CHAPTER - III

RESULTS

3.1 Evaluation of biochemical, haematological and immunological alterations in type 2 diabetes mellitus.

3.1.1 Biochemical alterations in type 2 diabetic patients.

In the present study the following biochemical alterations occur in type 2 diabetic patients. Fasting and postprandial blood glucose were found to be significantly elevated in type 2 diabetics (group II) when compared to group I normal subjects as given in table 1 and fig. 8. Urea and creatinine levels were elevated in type 2 diabetic patients (group I) when compared to group I as given in table 1 and fig. 10. The level of insulin in type 2 diabetic patients was found to be lesser than the normal range as given in group II.

Glycemic control was monitored by measuring glycosylated haemoglobin which showed poor control in type 2 diabetics (group II) as observed in table 1 and fig. 9. Poor glycemic control in type 2 diabetic patients is mainly produced by elevated levels of glycosylated Hb in group II subjects.

Table 2 reveals the status of lipid abnormalities seen in type 2 diabetic subjects (group II). The levels of total cholesterol, triglyceride, LDL and FFA were found to be significantly increased above the normal range in type 2 diabetic patients (group II) when compared to group I as given in fig. 11 and 12.

Table 3 and fig. 13 shows the alterations in the levels of uric acid, homocysteine and urine microalbumin in type 2 diabetic subjects (group II). The levels of all the three parameters were found to be significantly elevated in group II when compared with group I subjects (normal healthy subjects).
Elevated levels of hepatic enzymes such as AST, ALT and ALP indicate the LFT abnormalities associated with type 2 diabetic patients as given in table 4 and fig. 14.

3.1.2 Haematological alterations in type 2 diabetic patients

There was no alteration in the level of RBC in type 2 diabetic patients (group II) when compared to group I. WBC count was found to be significantly elevated in type 2 diabetic subjects when compared to normal (table 5).

In differential count, all the types of white blood cells were found to be elevated in group II (type 2 diabetic patients) except basophils which was found to be within the normal range as given in table 5. ESR was significantly elevated in group II when compared to group I (normal healthy subjects) as given in table 5 and fig. 15 and 16.

3.1.3 Alterations in the levels of various immunological parameters in type 2 diabetic patients.

The levels of immunoglobulins such as IgG, IgM, IgE and IgA were found to be significantly raised in group II subjects when compared to normal individuals (Table 6 and fig. 17 and 18).

Table 7 depicts the status of various inflammatory markers in type 2 diabetic patients as given in type 2 diabetic patients as given in group II. The inflammatory markers include CRP, cortisol, C3, ceruloplasmin, fibrinogen, haptoglobin, α1 antitrypsin and PAI-1.

The levels of all the above inflammatory markers were found to be significantly increased in group II (type 2 diabetic subjects) when compared to normal (group I) subjects as given in table 7 and fig. 19 and 20.
Alterations in cytokine mediators (IL-6 and TNF-α) and anti-inflammatory marker (adiponectin) was shown in table 8. This reveals that both the cytokine mediators were found to be significantly elevated in group II subjects when compared to group I. However, the anti-inflammatory marker (adiponectin) was found to be significantly decreased in group II subjects when compared to normal (group I) subjects as given in table 8 and fig 21.

3.2 Effect of rosiglitazone in type 2 diabetic patients.

3.2.1 Effect of rosiglitazone on biochemical parameters in type 2 diabetic patients

In the present study, rosiglitazone therapy (group III) was found to lower blood glucose concentration in both fasting and postprandial condition as given in table 1 and fig. 8. The levels of urea and creatinine were also significantly decreased by rosiglitazone treatment in group III subjects when compared to group II (type 2 diabetic patients). The level of insulin in rosiglitazone treated subjects was found to be within the normal range as given in group III.

Glycemic control by rosiglitazone therapy in group III subjects was monitored by the estimation of glycated hemoglobin. Rosiglitazone was found to provide a good glycemic control when compared to group II (type 2 diabetic patients) as given in table 1 and fig. 9.

Table 2 shows the effect of rosiglitazone on lipid profile in type 2 diabetic patients as given in group III. The levels of total cholesterol, triglyceride, LDL, FFA were found to be significantly decreased in group III when compared to group II as given in table 2 and fig 11 and 12. Rosiglitazone therapy in group III subjects was found to raise the HDL level significantly when compared to group II (type 2 diabetic patients).

Rosiglitazone therapy produces alterations in the levels of uric acid, homocysteine and urine microalbumin as shown in group III of table 3 and fig. 13. The levels of all the
three parameters were found to be significantly decreased in group III subjects when compared to group II.

On *rosiglitazone* therapy, the LFT abnormalities seen in type 2 diabetic patients was found to disappear as given in group III of table 4 and fig 14. AST, ALT and ALP were found to decrease as a result of *rosiglitazone* therapy in group III when compared to group II (table 4).

