

Original Article

Prevalence and clinical correlates of hypothyroidism in a school for children with mental retardation.

Shivani Jaswal^{1*}, Jasbinder Kaur¹, BS Chavan², Seema Gupta¹, Harjeet Kaur¹

1.Department of Biochemistry, Government Medical College & Hospital, Chandigarh

2.Department of Psychiatry, Government Medical College & Hospital, Chandigarh

*Corresponding Author: Dr. Shivani Jaswal, Department of Biochemistry, Government Medical College & Hospital, Chandigarh, India. Email: shivanirishiraj@yahoo.co.in

Abstract

Objective: Pediatrician is the first contact in the Pathway to Care in children with Mental retardation (MR). Following the recent advancements in the area of molecular genetics, understanding of specific conditions of MR or Developmental Delay (DD) is expanding. Hypothyroidism is a treatable metabolic/endocrinological cause of MR. The aim of this study was to determine the prevalence of hypothyroidism in school children with mental retardation.

Material & Methods: The study was conducted with 140 randomly selected school-going children with MR residing at the Government Institute of Mentally Retarded Children, Chandigarh. Thyroid Stimulating Hormone (TSH) levels were estimated to find out the prevalence of hypothyroidism.

Results: The prevalence of hypothyroidism in children with MR was 10.7% with mean TSH levels of 12.08 ± 4.58 mIU/ml. Majority of the children with Down syndrome had hypothyroidism. Developmental delay was found in all the children. Mean IQ levels were significantly lower in children with MR and hypothyroidism when compared with euthyroid children with MR. Significant negative correlation was present between IQ and TSH levels in the MR children with hypothyroidism

Conclusion: The results of our study suggest that hypothyroidism may be a causative or exaggerating factor of MR in these children. Hence, mass screening of this treatable endocrine disorder in newborns as well as children diagnosed with MR is strongly recommended for identification and intervention of developmental delay in the community.

Key Words: mental retardation, hypothyroidism, children, Down Syndrome

Conflict of Interest: None declared by the authors

Introduction

Family pediatrician is the first point of contact for any child with developmental delay (DD) and mental retardation (MR). Approximately 1-3% of children manifest some degree of MR [1]. Mental retardation originates during the developmental period and results in significantly sub-average general intellectual function with concurrent deficits in functional life skills. Following the recent advancement of molecular genetics, the understanding of specific mental retardation is expanding. Small chromosomal imbalances identified by microarrays constitute a significant cause of MR which is estimated to be in range of 10-15% [2]. MR is also due to the additive effect of one or more causative factors. In 10-15% of individuals with MR the cause lies in the CNS malformation; 5% have multiple congenital anomaly syndromes [1]. Inborn errors of metabolism contribute a small fraction of the causes of MR of which a congenital hypothyroidism is important [3]. Approximately 1 in 4000 newborn infants in the world have a severe deficiency of thyroid function; more have mild/subclinical hypothyroidism. [4]. In about 10% of the children diagnosed with hypothyroidism, the impairment at birth may be a transient phenomenon. The duration and severity of the transient neonatal hypothyroidism is greatly variable and its evolution is unpredictable; the most important cause being the trans-placental passage of maternal antibodies [5]. Congenital hypothyroidism is a potential treatable cause of developmental delay. Delay in diagnosis and treatment beyond the newborn period and early infancy has been linked to later and often substantial neuro-developmental sequelae [6]. Treatment is simple, effective and inexpensive. Developed countries have mandatory newborn screening to detect and treat congenital hypothyroidism in the first week of life. In some countries where comprehensive newborn screening programme is not in place, congenital hypothyroidism has been found to be responsible for 3.8% cases of cognitive delay [7].

Hypothyroidism if present may aggravate the retardation due to other causes as well. If diagnosed early and treated the severity of retardation in these children could be less. The present study was aimed to determine the prevalence of hypothyroidism in school children with mental retardation.

