Chapter No. 1

INTRODUCTION
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Leprosy (Hansens disease) is a chronic infectious disease of man caused by mycobacterium leprae.

Leprosy is essentially a disease of peripheral nerves but it also affects the skin and sometimes certain other tissues, notably the eye, the mucosa of the upper respiratory tract, muscle, bone and testes.

The spectrum of clinical manifestation of leprosy is broad. At one end is tuberculoid (TT) leprosy in which the clinical manifestations are localized to a single area skin and the associate nerve supply. At the opposite end is lepromatous (LL) leprosy, in which there is massive infection of the dermis by M.leprae as well as involvement of nerves system.

The intermediate forms of leprosy display mixture of clinical histopathologic and immunologic features typical of TT and LL diseases. The intermediate forms are less stable. Clinically and often progress towards the lepromatous type. Spontaneous improvement with a shift towards the
Trace Elements in Leprosy

Tuberculoid spectrum occurs less frequently unless antimicrobial therapy has been instituted.

Immunological instability and therefore the tendency to move in either direction along the borderline spectrum, with treatment towards the tuberculoid pole usually as a result of a reversal reaction (upgrading) while the untreated patients tends to move towards the lepromatous pole a (downgrading) within infected tissue the immunologic mechanism of which are poorly understood.

Such reactions involve considerable functional impairment when they involve the peripheral nerve trunks. Reactions of this types occurs in individuals with intermediate forms of leprosy but not in those with TT or LL disease. LL leprosy is associated with a different type of reaction, Erythema nodosum leprosum (ENL) that likewise may precipitate acute nerve dysfunction, possibly as a result of the humoral response to Antigens of M. leprae

The mycobacterium leprae contain mycolic acid and sugar known as mycosides. Mycolic acid is responsible for the organism is stained with carbol fuchsin. Leprosy is a disease which disable rather than causing death
adds up a lot of economic strain on health delivery system. The extent of research in the field requires continuous efforts to win over the problem. The presence bacilli and pathology in internal organs in the evidence systemic nature of disease, chronicity of leprosy infection and complex biochemical structure of mycobacterium leprae have directed interest for study of biochemical changes for the host.

Leprosy continue to remain major communicable disease problem particularly in developing countries physical deformity and social stigma are major concern in leprosy. Socioeconomic under development associated with disease has made its control very difficult all over the world. The global figure is an estimate of 10 to 12 million patients of whom about 2 to 3 million have physical deformities. Trace elements acts as catalyst in many biochemical reactions in our body. So the importance of trace elements in leprosy of different types have been taken to find out if any relation with.

Trace elements are required in small concentrations as essential components of biological enzymes systems or of structural proteins of biological constituents.
Trace elements in sick and healthy humans beings has been studied in relation to number of diseases, such as leukemia, diabetes, liver disorder cancer and leprosy.

Variations in diet and nutrition’s practices among different populations have been studied by Gabriel and Venkatraman. They reported, such variations have been associated with increased or decreased leprosy risk. Certain trace elements may act as antioxidants and inhibit activation of bacilli. Trace elements may also enhance the functional activities of immune system.

Copper is a trace element occurs in many enzymes like cytochrome oxidase, ferrooxidase, uricase, superoxide dismutase etc. variations in serum copper found in various disease involving leprosy.

Zinc is essentials for function of several enzymes it is involved in carbonic acid [carbonic unhydrase] and in [alcohol dehydrogenase] formation and helps in neovascularisations.

