ABSTRACT

Mental retardation (MR) is an impairment that affects brain function and reflects functional defects in cognitive and adaptive behavior such as daily living skills, social skills and communication. MR affects 1-3% of the general population. It is a common problem with major implications for a nation’s health, education and community services. MR is a clinically and etiologically heterogeneous group of conditions whose pathogenesis is poorly understood. A number of environmental, genetic or multiple factors can cause mental retardation. It is also believed that behavioral or societal factors such as poverty, malnutrition, maternal drug and alcohol use, as well as severe stimulus deprivation can contribute to MR. Anything that damages and interferes with the growth and maturation of brain can lead to MR and this might happen before birth (Prenatal), during birth (Perinatal) or after the birth (Postnatal) of the child. On the basis of IQ test score, MR has been classified as borderline (70-84), mild (IQ 50–69), moderate (IQ 35–49), severe (IQ 20–34) and profound (IQ < 20).

A number of inborn errors of metabolism (IEM) have been reported worldwide affecting approximately 1 in 5,000 live births. IEM causes excessive accumulation of intermediate which may possibly damage the central nervous system and cause mental retardation. Several disorders of intermediary metabolism have been reported which manifest mild mental retardation and behavioral disturbances. Several IEMs that may present or include features of autism and/or neuro developmental delay include disorders of mono amine oxidase (MAO), ornithine carbamoyl transferase (OCT), cystathionine β-synthase (CBS), phenylalanine hydroxylase (PAH), galactose 1-phosphate uridyl transferase (GALPUT). The present investigation was undertaken to observe whether some metabolic defects manifests in the general mentally retarded population, irrespective of the cause of mental retardation.

Ethical approval was obtained from the Institutional Human Ethics Committee, Kurukshetra University, Kurukshetra to work on mentally challenged Human Population. Blood samples from a total of 104 mentally retarded subjects (both male and female) aged
3 - 18 years were collected. Blood samples were also collected from an equal number of age and sex matched healthy subjects.

The MR population selected were studied for the presence of physical and behavioral anomalies. Most of the MR children had multiple abnormalities and the highest number of such children was observed in profoundly mentally retarded groups and the prevalence of these deformities decreased gradually in higher I.Q. groups. The lowest IQ groups displayed maximum prevalence of poor living skills, poor head balance, open mouth, drooling, microcephaly, macrocephaly, squint in eyes, very poor speech, frequent seizures, very poor reflexes, paralysis, deformities in toes and fingers, poor postures and gait owing to hypotonic trunk and stiffened limbs. Facial hypotonia resulted in open mouth and drooling, which were observed to be the common features of MR population.

Prevalence of these physical and behavioral anomalies was negligible in control subjects. Relationship of the above physical and behavioral symptoms was studied with the biochemical parameters which were mainly the metabolic disorders. Inborn errors of metabolism are an important cause of MR. The activities of all the enzymes under studies i.e. MAO, OCT, CBS, PAH and GALPUT were found to be significantly lower in MR population as compared to that of control.

Only 8-13 % of the normal enzyme activity was estimated in MR subjects. Rapers et al (2003) reported that if only 5-10 % of the normal enzyme activity is present, it leads to inborn errors of metabolism and our studies have shown that enzyme values in MR population is close to 5-10 %. The IEMs have highly diverse clinical manifestations like lethargy, decreased feeding and vomiting. As the metabolic illness progresses, it is associated with progressive abnormalities of tone, posture and moments (tongue thrusting and lip-smacking).

IEMs lead to neurological symptoms like macrocephaly, microcephaly, seizures, paralysis and other movement disorders and non-neurologic manifestation which include skeletal abnormalities, coarse facial features, retinal changes and corneal clouding. These clinical features have been observed in our population under study and correlate with low values of GALPUT and MAO.
Neuropsychiatric symptoms are a component of almost all IEM that affects the central nervous system. Many of these manifestations culminate in the common pathways of CNS dysfunction and coma. Phenylketonuria, if untreated result in MR with variable degrees of psychiatric pathway like depressed mood, anxiety and psychosocial difficulties. Very low levels of PAH in our study in the profound MR group correlates well with the physical behavioral abnormalities observed in this group.

The enzyme activities showed no significant trend in relation to age and sex in either population. The MAO activity in females of both control and MR population was found to be higher than the male subjects probably because of some hormonal factors. No significant trend in relation to different age groups could be deciphered.

The increased activity in the higher age group MR population is probably because majority of the subjects of this population are in mild and borderline MR group. A significant decrease in enzyme activity has been observed with decrease in I.Q correlating well with clinical and behavioral symptoms prevalent mostly in profound and severe MR group.

Two isozymic forms of MAO were observed as revealed by the presence of two bands. Only one band was observed for OCT, CBS, PAH and GALPUT. The intensity of enzymatic bands of MR subjects was less as compared to that of the control population.

Pearson correlation studies were carried out between different enzyme activities of MR population. MAO showed insignificant but positive correlation with OCT and GALPUT. A significant correlation between MAO and CBS, CBS and PAH and CBS and GALPUT was found. Insignificant but positive correlation was found with OCT and PAH, OCT and GALPUT and PAH and GALPUT. A negative correlation was found between MAO and PAH activities of MR population.

The cause of mental retardation varies with the severity of the disorder. The cause of profound to severe cases of mental retardation are much more likely to be diagnosed than are moderate, and borderline cases which are thought to be multifactorial in origin. A similar trend was observed in this population. It was difficult to relate the physical symptoms with biochemical abnormalities in higher IQ groups. Also, the most severe forms
of retardation are evident from birth and an early diagnosis of any metabolic disorder can be of help in treating or arresting that particular metabolic disorder. The milder the retardation, more time it is likely to take to emerge fully and come to the notice of the caregivers.

So, a study like this which attempts to correlate the abnormal and behavioral features with the disturbed biochemistry of MR subjects could add to the existing data pool of the information available on the biochemistry of mental retardation and further similar studies carried out in larger and diverse, multiethnic population could serve as a basis for molecular analysis of the genes of concerned enzymes.