Material & Methods

The sample for the study was drawn from Government Institute of Mentally Retarded Children (GIMRC), Chandigarh. The Institute serves 300 children in the age group of 7-18 years who are divided into 12 educational and 6 vocational classes, each consisting of 15-20 students. The Institute offers both day care as well as residential facilities. Approximately half of the students from each class were selected for the study with the help of a table of random numbers. Parents of the 150 subjects thus selected (including 20 from the residential facility) were contacted for informed consent for the study. 10 parents did not provide consent.

The children were screened for hypothyroidism with estimation of Thyroid Stimulation Hormone (TSH) levels along with the routine hematological and biochemical investigations required by the GIMRC. Venous sample was collected after observing all

the aseptic precautions and analyzed for TSH levels in the Department of Biochemistry, Government Medical College & Hospital Chandigarh. Analysis of TSH was done by Chemiluminiscence on BAYER ACS 180 analyzer. Detailed history of the children was taken from the parents and teachers. Children with TSH levels > 5.5 mIU/ml were labeled as hypothyroid [8].

Intelligence Quotient (IQ) levels of the children was assessed by the psychologist at GIMRC using the criteria of Vineland Social Maturity Scale & Gessell's Developmental Training Test [9,10].

Based on the IQ levels children were categorized as having mild, moderate and severe MR according to the criteria in International Classification Diseases - 10 [11].

IQ levels Mental retardation

50- 69 Mild
35-49 Moderate
20-34 Severe
<20 Profound

Statistical analysis was done using chi square and student's 't' test.

Results

During the study 140 randomly selected school children with mental retardation in the age group of 7-18 years were screened for hypothyroidism. The prevalence of hypothyroidism (TSH > 5.5 mIU/L) was found to be 10.7%. The mean TSH levels were 3.59 ± 1.51 mIU/ml in euthyroid children and 12.08 ± 4.58 mIU/ml in hypothyroid (Table 1)

Table 1: TSH levels & IQ scores in the study sample

| | Euthyroid n=125 | Hypothyroid n=15 | P value |
|--|--------------------|---------------------|---------|
| TSH levels in mIU/ml (Mean \pm SD) | 3.59 \pm 1.51 | 12.08 \pm 4.58 | p<0.001 |
| IQ (Mean \pm SD) | 54.6 \pm 13.38 | 42.6 \pm 13.24 | p<0.001 |

The mean age of children with hypothyroidism was 13.6 ± 1.8 years. 55.3% were males and 46.6% females, the M: F ratio being 1.1:1. Family history of hypothyroidism was found in only 14.2% cases while the rest were sporadic. MR in the children found to be hypothyroid was associated with various syndromes as shown in Table 2, of which the majority (40%) were Down's syndrome. The signs and symptoms observed in them are

shown in Table 3. Developmental delay was found in all the children and among other signs & symptoms the incidence of speech disorder was found to be the maximum.

Table 2: Reported co-morbidity at birth in the study sample with Hypothyroidism

| | Disease/Syndrome | Percentage |
|---|-----------------------------|-------------------|
| 1 | Down's syndrome | 40% |
| 2 | Birth asphyxia | 13.3% |
| 3 | Congenital Rubella Syndrome | 6.7% |
| 4 | Cause not known | 40% |