Low serum zinc concentrations have been shows by various workers in patients with leprosy. Selenium
has key role in activity of enzymes glutathione peroxidase. Supplementation of selenium with vitamin E, decreases the plasma concentration of lipid peroxides suggesting the antioxidative role of selenium work in redox reaction, enzyme is believed to account for catalysis the transfer of reducing equivalent from reducing glutathione [Gpr] to hydrogen peroxide or to lipid peroxide thus serving to protect cell and cell membranes against oxidative damage selenium or compounds may serve to protect animals against the toxicity of heavy metal such as cadmium and mercury.¹¹²

Magnesium plays key role as an essentials prosthetic group in at least 300 enzymatic reactions in intermediary metabolism [shills 1988] magnesium is cofactor in reaction involved in the transfer of energy by way of adenosine triphosphate [ATP] , chronic magnesium deficiency is associated with edema, hypertropic gums, leuocytosis, splenomegaly, thymic malignant lymphosarcoma [shills 1988] also significant decrease in serum magnesium is related to all clinical types of leprosy, associated with different biological processes in carbohydrate metabolism, deficiency are functional hypoparathyroidism and impaired endorgan responsiveness to parathyroid hormone.¹⁰²
Manganese occurs in many oxidation states but Manganous (+2) and manganic (+3) forms are of greatest biological interest activator for several enzymes as non specific divalent metal. The two manganese containing mammalian metaloenzymes, pyruvate carboxylase and superoxide dismutase are both located in the mitochondria, vanadium injected excrete through kidney in urine. Contents to vanadyl transferring and transferring complex precipitated in redox reaction within cell particularly with relatively small molecules that can reduce vanadate non enzymetically such as glutathione helps in preventing an increase in glucose decrease phospholipid and cholesterol levels, help in developing bone and teeth toxicity causes manic depressive illness deficiency cause neutritional oedema.

One of the cause of leprosy is damage to cell by free radicals. Free radicals are chemical species possessing an unpaired electron that can be considered as fragment of molecules and which are generally any reactive. They are produced continuously in cells either as accidental or deliberately e.g. phagocytosis. The most important reactant in free radical biochemistry in aerobic cells are oxygen and its radical derivatives. The most important free radical in
biochemistry are superoxide, hydrogen peroxide, transition metal ions and the hydroxyl radical which conspire by variety of reactions to generate the last.

**Superoxide**:

Superoxide although a free radical is not particularly damaging species, it is most reductive in nature and its main significance is probably as a source of hydrogen peroxide.

**Hydrogen peroxide**:

Hydrogen peroxide is an oxidizing agent but not especially reactive and its main significance lies in it being a source of hydroxyl radicals in the presence of transition metal ions.

**Hydroxyl Radical**:

Hydroxyl radical is an extremely oxidizing radical that will react with most biomolecules at diffusion controlled rates it has extremely short half life but is capable of causing great damage.
All major classes of biomolecules may be attacked by free radicals but the lipids are most susceptible. Poly unsaturated fatty acids (PUFA) which are readily attacked by oxidizing radicals and the oxidative destruction of PUFA known as lipid peroxidation it is particularly damaging because it proceeds as self perpetuating chain reaction.52

Chemical compounds and reaction capable of generating potential toxic oxygen species can be referred as pro-oxidants are simply oxidants. And on other hand compounds and reactions disposing of these species by scavenging them, suppressing their formation or opposing their action are antioxidants.

In normal cell the appropriate balance with in cell is maintained defenses against the deleterious action of free radicals are known as antioxidant defense and the two main categories are those, whose role is to prevent the generation of free radicals and those that intercept any, that are generated. They exist in both the aqueous and membrane compartments of cells and can be enzymes or non-enzymes.
Superoxide dismutase (SOD), Glutathione peroxidase and catalase play most important role in antioxidant defense system to intercept or scavenge free radicals whose substrate is free radical while role of in defense is removal of peroxides that reacts with transitional metal ions to produce reactive free radicals.

Adenosine Deaminase (ADA) is an enzyme involved in purine metabolism. A lack of ADA is responsible for deterioration in lymphocytes response as well as failure of lymphocytes to proliferate causing lymphopenia. ADA deficiency is associated with severe combined immuno deficiency Disease (SCID). The intracellular accumulation of adenosine interferes with critical metabolic function including DNA synthesis.

In present study attempt has been made to explore the role of lipid peroxidation, Adenosine deaminase activity, superoxide dismutase, catalase, glutathione peroxidase and trace elements in patients with leprosy, assessment correlate severity of disease.