The primary aim of the current study was to compare the plasma levels of pro- and anti-angiogenic factors and oxidative stress between normal subjects, diabetic patients without retinopathy, diabetic patients with non-proliferative retinopathy and those with proliferative retinopathy. Their levels in plasma were compared before and after LASER and anti-VEGF therapy.

- Higher levels of pro-angiogenic factors (VEGF-A, HIF-1α, MMP-9 and NO), lower anti-angiogenic factor (PEDF) and imbalance in the oxidative status in patients with NPDR and PDR indicated their involvement in the pathogenesis of retinopathy.

- The oxidative stress markers could effectively differentiate NPDR from PDR subjects. The angiogenic factors were found to be efficient in diagnosing PDR. This indicates initial changes in the retina of diabetic subjects might be initiated by oxidative stress, which is followed by hypoxia and the release of angiogenic factors in the advanced stages of retinopathy.

- The plasma levels of PDE was significantly decreased in patients with PDR indicating its involvement in pathogenesis of retinopathy.

- None of the demographic variables were found to have a clinically significant impact on any of the parameters considered for the study. This excludes their possible confounding effects on the variation observed in study parameters among different study groups.

- Plasma levels of angiogenic factors, VEGF-A, HIF-1α, MMP-9 and NO were significantly increased after anti-VEGF therapy for NPDR while levels of VEGF-A and NO were decreased significantly following LASER therapy for proliferative retinopathy. Plasma anti-angiogenic factor PEDF was unaltered following LASER therapy for proliferative retinopathy, but it was decreased after anti-VEGF therapy in case of NPDR. Malondialdehyde levels were increased after anti-VEGF therapy in case of NPDR while it is decreased flowing LASER therapy for proliferative retinopathy. Plasma levels of sRAGE and thiols remain unaltered. This may indicate persistent hypoxia and increased oxidative stress in the retina after anti-VEGF therapy.
• Levels of angiogenic factors were significantly increased and anti-angiogenic (PEDF) factors were decreased significantly irrespective of therapeutic outcome in patients who had undergone anti-VEGF therapy. LASER therapy resulted in a significant decrease in the levels of potent angiogenic factors, VEGF-A, HIF-1α irrespective of therapeutic outcome.

• This may imply that, irrespective of treatment outcome, anti-VEGF therapy can result in increased plasma levels of angiogenic factors, oxidative stress and a decrease in anti-angiogenic factors.

• How long the increase in the levels of these factors persists following the therapy and their impact on long term outcome needs to be evaluated.