### 3.2.2 Effect of *rosiglitazone* on haematological parameters in type 2 diabetic patients

In the present study, haematological alterations were observed as a result of *rosiglitazone* therapy as given in group III of table 5. The effect of *rosiglitazone* therapy in group III subjects was not significant as there was no variation in the RBC count of group III subjects. WBC count was found to be significantly decreased by *rosiglitazone* therapy in group III subjects as given in table 5 when compared to group II (type 2 diabetic patients).

In the differential count, all the components were brought back to the normal range (group III) except basophils as it was found to be normal in group II subjects as given in table 5 and fig. 15 and 16. ESR was also found to be within the normal range in group III subjects as given by table 5. This supports the anti-inflammatory activity of *rosiglitazone* in type diabetic patients.

### 3.2.3 Effect of *rosiglitazone* on immunological parameters in type 2 diabetic patients

This deals with the evaluation of the effect of *rosiglitazone* therapy on immunological status in type 2 diabetic patients. The levels of immunoglobulins (IgM, IgA, IgG and IgE) were found to revert back to normal range in group III subjects as given in table 6 and fig. 17 and 18. These results confirm improvement of immune status in type 2 diabetic patients on treatment with *rosiglitazone*. 
Table 7 reveals the status of inflammatory markers such as CRP, ceruloplasmin, C3, cortisol, fibrinogen, haptoglobin, α1 AT and PAI-I in type 2 diabetic patients on treatment with rosiglitazone (group III). The levels of all the above inflammatory markers were found to be significantly decreased by rosiglitazone therapy as given by group III of table 7 and fig. 19 and 20.

The effect of rosiglitazone therapy on the levels of cytokine mediators (IL-6 and TNF-α) and anti-inflammatory marker (adiponectin) was shown in table 8 and fig. 21. The results show that the levels of IL-6 and TNF-α were found to be significantly decreased by rosiglitazone, whereas adiponectin was significantly increased in group III subjects by rosiglitazone therapy.

3.3 Effect of pioglitazone in type 2 diabetic patients.

3.3.1 Effect of pioglitazone on biochemical parameters in type 2 diabetic patients.

In the present study, pioglitazone therapy was found to lower both fasting and postprandial blood glucose levels as given in group 4 and fig. 8 (Table 1). Pioglitazone therapy also significantly decreases the levels of urea and creatinine in group IV subjects when compared to group II as given in table 1. The level of insulin in pioglitazone treated subjects was found to be within the normal range as given in group IV.

Pioglitazone therapy was shown to provide an excellent glycemic control in type 2 diabetic patients (group IV) when compared to group II subjects (group II) as given by the measurement of HbA1C in table 1 and fig. 9.

Table 2 indicates the effect of pioglitazone on lipid levels in type 2 diabetic patients as given in group IV. The levels of total cholesterol, triglyceride, LDL and FFA were found to be significantly decreased in group IV subjects when compared to group II as given in table 2. But pioglitazone therapy in group IV subjects was found to raise HDL.
when compared to group II and hence serves as an effective scavenger of bad cholesterol. *Pioglitazone* therapy in group IV subjects contributes to significant decrease in the levels of uric acid, homocysteine and urine microalbumin when compared to group II subjects as given in table 3 and fig. 13.

On treatment with *pioglitazone*, abnormalities in liver enzymes were found to revert back to normal function. This is mainly due to decrease in the levels of AST, ALT and ALP seen in group IV mainly mediated by the effect of *pioglitazone* (Table 4 and fig. 14).

### 3.3.2 Effect of *pioglitazone* on haematological parameters in type 2 diabetic patients

In the present study, haematological alterations were produced by *pioglitazone* therapy in type 2 diabetic patients as given in group IV of table 5. RBC count was found to be significantly decreased by *pioglitazone* therapy in group IV subjects as given in table 5 when compared to group II (type 2 diabetic patients) ruling out the occurrence of anemia in such subjects. WBC count was found to be significantly decreased by *pioglitazone* therapy in group IV subjects as given in table 5 when compared to group II type 2 diabetic patients.

*Pioglitazone* therapy normalizes the elevated differential count in group IV subjects except basophils as it was found to be in normal percentage as given by group IV of table 5. ESR was also found to be within the normal range in group IV subjects as given by table 5 and fig. 15 and 16. This supports the anti-inflammatory activity of *pioglitazone* in type 2 diabetic patients.
3.3.3 Effect of pioglitazone on immunological parameters in type 2 diabetic patients

This deals with the evaluation of the effect of pioglitazone therapy on immunological status in type 2 diabetic patients. The levels of immunoglobulins such as IgA, IgM, IgG and IgE were found to be within the normal range in group IV subjects (table 6 and fig. 17 and 18) when compared to group II. The above observation was mainly attributed to improvement of immune status in type 2 diabetic patients on treatment with pioglitazone.

