

A study of therapeutic effect of the growth of children with hypothyroidism

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Abstract

Objectives: This study was done to see the therapeutic effect of the growth of children who was diagnosed as hypothyroidism.

Methods: Thirty-four children with primary hypothyroidism were included in this study. Height, weight and head circumference were measured at initial diagnosis and at every follow up visit. Thyroid function was done. The value was interpreted as abnormal if the range was above or below the normal (T3=70-200 u/L, T4=4-13 u/L, TSH=0.3-6 u/L). X-ray to see the bone age for the chronological age was performed. The value was interpreted as abnormal if the ossification center for the chronological age is inappropriate. Treatment was started with Eltroxine from the day of diagnosis. Dose was adjusted according to the response to the medicine. T3, T4 and TSH level was taken as the guideline to adjust the dose of the drug. X-ray was considered in the follow up where it was indicated.

Result: Marked improvement in the anthropometry was seen in comparison to the initial assessment which was well correlated with the normalization of the TSH level and the x-ray of the bone.

Conclusion: Serial follow up of these patients was necessary in order to assess the growth in height, weight and head circumference along with the repeated thyroid function to correlate the response of the drug.

Key words: Therapeutic effect, growth, primary hypothyroidism, TSH level

Hypothyroidism is the result of the deficient production of the thyroid hormone or a defect in thyroid hormone receptor activity. The disorder may manifest from birth called as congenital hypothyroidism. The incidence of congenital hypothyroidism (Fig. 1) world wide is about 1: 3000-4000 but some of the highest incidences (1 in 1400 to 1 in 2000) have been reported from various locations in the Middle East and 1 in 2481 from Mumbai^{1,2}. First clinical manifestation of hypothyroidism is retardation of the growth but the sign often goes unrecognized. Delayed Osseous maturation in the adolescent gives the clinical picture of short stature. However, younger children may present with pseudo precocious puberty characterized by development of breast in girls and macroorchidism in boys or galactorrea, which is the result of increased TSH stimulating prolactin secretion. All or many of the Myxedematous changes like coarseness of the skin, constipation, cold intolerance, decreased energy and increased need for the sleep are present. With adequate replacement of T4 all, these changes return to normal. However, catch-up growth may be incomplete in children with long standing hypothyroidism. During first 18 months of treatment, skeletal maturation often exceeds expected linear growth. In humans, T4 can be found in the first trimester coelomic fluid from 6 weeks of gestational

age, long time before the onset of secretion of T4 by the foetal thyroid, which occurs at the 24th week of gestation. The T4 and T3 found in early human foetuses up to mid gestation are likely to be entirely or mostly of maternal origin. This transfer is decreasing but persists during later gestation as Vulsma et al suggested. Up to 30 % of serum T4 in cord blood at birth could be of maternal origin, although Delange et al have reported a much lower percentage. Most cases of congenital hypothyroidism present clinically during the first year of life. Delay of diagnosis and treatment beyond the first 1-3 months of life is likely to result in irreversible neuropsychological deficits.

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Screening at birth may, in fact, occur too late to prevent important neurodevelopment deficits in some infants. A minimum interval of 6 months is recommended between height measurements for a reliable evaluation of growth velocity. The rate of growth varies considerably at different periods of childhood³. There should be consideration of the genetic consideration of the height for which the mid-parental height (MPH) be calculated for obtaining genetic of the individuals⁴.

Fig. 1: Congenital hypothyroidism



Material and methods

All the children with clinical features of hypothyroidism were included. Blood sample were sent for thyroid function test. The results were available within a week. X-ray of the left wrist and hand or other ossification center according to their chronological age was taken. They were compared in the follow up as per their availability. Height and weight of the father and mother were measured subject to the availability. Child's height was taken in a standing scale against the fixed wall, weight was measured in the weighing scale and head circumference was measured with the measuring tape. At each follow up all these parameters were measured in the same scale. Thyroid function test was done every 3 months to see the efficacy of the treatment. X-rays were repeated according to the need at the follow up. A lateral radiograph of the knee should obtain, looking for the presence of the distal femoral epiphysis. This ossification center appears at about 36 weeks' gestation. Its absence in a term or post term infant indicates prenatal effects of hypothyroidism, a poor prognostic sign.

