Is delayed diagnosis of hypothyroidism still a problem in Faisalabad, Pakistan

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Abstract

Objective: To determine the age at diagnosis of hypothyroidism, to signify the effect of delayed diagnosis on the clinical presentation of hypothyroidism and hence to emphasize the need for early diagnosis by cost effective neonatal screening.

Methods: The study was a descriptive case series carried out at the Department of Paediatrics, Allied Hospital, Faisalabad from 2004 to 2006. One hundred consecutive cases of hypothyroidism from birth to twelve years of life were included. The age at presentation and age related clinical features were determined.

Results: The age at diagnosis ranged from birth to 16 years. Male to female ratio was 1:1. Congenital hypothyroidism was more common than acquired(92% VS 8%). Maximum number of cases (42%) were diagnosed between 1-5 years of age while only 14% were diagnosed before 3 months of age . Developmental delay (66%), constipation (51%) and lethargy (37%) were more common symptoms while common signs were pallor (65%), short stature (61%), coarse facies (53%), wide anterior fontanellae (46%) and coarse skin (42%).

Conclusion: Early diagnosis by neonatal screening and commencement of treatment is recommended to prevent the effects of delayed diagnosis (JPMA 58:545; 2008).

Introduction

Hypothyroidism is one of the most common and treatable endocrine disease in which there is insufficient amount of thyroid hormones.[1] The thyroid gland is not essential for life but its absence causes mental and physical slowing, poor resistance to cold and in children, mental retardation and dwarfism.[2]

Iodine is an important trace element required for the synthesis of thyroid hormones. Daily requirement of iodine is normally met by a well balanced diet and drinking water except in hilly areas and around the rivers and great lakes where iodine has been leached out of soil so that food grown in soil is iodine deficient, resulting in increased incidence of hypothyroidism in these iodine deficient areas.[3,4] According to UNICEF (1998) , 70% of the total population in Pakistan is at risk of Iodine Deficiency Disorders (IDD).[5] Northern areas of Pakistan (Dir, Swat, Chitral and Gilgit) are highly endemic for IDD.[6] Iodine deficiency is also reported from other parts of country like Islamabad.[7]

The overall prevalence of Congenital Hypothyroidism (CH) is 1 per 4000 while that of acquired hypothyroidism is 1:500-1000.[1,8] The incidence of CH may be higher in children born to mothers of Pakistani, Indian and Bangladesh origin.[9] Studies in Pakistan to find the incidence have been few and on a smaller scale but predict a much higher incidence of 1:1000.[10]

Delay in the diagnosis and treatment results in a mentally deficient dwarf. The best result will be attained if treatment is started in first weeks of life.[11,12]

Routine neonatal screening is not available in Faisalabad even in tertiary care centers like Allied Hospital so the main stay for diagnosis is clinical awareness of this condition.The purpose of this study was to determine the age of presentation of congenital and acquired hypothyroidism and to determine their age specific clinical features in order to signify the effect of delayed diagnosis of congenital hypothyroidism on physical and mental growth, and hence to emphasize the need for establishment of cost effective neonatal screening nationwide as a routine.

Patients and Method

This study was conducted in the department of Paediatrics during 2004-2006 at the Allied Hospital, the largest teaching Hospital of Faisalabad (Pakistan) where patients are referred from rural as well as urban areas.

Hundered consecutive cases of hypothyroidism diagnosed on the basis of history, clinical examination and confirmed by thyroid profile, both from outpatient and emergency departments of the Paediatric Ward, Allied Hospital were evaluated to make the epidemiological significance of the study.

Age specific clinical presentations were identified. These children were divided into 4 groups. Group A (birth to < 3 months), Group B (3 months to < 1

year) Group C (1 year to < 5 years) and Group D (5 years and above).

History details were recorded. Questions specifically asked in group A were feeding problems (choking during feeding and poor feeding), respiratory problems (noisy breathing, apnoea and respiratory distress), delayed passage of meconium (> 72 hours after birth), prolonged neonatal jaundice (lasting for > 2 weeks) and hypothermia (baby being cold as reported by parents and/or documented by health staff). Constipation was considered when there was history of passage of stools after the interval of > 3 days and/or use of some laxatives or suppositories for the passage of stools. Eruption of teeth were considered to be delayed when there were no sign of eruption even after 12 months of age.