Table 3: Signs and Symptoms in the MR children with Hypothyroidism

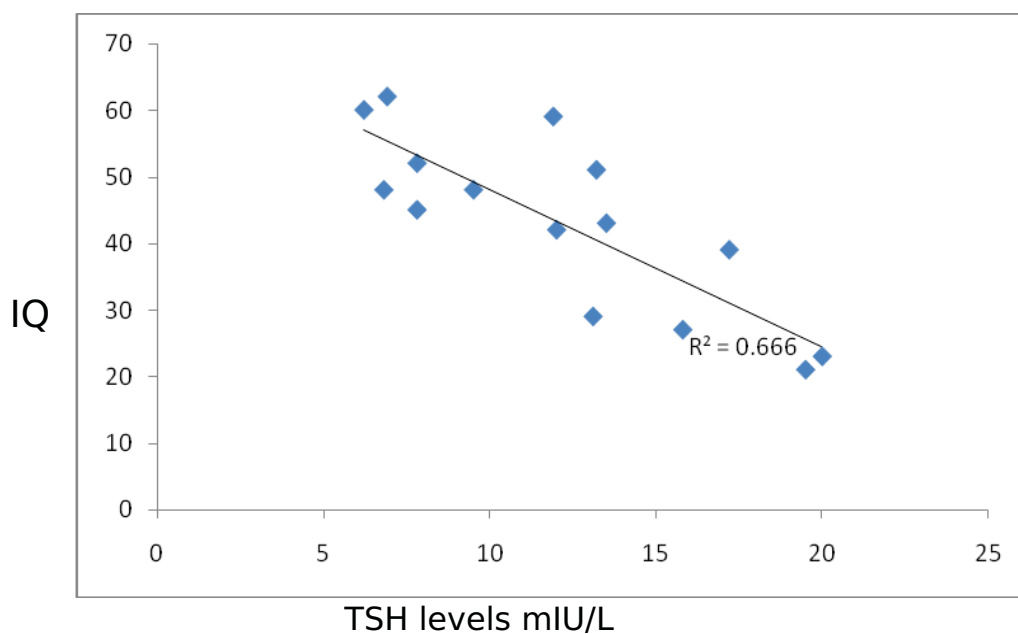
| | Signs & Symptoms | Percentage |
|---|-----------------------------|-------------------|
| 1 | Speech disorder | 40% |
| 2 | Developmental delay | 100% |
| 3 | Short stature | 20% |
| 4 | Constipation | 13.3% |
| 5 | Lethargy | 33.3% |
| 6 | Neonatal jaundice | 13.3% |
| 7 | Convulsive disorder | 26.6% |

The mean IQ in children with hypothyroidism was 36.6 ± 15.01 and in euthyroid children was 54.64 ± 13.38 (Table 1). 40% of the hypothyroid children had moderate mental retardation while mild and severe mental retardation was in 33.4% and 26.6% of the children respectively (Table 4). A negative correlation ($r = -1.2$) was found between the IQ levels and TSH levels in the mentally retarded children with hypothyroidism - higher the TSH levels were more severe was the mental retardation indicated by the IQ levels. (Fig.I)

Table 4: Mean TSH levels & IQ in the study sample with Hypothyroidism

| | Mild Mental Retardation | Moderate Mental retardation | Severe Mental retardation |
|---|-------------------------|-----------------------------|---------------------------|
| Proportion of children with MR and Hypothyroidism | 33.4% | 40% | 26.6% |
| TSH levels in mIU/ml (Mean±SD) | 9.2 ± 3.1 | 11.13 ± 3.8 | 17.1 ± 3.2 |
| IQ (Mean±SD) | 56.8 ± 4.96 | 44.16 ± 3.54 | 25 ± 3.6 |

Fig 1: Correlation between TSH levels and IQ in study sample with Hypothyroidism.



Discussion

Hypothyroidism in children and neonates is classified in three major groups: endemic, transient and sporadic hypothyroidism. Causes of sporadic hypothyroidism include hypothalamic-pituitary or thyroid dysgenesis and/or dysmorphogenesis as well as hyporesponsiveness or resistance to either TSH or thyroid hormones [12]. The genetic defect

of thyroxine synthesis can also occur within a structurally normal gland. Among specific defects are TSH resistance, iodine trapping defect, organification defect or thyroglobulin deficiency [4].

Hypothyroidism in the newborn period is often overlooked in our country as there are no mandatory screening procedures for neonates post-natally. Delayed diagnosis leads to severe outcome - mental retardation, emphasizing the importance of neonatal screening for congenital hypothyroidism [13]. Incidence of congenital hypothyroidism in children is as high as 1/593 [16]. In the current study of randomly selected school children with mental retardation, the prevalence of hypothyroidism was found to be 10.7%. This indicates that in children with MR, hypothyroidism may be a significant factor aggravating the mental retardation. Hsiao et al (1989) screened school children with MR for hypothyroidism, phenylketonuria, and galactosemia and found an incidence of 0.36% of congenital hypothyroidism in their study group [14]. In a similar study Wu et al (1991) found hypothyroidism in 0.2% of their study population [15]. Others have also identified that hypothyroidism to be a cause of mental retardation in children [17, 18]

