Chapter 8

Conclusions
Conclusion

In conclusion, this study demonstrates the utility of biomarkers CCL18 in patients with Gaucher Disease and Niemann Pick Disease and Heparin Cofactor II Thrombin in Mucopolysaccharidoses Type I and II.

We established the reference range of enzyme Chitotriosidase in our pediatric population. We observed that plasma Chitotriosidase levels were highly elevated in Gaucher and Niemann Pick patients as compared to control group and it was statistically significant in gaucher disease and high in patients with Niemann Pick disease. Chitotriosidase was easy to establish in the laboratory.

**Ease and Robustness of Measurement:** We also established the reference range of biomarker CCL18/PARC in our pediatric population. We observed that plasma levels of CCL18 were also highly elevated in Gaucher and Niemann Pick patients as compared to controls and it was statistically significant in Gaucher and elevated five fold in Niemann Pick patients.

**Predictive Efficacy:** During natural course of Gaucher disease over a 12 and 24 month period this marker failed to demonstrate a statistical change. While both Niemann Pick patients were lost to follow up for estimation of CCL18 level, we cannot decide regarding its utility in disease progression in NP disease. The trends demonstrate that if followed over longer periods on a larger sample size an appreciable difference may be visualized.
Utility and ease of Urinary GAG’s: GAG analysis for both types of MPS was done and the reference range of GAG in pediatric population of North Indian ethnicity was established. The data showed that the GAG levels were elevated in both of these set of patients when compared age matched controls However, during natural course of disease over a 12 and 24 month period failed to demonstrate a statistical change.

Utility of HCIIT: HTCII T levels were highly elevated in MPS Type I (Hurler) and MPS Type II (Hunter) patients as compared to controls and it was statistically significant in both types of MPS. However, during natural course of disease over a 12 and 24 month period, this biomarker also failed to demonstrate a statistical change while demonstrating a positive trend. A good correlation between GAG’s and HCII T was obtained. So it is concluded that assessment of HC II T level in patients with MPS patients can help in the diagnosis and monitoring of patients with MPS I and II.

Our finding of markedly elevated plasma CCL18 levels in patients with Gaucher and Niemann Pick disease and Heparin Thrombin II cofactor levels in patients with MPS warrants further investigations regarding its role in the clinical management of GD, NP and MPS as well as its role in the peculiar pathophysiology of these disorders. Larger studies adequately powered including inclusion of uniform disease phenotypes may confirm our contention.
To conclude CCL18/ PARC and HCIIT are reliable screening biomarkers for this complex multisystemic group of disorders. These are reliable secondary biomarkers that are reflectors of altered cellular tissue homeostasis, hence likely to be more informative. However, considering the limitation to differentiate well between subtypes and to predict the course in attenuated phenotypes, we probably need to move from organ or pathway specific biomarkers. We need to comprehend that rather than focusing on ‘one stop- shop biomarker’ we need to utilize a panel of biomarkers to correlate with prediction, typifaction, disease progression and response to therapy. Considering that individually these diseases are rare, we need to participate in the international disease consortiums for a definite answer.