Result

Total numbers of 34 children with clinical appearance of primary hypothyroidism were studied for the period of 3 years and 9 months (16.01.2059 - 01.10.62). Among them males were 59% and female 41% (Fig. 3). Females were more affected in other study but in this study we observed more males were affected.

Fig. 2: Photo of pseudo precocious puberty
Age 17 years, height 82 cm.



Age at first diagnosis was ranged from 45 days (.09 years) to 17 years with median age of 1.6 years. Their places or residence were from hill region 13(54) %, from terai 11(46%). 10 patients addresses were not recorded. The prevalence of hypothyroidism was slightly higher among terai castes (17.66%) compared to hill castes (15.17%) in a study which was undertaken to investigate the prevalence of thyroid dysfunction among the hill and terai (low land) castes of eastern Nepal who attended

The thyroid clinic at the BP Koirala Institute of Health Sciences (BPKIHS), Dharan 5. At the time of initial presentation 65% of the children were presented with delayed development, 44% with short stature, 12% each with protruded tongue and prolonged neonatal jaundice, 6% each with coarse skin and obesity, 3% each with poor school performance, constipation, delayed closure of fontanella beyond 18 months of the age and goiter (Fig. 4). Similar number of short stature was seen in a study done at referral centre in north India⁶. A girl of seventeen presented with short stature, obesity,

coarse feature, myxedematous pad of fat over the neck, oedematous feet, well developed breast who

Fig. 3: Sex distribution

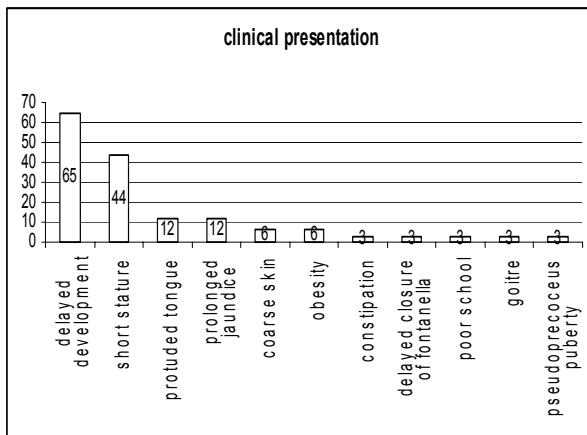
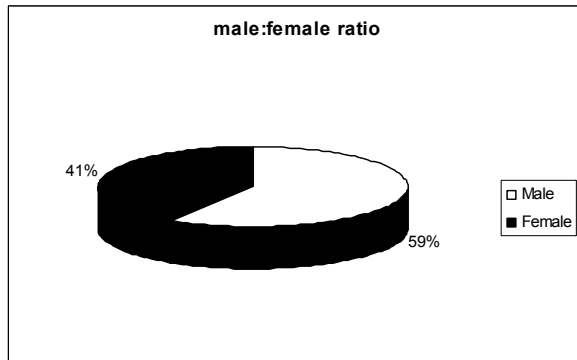


Fig. 4: clinical presentation

Average of 6.5 times (2-12 times) follow up these patients were done for about four years. In the initial assessment height of 67% of them were below two standard deviation as was true with their weight 59%, head circumference 50%. 24% were within two standard deviation for their height as was true for their weight 21% and head circumference 32%. In the second visit after the initiation of thyroxin height of 41%, weight of 38% and head circumference of 32% remained in the below two standard deviation were observed. In the third visit below two standard deviation was further lowered to 23%, 27%, and 10%. At sixth visit all three anthropometric parameters have overcome the below two standard deviation entering all into within two standard deviation (Fig. 5). Seventy six percent of the patients had TSH level high and decreased T3 and T4 level were seen in 35 and 44 % of the patients at their initial visit. In subsequent visit after 3 months high TSH level has decreased to 21 % and level of low T3, T4 has decreased 9 and 3 % respectively. In the third visit high TSH level decreased to 15%, which

had also started menstruations but absence of pubic hair⁷ (Fig. 2).