We, in this study report a prevalence of 10.7% hypothyroidism by TSH screening in the school children with mental retardation. This prevalence is about five times higher than the reported prevalence of hypothyroidism in school going normal children from India [19]. The thyroid status of these children in the study at birth was not known; so we cannot comment on the prevalence of congenital hypothyroidism, though it seems to be a probability. Winker et al (1993) in their study on children with congenital hypothyroidism found disorder of speech along with deficient psychomotor & intellectual development [20]. In our study we also found that 40% of the children with mental retardation with hypothyroidism had speech disorder. In another study Al Quadah (1998) screened cognitively delayed children for congenital hypothyroidism. They found main presenting symptoms were seizures, lethargy, poor feeding, constipation and prolonged jaundice [7]. We also found similar findings in the children with mental retardation with hypothyroidism, 26% had seizure disorder, 13.3 % had history of prolonged neonatal jaundice, 33% complained of chronic constipation and about 33% had lethargy. The chronic systemic signs and symptoms also suggest a probability of congenital hypothyroidism.

It has been reported that approximately 85 % of cases reported for hypothyroidism are sporadic and 15% hereditary [4]. We found similar results in our study group. Only 14.2% of the hypothyroid children had a family history of hypothyroidism.

It has been found that twice as many females as males are affected with congenital hypothyroidism [4]. In our study, however, we found a male: female ratio of 1.1:1 in children with hypothyroidism.

Untreated or unrecognized congenital hypothyroidism has grave consequences, with moderate to severe mental retardation, growth failure, deafness and neurological problems [21]. Evidence exists that infants with low serum T4 levels and high TSH levels have low IQ values [21]. In our study we found that in children with hypothyroidism the

mean IQ was significantly lower as compared to the euthyroid ($p < 0.001$). There was a statistically significant negative correlation between the IQ levels and the TSH levels. However, it was difficult to prove that the lower IQ of these children was the result of hypothyroidism alone. For example, 40% of the children with MR and hypothyroidism in this study had Down's syndrome that is known to be associated with low IQ [22, 23].

It is likely that hypothyroidism not detected and treated, could have aggravated the delayed development leading to MR in the study sample. Early detection and treatment could have provided definite benefit. Thus the severity of hypothyroidism at diagnosis is the most important prognostic factor affecting the intellectual outcome.

Conclusion

Prevalence of hypothyroidism determined by high TSH levels was as high as 10.7% in a randomly selected 140 school going children with mental retardation. Most of them were sporadic hypothyroidism. This prevalence was much higher than the reported prevalence rate of hypothyroidism in school going normal children in India. The cognitive abilities of the MR children with and without hypothyroidism were significantly different – those with hypothyroidism scored lower on IQ tests. 40% of the MR children with hypothyroidism in the study also had Down Syndrome indicating a high co-occurrence of the three conditions. It is possible, that hypothyroidism exaggerates the delay and retardation in children with Down's syndrome.

The limitations of our study were that the thyroid status of the children screened at birth was not known, so we cannot comment on the hypothyroidism as the sole cause of the mental retardation. The study methodology did not include assessment of T3, T4 and anti-thyroid antibodies that are known to be high.

The study reiterates the need for screening, early detection and timely treatment for hypothyroidism in newborns to prevent mental retardation. It also indicates the need for regular screening of thyroid dysfunction in children with mental retardation including Down's syndrome as treatment may improve learning the cognitive abilities in these children.

References

1. Volkmar FR, Lewis M. Mental retardation. Child and Adolescent Psychiatric Clinics of North America. Philadelphia: WB Saunders Company 1996;5: 769-993.
2. Zahir F, Friedman JM. The impact of array genomic hybridization on mental retardation research: A review of current technologies and their clinical utility. Clinical Genetics 2007; 72(4): 271-87.
3. Shevell M, Ashwal S, Donley D, Flint J, Gingold M, Hirtz D et al. Practice parameter: Evaluation of the child with global developmental delay: Report of the Quality Standards Subcommittee of the American Academy of Neurology and The Practice committee of the Child Neurology Society. Neurology 2003; 60:367-380.
4. La Franchi S. Congenital hypothyroidism: Etiologies, diagnosis and management. Thyroid 1999;9(7):735-40.

