5. SUMMARY

5.1 Malaria has been afflicting human population and it has surfaced as a growing problem in Madras city.

5.2 173 patients infected with *P. vivax* were taken for the study and the antioxidant status of infected RBC was compared with that of 63 age and sex-matched healthy controls. 20 negative controls were also included. Out of 173 recurrent malaria patients, 49 patients had only one attack, 46 two attacks, 37 three attacks and 41 more than three attacks. Vitamin E supplementation therapy was carried out in a section of the infected patients, and follow-up study was done to assess the efficacy of vitamin supplemented antimalarial regimen.

5.3 A steady fall in the level of haemoglobin was observed with increasing number of attacks. A significant decrease (p<0.05) in PCV level was observed during the first and second attack, and it lowered further with the third (p<0.01) and multiple attacks (p<0.001). The malarial patients showed a progressive decrease in RBC level with increasing number of attacks. The decrease in the haematological indices was statistically significant at all levels of parasitaemia. During vitamin E supplementation, haemoglobin, PCV and RBC levels were regained to normalcy, in comparison to patients treated with chloroquine alone.
5.4 There was a marked increase in the osmotic fragility of the malarial erythrocytes (I attack - p<0.05; II attack - p<0.01; III attack - p<0.01 and IV attack - p<0.001) when compared to that of controls. However, during the first two attacks, MCH and MCHC did not show any significant change but during repeated attacks, a remarkable decrease in MCH (p<0.05) and MCHC (p<0.01) levels were observed. During all attacks, an increase (p<0.050) was observed in the MCV level of the recurrent malarial patients. Pronounced Heinz body formation (p<0.001) was observed from the primary attack onwards and it augmented in patients with repeated attacks.

Parasite density significantly influenced the fragility of the erythrocytes, Heinz body formation, MCV, MCH and MCHC levels. Vitamin E administered patients showed a speedy recovery with reference to these haematological indices.

5.5 Malaria had negligible effect on blood glucose level. The increase in uric acid level was more pronounced with increasing number of attacks. Though a marginal insignificant decrease was observed in the globulin fraction during malarial infection, the albumin fraction exhibited a steady fall with increasing number of attacks. Cholesterol levels showed a marked decrease from the II attack onwards. These biochemical parameters manifested significant changes at all levels of parasitaemia. Chloroquine when administered alone and along with vitamin E, brought their levels to normal limits.
5.6 The concentration of total bilirubin level was significantly elevated from the primary attack onwards. This increase was associated with significant (p<0.01) increase in both conjugated and unconjugated levels. With reference to the liver marker enzymes, ALT level was significantly elevated during the IV attack (20.33 units/ml) when compared to the control (11.52 units/ml), II attack (14.73 units/ml) and III attack patients (16.96 units/ml). However, AST level was significantly elevated (p<0.01) relative to the control only in the fourth attack patients. The serum cholinesterase activity was found to be decreased while acetylcholinesterase increased compared to that of control subjects, during malarial infection. The biochemical markers showed a progressive decrease with increasing levels of parasite density.

These indices were brought back to near normal levels after drug treatment.

5.7 Plasma lipid peroxidation was increased both in fresh (p<0.05) and recurrent malaria (p<0.001) patients. The increase was dependent on the number of attacks. The mean GSH values decreased progressively with the increase in the number of attacks. The concentrations of plasma vitamin E, A and ascorbate, manifested a linear decrease with increase in the number of attacks. Similarly, the RBC GSH and TSH contents were also markedly depleted during fresh (p<0.01) and recurrent malaria (p<0.001), when compared to that of the control. It is significant to note that RBC vitamin E level increased in the recurrent malarial patients.
Unlike the fresh malaria patients, parasitaemia significantly influenced plasma. MDA levels in the recurrent malaria patients. The concentration of the antioxidants were significantly reduced in both fresh and multiple attack patients, at all levels of parasitaemia.