Examination details were also recorded. Growth parameters were plotted on standard weight and height charts and classified according to modified Gomez classification(Grade I:70-80% of the expected weight,Grade II:60-70% of the expected weight and Grade III:less than 60% of the expected weight). Children were classified having short stature when their height was below 3rd centile on growth charts.[13,14] Development was assessed according to Denver development scoring. Hearing was assessed by distraction hearing test and by audiometry in children above 5 years. Pallor was identified by clinical examination and confirmed by haemoglobin estimation and peripheral film. Facies were considered coarse if these were not resembling with other family members and included depressed nasal bridge, macroglossia and lowset anterior hair line.

Anterior and posterior fontanellae were considered wide if these measured above normals (Normal range for anterior fontanellae is 20 + 10mm and for posterior fontanellae is < 0.5cm) and patent if AF remained open after 18 months and PF after 3 months of life. Goitre was classified into grade I-IV according to WHO classification. (Grade0:no goiter,Grade I:palpable of thumb size,Grade II:visible with neck in extended position, GradeIII:visible with neck in normal position,GradeIV:visible fom distance of 10 m).[15]

Thyroid profile including free T3, T4 and TSH were done in all cases. T3 and T4 were assayed using RIA (radioimmunoassay) while TSH was assayed using IRMA (immunoradiometric assay). Reference values for T3,T4 and TSH were 2.5 -5.8 pM, 11.5-23.0 pM and 0.17-4.05 mIU/L respectively. We considered TSH value of >20 mIU/ L for the diagnosis of hypothyroidism.

In children above 5 years differentiation between congenital and acquired hypothyroidism was based on normal physical and mental development. Thyroid antimicrosomal and antithyroglobulin antibodies were tested under the suspicion of autoimmune thyroiditis. Endemic cretinism was diagnosed in cases of acquired hypothyroidism on the basis of presence of deafness and neuromuscular disorders

Ultrasonographic or TCM 99 scanning of thyroid gland and FNAC were done as indicated. Other related investigations included haemoglobin, peripheral film and Xrays for assessment of bone age.

Data was entered and descriptive statistics were analysed using SPSS soft ware version 10 and presented through frequency tables.

Results

One hundred cases of hypothyroidism were diagnosed during the 3 year period of this study. Male to female ratio was 1:1. Congenital hypothyroidism was present in 92% (n=92) cases while remaining 8% (n=8) cases were of acquired hypothyroidism.

Most of the patients were in the age group C (42%) as shown in figure. The common symptoms and signs were developmental delay, constipation, lethargy, pallor and short stature (Table-I).

Congenital hypothyroidism was the associated problem in patients with Down syndrome (n=2) and nephrotic syndrome (n=2). Hashimoto's thyroiditis was associated with Turner syndrome in one case and another with Addison disease and diabetes mellitus as a part of polyglandular autoimmune disease type II (Schmidt syndrome). All these presented and were diagnosed after 5 years of age.

Goitre was seen in 14% (n=14) cases.Tc 99 scanning was done in all these cases. Out of these, 6% (n=6) were of congenital and 8% (n=8) of acquired hypothyroidism. Thus goitre was present in 100% cases of acquired hypothyroidism. Hearing was affected in 2 cases and both were of endemic goitre.

T3 value <1.5pM was found in 67% and between 1.5-2.5pM in 33% cases.T4<5.5 pM was found in 75% and between 5.5 - 11.5pM in 25% cases. Elevated TSH level of greater than 50mIU/L was found in 100% cases.

Pallor with Hb<10g/dl was present in 65 %,42% were normochromic and normocytic while 23% were of hypochromic and microcytic type.