5. Sava L, Delange F, Belfiore A, Purrello F, Vigneri R. transient impairment of thyroid function in newborn from an area of endemic goiter. *Journal of Clinical, Endocrinology and Metabolism* 1984;59:90-5
6. Tarim OF, Yordam N. Congenital hypothyroidism in Turkey: a retrospective evaluation of 1000 cases. *Turkish Journal of Pediatrics* 1992;34: 197-202.
7. Al Qudah AA. Screening for Congenital hypothyroidism in cognitively delayed children. *Annals of Tropical Pediatrics* 1998;18(4):285-8.
8. Chen IW, Heminger LA. Thyroid stimulating hormone. In: Kaplan LA, Pesce AJ, eds. *Clinical chemistry: theory, analysis, and correlation*. 2nd edition. St Louis: CV Mosby, 1989:952-55.
9. Song AY, Jones SE. Vineland Social maturity Scale norm examined. The Wisconsin experience with 0-3yrs old children. *American Journal of Mental Deficiency* 1982;86(4):428-31.
10. M Wilson. Gessel Developmental testing. *The Journal of Pediatrics*. 1963;62(1):162-64.
11. ICD 10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. Geneva World Health Organization 1993.
12. Solis JC, Valverde C. Neonatal hypothyroidism: Pathophysiogenic, molecular and clinical aspects. *Rev Invest Clin* 2006;58(4):318-34.
13. Buyukgebiz A. Newborn screening for congenital hypothyroidism. *Journal of Pediatric Endocrinology and Metabolism* 2006;19(11):1291-8
14. Hsiao KJ, Chen CH, Liu TT, Wu SJ, Plettner C, Clemens P. Screening of Congenital hypothyroidism, phenylketonuria, galactosemia, homocystinuria and maple syrup urine disease in moderate to severe mentally retarded Chinese children. *Taiwan Yi Xue Hui Za Zhi* 1989;88(1):18-22.
15. Wu KD, Chiu PC, Li SY, Chen JY, Chao MC, Ko FJ, Wang TR, Hsiao KJ. Chromosomal and biochemical screening on mentally retarded school children in Taiwan. *Jinrui Idengaku Zasshi* 1991; 36(3):267-74.
16. Wu KD, Hsiao KJ, Chen CH, Hsiao TS, Chang CY, Chu YK. Screening for inherited metabolic diseases and congenital hypothyroidism in 4744 mentally retarded school children in Taiwan. *Journal of Human Genetics* 1981; 33 :33-40.
17. Hube JA , Grant DB, Clayton BE, Lilly P, Jackson D, Spracklan A. Population screening for congenital hypothyroidism. *British Medical Journal*; 1980;675-78
18. Hube JA. Outcome for Congenital hypothyroidism. *Archives of Diseases in Childhood* 1984;59(1):23-9
19. VK Chauhan, RK Manchanda, Archana Narang, RK Marwaha, Saurav Arora, Latika Nagpal. Prevalence of Thyroid Disorders in School children in Delhi – Post Iodization Scenario. *Indian Journal of Research in Homeopathy* 2009;3 (3)
20. Winker I, Bank S, Bremer-Hubler U, Brodehl J, Sander J. Physical and mental development of children with congenital hypothyroidism. *Monatsschr Kinderheilkd* 1993;141(10):799-804.
21. Wang ST, Pizzolato S, Denshar HP. Diagnostic effectiveness of TSH screening for newborn congenital hypothyroidism. *Clin Chim Acta* 1998;274(2):151-58.
22. Chen MH, Chen SJ, Su LY, Yang W. Thyroid dysfunction in patients with Down's Syndrome. *Acta Paediat Taiwan* 2007;48(4):191-5.

23. SE Noble^a, K Leyland^c, CA Findlay^e, CE Clarb^b, J Redfern^{a,c}, JM Mackenzie^d, RWA Girdwood^d, MDC Donaldson^e School based screening for hypothyroidism in Down's syndrome by dried blood spot TSH measurement Archives of Diseases in Childhood 2000;82:27-31 doi:10.1136/adc.82.1.27