CHAPTER – VI

SUMMARY AND CONCLUSION

Uptil now studies have performed addressing the role of Glycosylated Hemoglobin in Diabetes mellitus as an index of glycemic control. However, data regarding the role of Glycosylated Hemoglobin in diabetes with microvascular and macrovascular complications and in non-diabetic disorders like chronic renal failure and iron deficiency anemia are scanty.

The present study was carried out to evaluate Glycosylated Hemoglobin level in diabetic patients with microvascular and macrovascular complications, chronic renal failure and iron deficiency anemia patients. Age and sex matched control cases comprised of healthy individuals were also studied to establish the normal range of Glycosylated Hemoglobin. In all these patients Glycosylated Hemoglobin was measured by affinity chromatography. The technique of affinity chromatography definitely offers significant advantage over other techniques.

Findings of the present study were tabulated and statistically analysed by performing students’ t’ test.
Chapter-III: Glycosylated Hemoglobin in Complications of Diabetes

Diabetes mellitus is a life-long disease which many people worry about the quality and longevity of their life after being diagnosed with it. The microvascular (retinopathy, cataract, nephropathy and neuropathy) and macrovascular (hypertension, dyslipidemia, ischemic heart disease, coronary artery disease, peripheral vascular disease and cerebrovascular disease) complications of Diabetes are influenced not only by the duration of Diabetes but also by the average level of chronic glycemia which is measured most reliably with Glycosylated Hemoglobin assay.

By performing Glycosylated Hemoglobin test, health providers can measure a patient’s average glycemia over the preceding 2-3 months and thus, assess treatment efficacy. Glycosylated Hemoglobin testing should be performed routinely in all patients with Diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Glycemic control is best judged by the combination of the results of the patients Self Monitoring of Blood Glucose testing and the current Glycosylated Hemoglobin.

Each 1% reduction in mean Glycosylated Hemoglobin concentration is associated with a reduction in risk of 20% for any end point complications related to Diabetes.
Glycemic control as reflected by Glycosylated Hemoglobin is strongly associated with microvascular disease in individuals with Diabetes, but its relation to macrovascular disease and atherosclerosis is less clear.

From the Diabetes Control and Complication Trial (DCCT) and the United Kingdom Prospective Diabetes study it is clear that the degree of metabolic control influences the development of complications, particularly microvascular complications. A similar protective effect on macrovascular complication has not been reported.

By considering the importance of Glycosylated Hemoglobin in Diabetes, the present study was planned to evaluate the biochemical correlation of Glycosylated Hemoglobin and other blood/serum parameters (Lipid profile, kidney function test, and sensitivity of erythrocytes to peroxide hemolysis) in diabetic patients having microvascular (retinopathy, cataract, nephropathy and neuropathy) and macrovascular (hypertension, dyslipidemia, ischemic heart disease, coronary artery disease, peripheral vascular disease and cerebrovascular disease) complications.

The observations of the present study in diabetic patients with microvascular (retinopathy, cataract, nephropathy and neuropathy) and macrovascular (hypertension, dyslipidemia, ischemic heart
disease, coronary artery disease, peripheral vascular disease and cerebrovascular disease) complications are:

1. The level of glycosylated hemoglobin in healthy controls was found to be $4.6\% \pm 0.82\%$.

2. Majority of patients with these complications had poor diabetic control in form of hyperglycemia and elevated Glycosylated Hemoglobin levels. More pronounced effect was observed in diabetic macrovascular complication i.e. diabetic cerebrovascular disease patients with mean value of Glycosylated Hemoglobin $9.96\% \pm 2.44\%$. These findings will provide new dimensions to the role of Glycosylated Hemoglobin.

3. Most of the patients with these complications had elevated lipid profile but more pronounced atherogenic lipid profile was seen in diabetic dyslipidemia patients. A positive correlation was obtained between Glycosylated Hemoglobin and lipid profile in all the subjects. *These findings clearly indicate that Glycosylated Hemoglobin is not only a useful biomarker of long-term glycemic control but also a good predictor of lipid profile.* Thus monitoring of glycemic control using Glycosylated Hemoglobin could have additional benefits of identifying diabetic patients with complications who are at a greater risk of cardiovascular complication. *These results allow us to point out the usefulness and the application of Glycosylated Hemoglobin*
determination in evaluating the relationship between carbohydrate and lipid metabolism, particularly in complications of diabetes.

4. Severe renal impairment was observed in case of diabetic nephropathy subjects. Diabetic patients with complications along with renal impairment have an increased risk for cardiovascular disease. A positive correlation was obtained between Glycosylated Hemoglobin and renal function in complications of diabetes indicating that Glycosylated Hemoglobin may be a clinically useful tool for assessing diabetic renal complications.