Absent distal femoral epiphysis was seen in 71%

Table-I: Frequency of Symptoms and Signs According to the Age at Diagnosis

Clinical Features	Group A (n=14)	Group B (n=12)	Group C (n=(42)	Group D (n=32)	Total % (n=100)
SYMPTOMS					
Developmental Delay		10 (83%)	42 (100%)	14 (44%)	66 (66%)
Constipation		8 (66%)	39 (93%)	4 (13%)	51%
Lethargy		10 (83%)	12 (29%)	15 (47%)	37%
Hoarseness of Voice	12 (86%)	4 (33%)	18 (43%)		34%
Abdominal Distension		4 (33%)	30 (71%)		34%
Failure to Thrive		10 (83%)	19 (45%)		29%
Feeding Difficulties	10 (71%)				10%
Respiratory Difficulties	8 (57%)				8%
Prolonged Jaundice	8 (57%)				8%
Generalized Body Swelling				8 (25%)	8%
Delayed Passage of Meconium	6 (43%)				6%
Delayed Dentition			6 (14%)		6%
Delayed Cry	2 (14%)				2%
Hearing Impairment				2 (6%)	2%
Menorrhagia				1 (3%)	1%
SIGNS					
Pallor	6 (43%)	8 (66%)	42 (100%)	9 (28%)	65%
Short Stature			42 (100%)	19 (59%)	61%
Coarse Facies		6 (50%)	36 (86%)	11 (34%)	53%
Wide / Patent AF	14 (100%)	8 (66%)	24 (57%)		46%
Coarse Skin		6 (50%)	36 (86%)		42%
Goitre			3 (7%)	11 (34%)	14%
Wide / Patent PF	12 (86%)				12%
Periorbital Puffiness	2 (14%)			8 (25%)	10%
Umbilical Hernia	6 (43%)		3 (7%)		9%
Obesity				8 (25%)	8%
Hypothermia	2 (14%)				2%
Delayed Puberty				1(3%)	1%

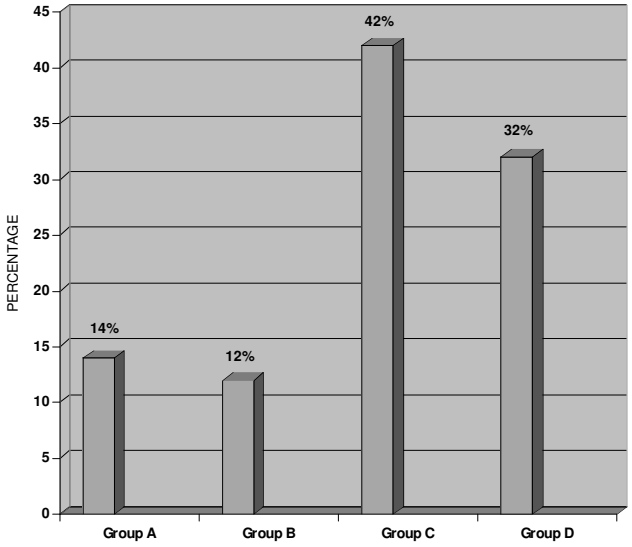

Figure: Frequency of hypothyroidism in different age groups.

(n=10) cases of congenital hypothyroidism in group A, while delayed bone age was found in 78% (n=61) cases of congenital hypothyroidism above 3 months of age. The results have been compared with a similar study from India. Table 2.

Table 2: Comparison of Present Study with that of Havaldar PV et al[16].

	Present Study n=100	Indian Study n=20
AGE AT DIAGNOSIS	**Percentage**	**Percentage**
< 3 months	14	10
3 months to < 1 year	12	20
1 - < 5 years	42	45
> 5 years	32	25
CLINICAL FEATURES		
SYMPTOMS		
Pallor	65	-
Constipation	51	60
Delayed milestones	66	60
Failure to thrive	29	20
Abdominal distension	34	15
Feeding difficulties	10	N.A*
Learning problems	N.A*	15
Periorbital puffiness/Oedema	8	15
Recurrent infections	N.A*	15
SIGNS		
Wide AF	46	65
Hypothyroid facies	53	100
Coarse skin	42	60
Stunted growth	61	60
Umbilical hernia	9	15
Muscular hypertrophy	None	15
I.Q 30 - 40	NA*	60
40 - 60		30
Hypotonia	N.A*	20

NA* = not assessed; AF = Anterior Fontanelle; IQ = Intelligence Quotients

Discussion

Hypothyroidism and its late diagnosis is still a problem in our set up as 100 cases of hypothyroidism were diagnosed over a 3 year period.

Congenital hypothyroidism is more common than acquired[1] consistent with the present study where 92% cases of congenital hypothyroidism versus 8% cases of acquired hypothyroidism were seen. Autoimmune thyroiditis is reported to be the most common cause of acquired hypothyroidism in children above 5 years,[8,16] contrasts with this study where Hashimotos thyroiditis and endemic goiter were present in equal proportion. The increased incidence of endemic cretinism in this study is because of referral of large number of patients from Gojra, Toba Tek Singh, Jhang, Chiniot and Sargodha being situated along the river banks and considered as iodine deficient areas.

