Malaria continues to be one of the major killer disease inflicting human race in tropical countries. Malarial infection causes structural and functional alteration in different organs of host viz. liver, spleen and kidney. Several attempts have been made at structural and biochemical levels to understand mechanism for liver damage in malaria infected host, since liver is the primary organ of homeostasis in mammals. However its complications remains the prominent cause of morbidity and mortality in the developing world.

In the present study, cell-line of rodent malaria parasite, *Plasmodium berghei* (NK-65 strain, India) was maintained. The parasite upon inoculation caused 100 percent mortality in white albino mice. The percent parasitaemia was evaluated by Leishman stained thin smears of infected blood, when parasitaemia reached upto 60-70 percent, animals were sacrificed by cervical dislocation, their liver were excised and then homogenized for estimating the different biochemical constituents.

During the infection the total lipid content in liver was increased significantly by (84.49%). The present study showed that liver cholesterol content in albino mice was depleted significantly, similarly phospholipids content of liver was found to decrease by (19.90%). The study further revealed
that liver from *P. berghei* infected mouse produces more lipid peroxidation as compared to control animals (314%). The effect on carbohydrate metabolism was also indicated by decrease in glucose and glycogen contents by (78.76%), (84.87%) and (78.6%) respectively. As regards to protein metabolism significant decrease in liver protein values was observed, indicating extensive proteolysis of amino acids for proliferation of parasite. Another reason for decrease in protein synthesis might be due to decrease in content of nucleic acid. DNA decreased by (79.58%) and RNA by (29.7%). With the onset of infection, a statistically significant decrease in GPT and GOT level by 22% and 42.5% respectively, were found in liver. Similarly, content of acid and alkaline phosphatases were estimated during severe infection. Acid phosphatase and alkaline phosphatase content of liver during *P. berghei* infection increased significantly, the acid phosphatase by 75% and alkaline phosphatase by (90%).

On the other hand, the liver damage caused by invading parasites was demonstrated by performing several liver function tests in serum to evaluate the levels of SGPT, SGOT, acid phosphatase and alkaline phosphatase. SGPT level in serum was found to increase by (188%). SGOT level increased by (84%), acid phosphatase by (215%) and alkaline phosphatase by (99%).
Total lipid, and nucleic acids contents in tissue were also demonstrated by some histochemical technique. Histochemical studies revealed that liver section showed large amount of deposition of lipid droplets throughout the lobules, which mainly causes fatty liver. We have also confirmed decrease in nucleic acid content in infected liver tissue section by above technique.

The role of immunity in protection or at least in minimizing biochemical alteration was studied in immunized animals. Albino mice were immunized against *Plasmodium berghei* using soluble *P. berghei* antigen in combination with TDM (6'6'-Trehalose Dimycolate). The intracellular parasite, *P. berghei* was isolated from infected RBC by means of multistep experimental protocol. The infected blood was collected in ACD (Acid citrate dextrose), 85 percent platelets and 98.9 percent leucocytes were removed by passing the infected blood through column packed with C~cellulose and microcrystalline cellulose.

Saponin was successfully used to induce the lysis of red blood cells. About 100% erythrocytes were lysed and the RBC debris was removed by washing with chilled normal saline. Parasites were separated from this lysate by density gradient centrifugation on Histopaque. The parasites appearing in a brown band at interface were withdrawn carefully and washed three times with normal saline (0.154M NaCl, pH 7.2). The purity of isolated parasite preparation was checked microscopically.
There were no apparent host cell contaminants in Leishman stained smears prepared from isolated parasite material. For the preparation of antigen, the isolated parasites were disrupted by ultrasonication at 9KHz for 6 mts. This preparation centrifuged at 10,000 rpm for 1 hour. The supernatant thus obtained was used as soluble antigen in these investigation.

The purity of isolated *P. berghei* antigen was checked by immunodiffusion (ID), counter immuno-electrophoresis (CIE) and PAGE analysis. Nonwithstanding the host cell contaminants, it was assumed that the isolated antigen preparation were comparatively pure by using above techniques.

Concentration of protein, DNA, RNA and hexoses in soluble antigen extracts was estimated as 2,500 ug, 200 ug, 400 ug and 200 ug respectively. Antigen characterization was also carried out on sodium dodecyl polyacryl amide gel electrophoresis. The parasite antigen extracts resolved into eleven protein bands in the molecular weight range of 12,000 to 150,000 daltons.

In the immunized animals, total leucocyte count was found to increase. The increase in total leucocyte count was highest in animals immunized with Ag plus TDM. Biochemical assays were carried out in animals after completion of immunization. Serum transaminase, phosphatase contents of
albinomice after immunization were found nearer to control values.

Inoculation of 500 ug TDM alone also provide 100% protection by providing non-specific resistance in host against the infection.

Detection of humoral immune response was carried out by immunodiffusion, indirect haemagglutination (IHA) tests and enzyme linked immunosorbant assays (ELISA). Animals which were immunized with Ag-TDM preparation showed precipitin bands in ID test. Highest reciprocal titre of 512 by IHA and 1024 by ELISA tests was detected in animals which were immunized with Ag-TDM combination. Specific antibody titre values were comparatively lower in animals immunized with antigen and adjuvant alone.

The cell mediated immune response in the immunized animal were detected by delayed type skin hypersensitivity (DTH) reaction and leucocyte migration inhibition (LMIT) test. The delayed type skin reaction reached a maximum at around 24-48 hours in animal immunized with Ag-TDM combination. Other experimental group showed weak skin reaction indicating the absence of proper CMI response. The migration of peritoneal exudate cells obtained from the animals immunized with Ag-TDM was greatly inhibited in presence of P. berghei antigen. There was no significant
migration inhibition of cells from other control groups.

Further, histopathological studies revealed that the liver parenchyma showed patchy necrosis in centrilobular region indicating hepatocellular damage. Sinusoids were dilated, filled with hypertrophied kupffer cells containing phagocytosed parasites, malarial and hemosiderin pigments.

Immunized animals did not show any parasitic infiltration in liver. No pathophysiological changes were observed in immunized liver sections. Haematoxylin and eosin stained sections of liver from immunized animals showed normal architecture.

The findings made from various experiment has helped in understanding the aetiology of the massive changes that takes place at high parasitaemia, in mice during *P. berghei* infection. The immunological studies further showed that immunization against malarial infection helps in minimizing morbidity and mortality due to *P. berghei* infection.