physiological activities like cellular destruction such as Erythrocytes may also release acid phosphatase into the serum (Schumann. G, A and Henry 1986).

The macrophages can release a number of performed mediators, chiefly enzymes and perhaps some cytokines the granules contain both hydrolytic and proteolytic as well as some enzyme inhibitors. These have a role in the metabolism of engulfed particles, however some are released into the supernatens of cultured cells following the engulfing of some particles (Meagher etal 1989).

Cells covered with material such as collagen has also shown the release of enzymes which can metabolize the substrates, leading to the

hypothesis that such release may be part of the pathological process as well as part of the mechanism of migration of cells (Brick R Mandel H 1993).

Occupational Asthma affected by chemicals, airborne particles, exposure to cobalt, chromium leads to an alveolisis and pulmonary fibrosis stimulate the formation of autophagic vacuoles and increase the activity of lysosomal enzymes (Woodard. H .Q. 1989).

Most of the lung diseases originate with the infections with stephalocoeii (Krause and Mahn - 2000). So generally pulmonary patietns were treated initially with 'corticosteroid' that results in increased osteoclastic activity of the bones. This perhaps resulted in increase phosphatase level in the serum (Suda. T, Takahashi N, Mortin T.J. 1992).

Lactate Dehydrogenases: - Lactate dehydrogenase was higher in clinical serum than normal serum in all the clinical states. It is widely distributed, being found in all cells in man, but is plentiful in cardiac and skeletal muscle, liver, kidney and the red blood cells.

LDH exists in two sub units forms an 'H' form which predominates in 'heart' and an 'M' form which predominates in skeletal muscle. The active form of the enzymes is a tetramer such that in most tissue a spectrum of isoenzymic forms appear include H_1, H_3M, H_2M_2, H_1M_3 and M_4. Separate deficiencies have been described for the two subunits forms of this enzyme. (Herman FF, 1988)

In one case report, four sibs were totally lacking detectable activity of the M subunit form of the enzyme, and all activity detected in red cells, white cells and muscles was of the H_4 form (Stremmel. W; Strohymeyer G. Berk P. 1986).

One sib had pigmenturia and easy fatigue on exercise ischemeic exercise of the forearm lead to an exaggerated pyruvic acidmia and to a muted elevation of blood lactic acid because muscle damage was evident in this patients, the residual H_4 isoenzyme of lactic dehydrogenase present in exercising muscle must have had less than adequate activity to sustain NADH reoxidant rates, thus leading to an early curtailment of glycolysis and loss of intramuscular ATP. (Olkaner RK; Kaikus RM. 1992)

During the oxidation process electrons are transferred to oxygen via the energy transducing complexes of the respirator chain. Since the respiratory chain transfers NADH to oxygen, a disorder of oxidative phosphorylation should result in 1) an increase reducing equivalent in both mitochondria and cytoplasm and 2) the functional impairment of the citric acid cycle, due to the access of NADH and the lack of NAD. Therefore, an increase of ketone body and lactate / pyruvate molar ratios with secondary elevations of blood lactate might be found in the affected individuals. (Hargrove J. L, Scoble HA, Mather WR, 1989) .

In all pulmonary diseases complete and partial anoxia precipitate metabolic changes. Due to the deficiency of oxygen the cellular metabolic fuel, glucose does not get completely oxidize, which results in increased accumulation of lactate at the cellular level, hence in hypoxic condition, the serum LDH level increases significantly due to metabolic stress. (Elliot and Wilkinson;1988).

In advance cases of pulmonary diseases, Emphysema and muscular dystrophy were noted in the study group. Emphysema affects cardiac functioning and muscular dystrophy affects the metabolic pattern, both these changes precipitate circulatory and metabolic disturbances simultaneously. These drastically change the oxygen level and finally the

changed metabolic pattern elevates serum LDH level (Dickens F, Randle P. J;1978).

In the present study also lactate dehydrogenase showed significantly higher levels in Bronchiectasis by 36.4% and in Emphysema patients it was elevated (36%) than the control subjects. During these inflammatory condition muscle tissues damage and alveolar fibrosis activity that might be elevated LDH activity in the blood. The 36% increase in LDH is suggestive of an intense muscular activity. In Asthma and Tuberculosis lactate dehydrogenase increased by 19% and 18.4% respectively.

In conclusion the blood counts may be useful for predicting the presence or severity of inflammation in lungs patients. The study profile of enzymes activity bring to the forebiological and functional pathological conditions which can be used for the biomonitoring of lungs patients.

It is perequisite for understanding their functional significance in the patients. Understanding the nature of the enzymes activity will lead to the development of novel and precise therapy for the different inflammatory conditions of the lung. This study search will eventually lead to better control of lung diseases in which these tools play a leading role.

The enzyme investigating in the present studies for example Aminotransferases (SGOT, SGPT) Acid Phosphatase and Lactate dehydrogenase can prove to be good diagnostic tools for evaluating the severity of the lung related diseases based on the serum levels. The evaluation protocols may also include immunodiagnostic kits that are already available or can be formulated using commercially available reagents and specific antibodies. The study holds great promise for clinical biochemistry in regard to diagnosis of a number of lung diseases including the ones in present study.