Female to male ratio in CH is 2:1 while in acquired hypothyroidism it is 3-4:1,[1,8] but in this study it was 1:1, similar to that reported by Hachicha M et al.[17] This is due to seeking medical advice more for males in our society.

Given the protean clinical manifestations, detection of CH based on signs and symptoms alone, many cases may be delayed to 6-12 weeks of age or older.[1,18,19] Same is evident from our study where only 14% (n=14) were detected before 3 months of age.

Delay in the diagnosis and hence treatment is still a common problem in our community as only 26% (n=26) were under one year and 74% (n=74) were diagnosed after one year of age. The majority, 42% (n=42) fell into the age group C (1-<5years). The reasons for the delayed diagnosis are the uneducated parents, who rarely notice or give less importance to the mild to moderate deviation of physical and mental growth as well as constipation, feeding difficulties and other vague non-specific symptoms in infancy.Parents are unaware regarding importance of early diagnosis and commencement of therapy. Lastly, hypothyroidism is usually considered as an uncommon problem among the general practitioners and its clinical features are related to other common illnesses. Thus it is essential that all paediatricians and clinicians be vigilant in recognizing the early clinical manifestations of congenital hypothyroidism. It is the awareness which needs to be enhanced among general practitioner and parents regarding the importance of early diagnosis and commencement of therapy to prevent the effects of delayed diagnosis.

The early symptoms and signs of hypothyroidism are prolonged gestation, delayed passage of meconium, prolonged unconjugated hyperbilirubinaemia, hypothermia, feeding problems, noisy breathing, hoarse cry, large fontanellae, umbilical hernia and cold dry skin1,[20] similar to that reported in the present study.

Delayed diagnosis of hypothyroidism can lead to retardation of physical and mental growth,[21-23] evident from the fact that as compared to children under one year of age in this study developmental delay was present in 38% (n=10) cases, while it was present in 100% (n=42) cases from 1-< 5 years of age. Developmental delay was present in 56% (n=14) cases in children above 5 years due to inclusion of acquired hypothyroidism with normal D.Q(developmental quotient) in this age group.

Kandemir N24 has revealed permanent height deficit in late diagnosed congenital hypothyroidism. Similary short stature was present in 100% cases (n=42) from one to 5 years of age signifying the need for early diagnosis and treatment of congenital hypothyroidism for prevention of physical and mental retardation.

Pallor is a common clinical feature of hypothyroidism secondary to defective stimulation of bone marrow by low thyroxine level and is refractory to treatment with haematinics.[25] For the same reasons pallor was noted in 65% (n=65) cases of hypothyroidism.

Goitre is seen in congenital hypothyroidism especially those with thyroid dysgenesis and in acquired hypothyroidism (autoimmune thyroiditis and endemic cretinism).[26] In the present study, goiter was present in 7% (n=6) cases of CH and 100% (n=8) cases of acquired hypothyroidism. Not all newborn infants with thyroid dyshormonogenesis have a palpable goiter[1] which is similar to our study, possibly because the palpation of thyroid in infants is difficult and that goiter had not been searched for carefully enough in every case.

Less frequent manifestations of hypothyroidism include menorrhagia present in one case in this study. Delayed puberty is a sequelae of untreated hypothyroidism also present in one case.

An increased frequency of hypothyroidism occur in children with trisomy,[21] Turner syndrome, Klinefelter syndrome or other autoimmune diseases including diabetes mellitus type I.[27,28] Same is evident from this study that out of 92 cases of CH, 2 were associated with Down syndrome and two with nephrotic syndrome. Out of 4 cases of autoimmune thyroiditis one was associated with Turner syndrome and another with type I diabetes mellitus and Addison disease as a part of polyglandular autoimmune disease type II. The presence of associated

syndromes lead to delayed recognition of hypothyroidism as features of hypothyroidism are related to the associated syndrome. This was the reason that all these patients presented and were diagnosed after 5 years of age.

Delayed bone age was consistent in all cases of CH, similar to other studies described.[1,19] Data suggesting clinical features and age at diagnosis of hypothyroidism is lacking in Pakistan, so we compared the results with those of Havaldar PV et al.[19]

Conclusion

Delay in the diagnosis and the sequelae of untreated CH on physical and mental growth are of utmost concern and their prevention is desirable, therefore high index of clinical suspicion with a close observation for early features of congenital hypothyroidism is warranted for early intervention. In the future, nation wide screening for hypothyroidism is strongly recommended.

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