5. An association of poor glycemic control with increased lipid peroxidation in erythrocyte membrane of diabetic patients was obtained. Non-enzymatic glycosylation also induces the formation of oxygen derived free radicals which bring about a variety of hematological abnormalities in Diabetes. One such abnormality is increased lipid peroxidation of erythrocyte membrane resulting in their hemolysis. This focuses the new role of Glycosylated Hemoglobin in lipid peroxidation.

The measurement of Glycosylated Hemoglobin not only shows promise of being a successful approach to the monitoring of diabetic patient but also provides a conceptual framework for the pathogenesis of microvascular as well as macrovascular complications of
**Diabetes.** Further, the findings of the present study also indicate that **Glycosylated Hemoglobin is not only a marker of glycemic control but also a marker of dyslipidemia and renal dysfunction in microvascular as well as macrovascular complications of Diabetes.**

**Chapter IV: Glycosylated Hemoglobin in Chronic Renal Failure:**

Hyperglycemia is prevalent in chronic kidney disease. Glycosylated Hemoglobin used as a measure of chronic hyperglycemia is a sensitive and reliable marker of impaired glucose metabolism. Further, Glycosylated Hemoglobin can be used as a predictor of **future CAD events among nondiabetic patients in the general population.**

The observations of the present study in *chronic renal failure patients* are:

1. The mean Glycosylated Hemoglobin level in chronic renal failure patients was 6.0 ± 1.16% as compared to the control.

2. The plasma glucose levels of the patients were significantly higher as compared to the control and showed positive correlation with Glycosylated Hemoglobin.

3. The levels of serum triglyceride as well as serum cholesterol (which is a well established marker of cardiovascular disease)
were positively associated with Glycosylated Hemoglobin in these patients.

4. The serum HDL-C level was significantly decreased as compared to the control.

5. The blood urea and serum creatinine levels were significantly higher as compared to the control indicating that patients had more severe renal damage.

In view of the recent recognition of elevated plasma glucose and Glycosylated Hemoglobin as an independent indicator of cardiovascular morbidity and mortality, the present study recommend regular monitoring of plasma glucose and Glycosylated Hemoglobin in all cases with non diabetic CKD to help stratify patients for aggressive monitoring and reduction of cardiovascular risk.

**Chapter V: Glycosylated Hemoglobin in Iron Deficiency Anemia.**

**Iron deficiency anemia** occurs when iron deficiency is sufficiently severe to diminish erythropoiesis and cause the development of anemia. Iron deficiency is the most prevalent single deficiency state on a worldwide basis. It is important economically because it diminishes the capability of individuals who are affected to perform physical labor, and it diminishes both growing and learning in children. Some studies suggest that iron metabolism influences glycosylation of hemoglobin.
The findings of the present study in iron deficiency anemia patients are:

1. The values of Hemoglobin, Hematocrit and red blood cell indices were significantly decreased as compared to the control, suggesting presence of iron deficiency anemia.

2. The Glycosylated Hemoglobin levels in iron deficiency anemia patients were found to be 5.5 ± 1.0% showing higher values as compared to the control.

Iron metabolism influences glycosylation of hemoglobin in iron deficiency anaemia. However, the blood glucose concentration is normal as that in the control group. Therefore iron deficiency must be corrected before any diagnostic or therapeutic decision is made based on Glycosylated Hemoglobin.

The present study clearly establishes that estimation of Glycosylated Hemoglobin by affinity chromatography offer an advantage of superior technique over other methods.

The overall results of the present study demonstrate that increased Glycosylated Hemoglobin level is associated with long-term microvascular (retinopathy, cataract, nephropathy and neuropathy) and macrovascular (hypertension, dyslipidemia, ischemic heart disease, coronary artery disease, peripheral vascular disease and cerebrovascular disease) complications of Diabetes under study. The study also emphasizes that Glycosylated
Hemoglobin is not only a marker of glycemic control but also a marker of dyslipidemia and renal dysfunction in macrovascular as well as microvascular complications of Diabetes.

The increased levels of Glycosylated Hemoglobin in chronic renal failure and iron deficiency anemia patients suggest that chronic renal failure itself causes an increase in Glycosylated Hemoglobin level and iron deficiency anemia also influences glycosylation of hemoglobin.

Glycosylated Hemoglobin is significantly elevated not only in Diabetes but also in nondiabetic disorders like chronic renal failure and iron deficiency anemia. This shows that increased Glycosylated Hemoglobin level may be due to metabolic disturbances caused by these disorders. These aspects of the present study are novel.