“A Study on glycosylation pattern of Serum Transferrin in patients with clinically suspected Congenital Glycosylation disorders”

Introduction:

Congenital disorder of glycosylation (CDG) is an inborn error of metabolism due to defective glycosylation of glycoproteins/glycolipids.It is a multisystem disorder with wide range of clinical presentations. Glycosylation pattern of a glycoprotein should be evaluated to diagnose this disorder.Transferrin is a glycoprotein whose glycosylation pattern does not changes with age. Therefore isoelectric focussing of serum transferrin is the gold standard technique to diagnose this disorder.

CDG prevalence is undoubtedly underestimated in our population due to lack of awareness & availability of automated, quick access diagnostic techniques.

Materials and Methods:

This study consists of two groups. Control group with 30 samples of apparently healthy individuals and cases group with 30 patients who were clinically suspected to have congenital disorders of glycosylation. Other differential diagnosis of their symptoms such as disorders of aminoacid metabolism, fatty acid oxidation defects, organic acidemias and structural anomalies of brain were excluded using possible investigations such as Urine metabolic screening, Tandem mass spectrometry, CT-Brain, ophthalmological and ENT evaluation. The cases were then screened for congenital disorders of glycosylation using capillary zone electrophoresis (CZE) of serum transferrin.

Results:

Statistical analysis was done using SPSS software version 20.0 by Independent sample T test and Chisquare test.

- Out of 30 cases three patients had abnormal transferrin pattern i.e. Carbohydrate deficient transferrin (CDT) - 7.5%, 66.4%, 56.4 %. (The reference interval of CDT is <1.3%)
- No statistical significant difference in the distribution of transferrin isoforms between different age groups and sexes in the control group.
- Statistically significant increase in the distribution of asialotransferrin was found in the group with history of consanguinous marriage in parents and in the group with cerebral atrophy as a radiological finding.

Discussion:

Out of 30 cases three cases showed increased Carbohydrate deficient. This observational study concludes that the prevalence of CDG is about 10% among the 30 cases which is a statistically significant finding. This finding inferes CZE of serum transferrin can be used as a simple technique to screen this disorder.

There is no statistical significant difference in the distribution of transferrin isoforms between different age group and sexes in the control group.Therefore age and gender specific reference interval for transferrin isoforms may not be important in the diagnosis of CDG

There is statistically significant increase in the aisialotransferrin isoform is present in the group with H/O of consanguinous marriage and in the group with positive radiological findings (cerebral atrophy). Since asialo transferrin contributes to the CDT measure, this finding infers that consanguinous marriage is a significant risk factor for congenital disorder of glycosylation and presence of radiological features adds as a supportive evidence for the diagnosis of CDG.

Conclusion:

- From this study we have first reported the presence of congenital disorders of glycosylation in our country
- The prevalence of congenital disorders of glycosylation is high in the study population.
- Capillary zone electrophoresis of serum transferrin can be used as a reliable screening technique to screen this disorder in our population
- Transferrin isoform levels do not vary between ages or sexes. Therefore age or gender specific reference interval for transferrin isoforms is not mandatory for the diagnosis of congenital disorders of glycosylation.
- Consangineous marriage is a significant risk factor for congenital disorders of glycosylation.
- Radiological finding of cerebral atrophy serves as a supportive evidence for the diagnosis of congenital disorders of glycosylation.

Key words: congenital disorders of glycosylation, carbohydrate deficient transferrin, capillary zone elctrophoresis, isoelectric focussing, screening, prevalence.