remained till 9th visit and returned to zero percent but at this point the abnormal TSH was seen in only one patient (Fig. 6) that could be due to slow increase in the dose of the drug. 53% X-rays for bone age in initial visit were abnormal. After 3months of treatment, only 15% x-ray remained abnormal and after 3 rd visit, only 12% remained abnormal (Fig. 7). One patient needed 1.5 years to return to normal. The Drug was started after confirmation of diagnosis the gold standard of diagnosis being thyroid function test and x-ray abnormality of the relevant bone appropriate for their chronological age. Dose adjustment was done according to the TSH level and weight of the child in the follow up clinic. Growth increment of the children were markedly improved after the treatment which is shown in comparison with normal growth pattern seen in a period of one year (Fig. 8)

Fig. 5: Height, weight and head circumference observed below two standard deviation at initial visit

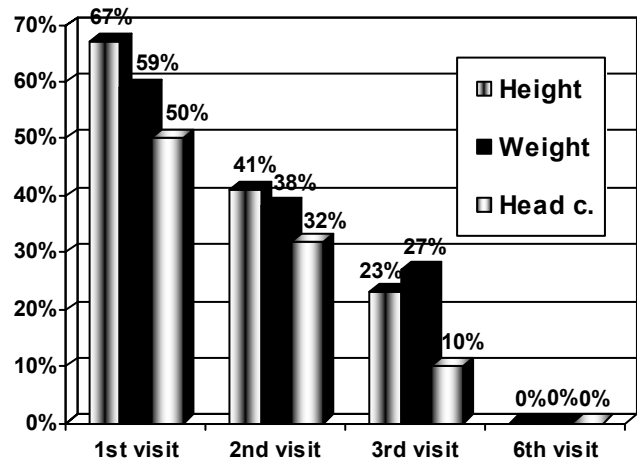


Fig. 6: Normalization of thyroid function test after the treatment

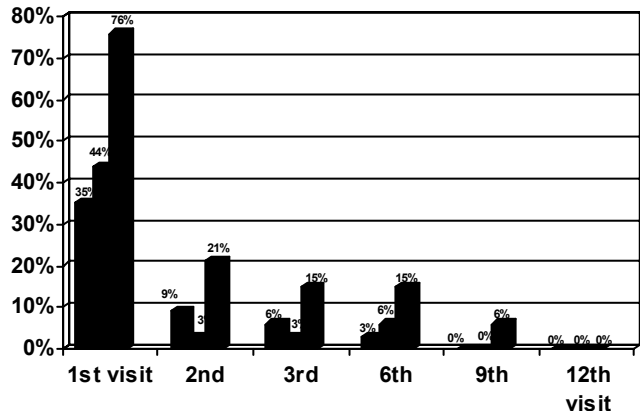


Fig. 7: Gradual normalization of abnormal x-ray findings by 1.5 years.

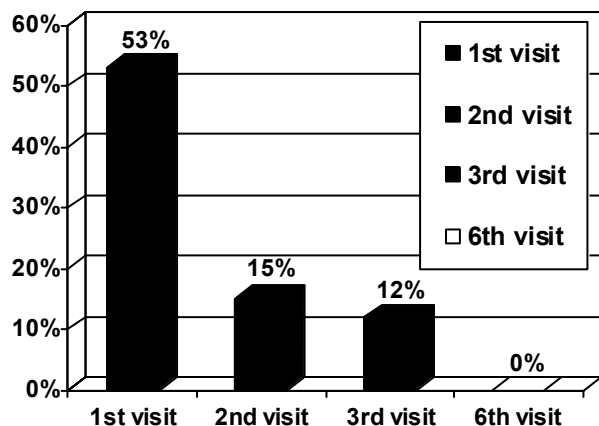
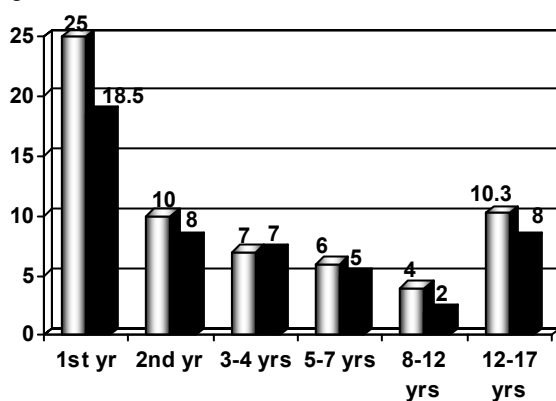