Table 7 reveals the levels of inflammatory parameters such as CRP, cortisol, C 3 , ceruloplasmin, fibrinogen, haptoglobin, alpha 1 anti - trypsin and PAI - 1 in type 2 diabetic patients on treatment with pioglitazone (group IV). The levels of all the above inflammatory markers were found to be significantly decreased by pioglitazone therapy when compared to group II as given in table 7 and fig. 19 and 20.

The results of the effect of pioglitazone in type 2 diabetic patients (group IV) reveals a significant decrease in the levels of adipokine mediators such as IL-6 and TNF-α and a significant decrease in the level of adiponectin (anti-inflammatory marker) when compared to group II subjects as given in table 8 and fig. 21.

3.4 Comparison between the effect of rosiglitazone and pioglitazone in type 2 diabetic patients.

3.4.1 Effect of rosiglitazone and pioglitazone on biochemical parameters in type 2 diabetic patients.

In the present study, both pioglitazone and rosiglitazone therapy were found to produce a similar decrease in the levels of fasting and postprandial blood glucose as given in table 1 and fig. 8 (group III vs IV group). Pioglitazone therapy was found to
produce significant decrease in the levels of urea and creatinine and significant increase in insulin when compared with *rosiglitazone* therapy (group III vs IV).

*Pioglitazone* therapy was found to offer an excellent glycemic control (HbA1c) which was found to be equivalent in comparison with *rosiglitazone* treatment in type 2 diabetic subjects as given in table 1 and fig. 9.

Table 2 indicates the effect of *pioglitazone* and *rosiglitazone* on lipid levels in type 2 diabetic subjects (group III and IV). *Pioglitazone* treatment was found to be superior over *rosiglitazone* treatment (group III) in normalization of altered lipid profile in type 2 diabetic subjects (Table 2) thereby contributing to cardioprotection.

*Pioglitazone* therapy in group IV subjects showed a greater decrease in the levels of uric acid, homocysteine and urine microalbumin when compared to group III subjects treated with *rosiglitazone* therapy (Table 3 and fig. 13).

Both *pioglitazone* and *rosiglitazone* treatment supports normal liver functioning by maintaining the levels of hepatic enzymes such as AST, ALT and ALP within the normal range thereby ruling out the effect of hepatotoxicity (Table 4 and fig. 14).

### 3.4.2 Effect of *rosiglitazone* and *pioglitazone* on haematological parameters in type 2 diabetic patients.

In the present study *pioglitazone* treatment was found to be superior over *rosiglitazone* in normalizing the hematological status in type 2 diabetic subjects (group III vs IV) as given in table 5. Anemia was eliminated in both the treatments as they maintain a normal RBC count in type 2 diabetic patients. The decrease in WBC count was found to be more significant with regard to *pioglitazone* therapy when compared to *rosiglitazone* therapy (group IV vs III) as given in table 5.

Group III and IV subjects showed a normal differential count as both the thiazolidinediones - *rosiglitazone* and *pioglitazone* maintain the number of different types
of white blood cells within the normal range (Table 5). ESR was found to be within the normal range in both group III and group IV as given in table 5 and fig. 15 and 16. The effect was found to be better and effective in the case of group IV subjects treatment with \textit{pioglitazone}.

### 3.4.3 Effect of \textit{rosiglitazone} and \textit{pioglitazone} on immunological parameters in type 2 diabetic patients

This deals with the comparison of efficacy between \textit{pioglitazone} and \textit{rosiglitazone} on immunological status in type 2 diabetic patients. The levels of IgA, IgM, IgG, IgE were found to be within the normal range in both the groups (group III and IV). The decrease of immunoglobulin levels were found to be greater in the case of \textit{pioglitazone} when compared to \textit{rosiglitazone} therapy as given in table 6 and fig. 17 and 18.

Table 7 reveals the superior role of \textit{pioglitazone} therapy on the effect of inflammatory markers in type 2 diabetes mellitus when compared to \textit{rosiglitazone} therapy (group III vs group IV). The levels of both adipokine mediators (IL-6 and TNF-\textalpha) in group IV and V subjects were found to be significant different from group II subjects. The decrease in the levels of the above mentioned cytokine mediators were higher in \textit{pioglitazone} treated group IV when compared to \textit{rosiglitazone} treated group III as given in table 8 and fig. 17 and 18. The increase of adiponectin was found to be greater in the case of \textit{pioglitazone} when compared to \textit{rosiglitazone} therapy as given in table 8 and fig. 21.

Thus \textit{pioglitazone} therapy was found to be more effective than \textit{rosiglitazone} therapy in type 2 diabetic subjects.