Chloroquine administration lowered the plasma lipid peroxidation content (11% decrease compared to malarial patients), and this peroxide scavenging action was more profound in chloroquine and vitamin E administered patients (18% decrease compared to malarial patients). Quinine therapy brought about only a marginal increase in the antioxidant status, but when coadministered with vitamin E, a remarkable hike in the levels of the antioxidants was observed in comparison to the untreated malarial patients.

5.8 A linear increase in TBARS release was observed with increasing number of attacks. The percent maximal release was found to be significantly high in I (8.90, p<0.01), II (9.22, p<0.01), III (8.76, p<0.01) and IV attacks (9.31, p<0.001), when compared to that of the healthy subjects (7.46). Patients exhibited an increased TBARS level when compared to the controls and fresh malaria patients, at different parasite densities.

5.9 SOD showed a significant decrease in its activity during the primary (p<0.05), second (p<0.01), third (p<0.001) and multiple infections (p<0.001) when compared to the healthy controls. The catalase activity in the normal subjects (791.99 μmoles/min/mg protein) was significantly
inhibited during I (687.47 μmoles/min/mg protein), II (604.40 μmoles/min/mg protein), III (513.84 μmoles/min/mg protein) and IV attacks 942.0 μmoles/min/mg protein) as evidenced by the F ratio (p<0.001). Ceruloplasmin levels showed an increase with the number of malarial attacks.

During the initial attack, parasitaemia had little effect on the enzyme activities but during later infections, a profound inhibition was noticed. In the vitamin E supplemented group, the elevation of the enzyme activities encountered was higher than in patients administered chloroquine alone. RBC acetyl cholinesterase, which was increased in vivax malaria (p<0.05), manifested a further increase (p<0.01) during chloroquine treatment. Chloroquine and vitamin E combination therapy established its efficacy in lowering (p<0.05) RBC acetyl cholinesterase activity, when compared to malarial patients treated with chloroquine alone.

5.10 Relative to the control (29.92 μmoles/g Hb), malarial infection caused a profound decrease in GPX activity in the I attack (26.97 μmoles/g Hb; p<0.05), II attack (25.20 μmoles/g Hb; p<0.01), III attack (24.41 μmoles/g Hb; p<0.001) and IV attack (24.97 μmoles/g Hb; p<0.001) patients. An inverse interaction between malarial recurrence and G6PD and GR activities was observed (I and II attacks - p<0.01; III and IV attacks - p<0.001). Recurrent malarial patients showed significantly low (p<0.05) GST activity when compared to the healthy controls. A
significant inhibition of the enzymes was observed in the recurrent malarial patients at all levels of parasitaemia.

Chloroquine treatment was effective in raising the activity of the glutathione metabolising enzymes. However, vitamin E supplementation afforded better protection than chloroquine alone.

5.11 To test whether blood groups influence recurrence of *P. vivax* malaria, analysis was done in 76 control subjects and 49 cases of I attack, 46 cases of II attack, 37 cases of III attack and 41 cases of more than III attack patients. It is evident that blood groups A,B and AB had negligible influence on the rate of recurrence. Interestingly, almost a direct correlation was observed between the percentage of incidence of blood group O and the number of malarial attacks.

5.12 The parasite count did not vary much during the I and II attacks. During the III attack, the mean parasite density observed in patients with blood group O was higher (p<0.05) than the mean parasite density of blood groups AB, A and B. During the IV attack, mean parasite density differed significantly in blood group A (p<0.05), B (p<0.05) and O (p<0.01), when compared to blood group AB. Furthermore, the parasite count of blood groups A and B were significantly low (p<0.05) in comparison to blood group O.
5.13 No significant variation was observed in the haemoglobin levels during the I and II attacks. During the III and IV attacks, the mean haemoglobin levels observed in blood groups B and AB were significantly higher than the mean haemoglobin level of blood group O.

5.14 In the control subjects and fresh malaria patients (I attack), the blood groups did not influence plasma MDA formation. The MDA content was higher in blood group A during the II and IV attacks, when compared to blood group AB. A significant elevation in MDA levels was observed in blood group O than in blood group AB, during the III and IV attacks.