Fig. 8: Comparison of height normal pattern and pattern after treatment



Discussion

There had not been any studies on congenital hypothyroidism in Nepal as the screening for hypothyroidism is not carried out in Nepal but there has been work on iodine deficiency hypothyroidism in Nepal. In India congenital hypothyroidism were studied and reported in sporadic centres. Similar works were seen from Bangladesh. Because of the high cost neonatal screening for congenital hypothyroidism has been routinely done only in the developed country where they use TSH as the screening but in United States, they use T4 level. There has been reported cases of acquired neonatal hypothyroidism due to maternal consumption of expectorants⁸.

The response of the thyroxin treatment in the children with hypothyroidism is very impressive and encouraging. Anthropometric changes are seen even from the first subsequent visit after the start of the treatment. With early institution of adequate

treatment, most patients will have neuro psychological development as well as overall growth, sexual maturation and final growth⁹. Levothyroxine is the preferred form of thyroid hormone replacement in all patients with hypothyroidism which is a synthetic thyroid hormone with proven record of safety, efficacy and easy to take orally.

Conclusion

Children with hypothyroidism should be monitored clinically and biochemically. Clinical parameters should include linear growth, weight gain, developmental progression, and overall well-being. Laboratory measurements of T4 (total or free T4) and TSH should be repeated 4-6 weeks after initiation of therapy then every 1-3 month during the first year of life. The time interval between measurements may be increased but should not exceed 4-6 months. As dosage changes are made, testing should be more frequent. Formal developmental and psycho neurological evaluations should be considered in all infants with congenital hypothyroidism. Such evaluations are especially important in children whose treatment was delayed or inadequate. Infants diagnosed early but with detectable signs of hypothyroidism at the time of diagnosis are also at increased risk of developmental problems. School progression should be monitored and parents encouraged seeking early evaluations and interventions as soon as problems are recognized. Thyroid hormone replacement and medical monitoring are required for life.

Outcome

Early diagnosis and treatment of hypothyroidism prevents severe mental retardation and other neurological complications. Even with early treatment, some children demonstrate mild delays in areas such as reading comprehension and arithmetic in third grade. Some of these delays had improved by sixth grade. As might be expected, infants with delayed bone age at diagnosis or a longer time to normalize thyroid hormone levels had poorer outcomes. While continued improvement in IQ has been documented in treated patients through adolescence, some cognitive problems may persist. These may include problems in visuospatial, language, and fine motor function. Defects in memory and attention may also be present. Early detection of the children with hypothyroidism has greater implication in the improvement of physical development as well as neurological development.

Recommendation

Though most of the hypothyroid patients are not affected mentally, it is still our responsibility to

diagnose these cases as early as possible because neurological handicap is significant and can be irreversible if the diagnosis is delayed. Physical catch-up growth can be expected as early as 3 months of the treatment but one should wait for the expected growth in height for about 6 months.

Screening for congenital hypothyroidism with thyroid function test (TSH) performed on dried-blood spot specimens is recommended for all newborns, optimally between days 2 and 6.

Children with congenital and primary hypothyroidism should be monitored clinically and biochemically. Clinical parameters should include linear growth, weight gain, developmental progression, and overall well-being. Laboratory measurements of T4 (total or free T4) and TSH should be repeated 4-6 weeks after initiation of therapy, then every 1-3 month during the first year of life and every 2-4 months during the second and third years. In children aged 3 years and older, the time interval between measurements may be increased but should not exceed 4-6 months. Test should be done more frequent according to the change of dosage. Formal developmental and psychoneurological evaluations should be considered in all infants with congenital hypothyroidism. Such evaluations are especially important in children whose treatment was delayed or inadequate. As mentioned previously, infants diagnosed early but with detectable signs of hypothyroidism at the time of diagnosis are also at increased risk of developmental problems. School progression should be monitored and parents encouraged seeking early evaluations and interventions as soon as problems are recognized.

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