



Original Article

Congenital Hypothyroidism in the Southern Bangladesh

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Abstract

Congenital hypothyroidism is the commonest preventable cause of mental retardation. It is more prevalent in endemic goiter regions like Bangladesh. But magnitude of the problem has not been studied at national level. This study was done to detect the frequency of congenital hypothyroidism in southern part of Bangladesh & to develop neonatal screening program. All the living newborns delivered between Oct 01 to June 05 Khulna Medical College Hospital were included in the study, After taking the relevant information from mother, cord blood sample were collected from the newborn within 120 hours of birth and kept in freezer. At the end of collection of each two months, the lot was sent to the laboratory of Institute of Nuclear Medicine, Dhaka for radioimmunoassay of TSH. Potential cases with TSH above 10 MIU were recalled for thyroid function test for confirmation of diagnosis. Fifteen hundred samples were collected in total during 45 months of study. One forty seven unsatisfactory samples were discarded; thereby 1353 samples were eventually assayed for TSH. Among the study population 88.2% hailed from Khulna district and the rest of the cases came from neighboring districts. Male to female baby ratio was 1.2:1. Regarding the birth weight 33.4% babies were low birth weight. TSH above 10 was found in 35 babies among whom one baby was hypothyroid and the other member of the twin was also hypothyroid although the TSH level was below 10. None of newborn had TSH level above 20. Thus frequency of congenital hypothyroidism was 1.5 per thousand living newborn. Congenital hypothyroidism in southern part of the country is quite high in relation to global incidence. Although this is not the national picture but the high figure is alarming. Therefore neonatal screening program should be implemented as soon as possible to reduce the number of mentally retarded child.

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Introduction

Congenital hypothyroidism (CH) is the most common congenital metabolic disorder seen in the newborn (1 in 4,000 births). It causes irreversible mental & physical disability if remains undetected. Diagnosis and treatment of CH before 3 months are mandatory to avoid cretinism¹.

Iodine deficiency is the most important and easily preventable cause of mental retardation. Globally

about 10% population are suffering from iodine deficiency disorder and lack of iodine in mother leads to 30,000 still birth and 1,20,000 CH². Bangladesh is known to be one hyper endemic zone for iodine deficiency. Goitre and other iodine deficiency disorder are very common in our country³. The national survey for Iodine deficiency Disease in 1993 shows that the incidence of cretinism in our country is 0.5%. But it was

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though that the incidence would be much higher and one small study done at institute of nuclear medicine, Dhaka shows that prevalence rate of CH in Bangladesh is 0.9% which is a cause of concern for Physicians^{4,5}.

In Bangladesh there is few institute based report on thyroid disorder. In recent community based study in southern part of Bangladesh it was revealed that 3.3% of school going children are suffering from thyroid insufficiency including hypothyroidism and subclinical hypothyroidism⁶.

Neonatal screening program for CH is highly cost effective for a nation because it prevents the mentally retarded persons⁷. Therefore screening program has become a routine practice in all developed countries and a many a developing country in South East Asia have inducted neonatal screening for CH as an essential part of their health service⁸.

The objective of this study was to evaluate the situation of CH in southern part of Bangladesh to rationalize the importance of neonatal screening program in this part of the country.

Patients & Methods

Place & population: This study was carried out in Khulna medical college Hospital (KMCH) jointly by the department of Obstetrics & Gynae. Department of child health and, center for nuclear medicine in collaboration with institute of nuclear medicine, Dhaka. Period of study continued for 45 months extending from October '01 to June '05. Newborn live infants of both sexes aged between 0 to 120 hours delivered in hospital during the time were included in the study. Two doctors in each year had given voluntary service for this study. Detailed information including the history and clinical findings were recorded in a predesigned clinical format in order to detect predisposing factors in relation to hypothyroidism.

Methods of Sample Collection

a) A drop of blood from baby's cord end was put to each circle of filter paper and five circles were filled in similar way.

- b) After collection, filter paper was dried in open air for 30 minutes; it was labeled for identification and kept in normal refrigerator.
- c) At the end of two months collected samples were sent to Dhaka in the laboratory of institute of nuclear medicine for estimation of TSH. The reports were sent back within two weeks.

Lab Test: In this method two antibodies are used against different portions of same antigen, polyclonal antibody is coupled with magnetic iron oxide particle & monoclonal antibody is coupled with 1-125. Thus when an antigen is present in the test material, it simultaneously binds with both antibodies in a double site sandwich fashion. The formed antigen-antibody complex is separated by placing the assay tubes in magnetic separator and decanting the supernatant. The radioactivity of tracer in the tube is directly proportional to the concentration of TSH in the specimen.

The TSH level above 10 were considered as significant and the babies were recalled for final diagnosis by doing the serum thyroid function test (T₃, T₄ & TSH) by standard method. The diagnosed cases were treated with levothyroxin (10-12µg/kg/day) and followed up at monthly interval to monitor the neurodevelopmental outcome for one year. Search for cause of hypothyroidism (Scintigraphy, ultrasonography, Tb antibody) has not been done in this study.

Results

During forty five months of study, cord blood was collected from 1500 cases of live newborn. Faulty technique in blood collection led to laboratory rejection of 47 samples. Thus 1353 cases were included in the screening program. Majority of the newborn were male and the male female ratio was 1.2:1 (Table I). Most of the patients (88.2%) were from Khulna city and adjacent villages within Khulna district except a few (11.8%) from neighboring districts such as Bagerhat, Satkhira, Jessore and Narail. The sample population by it's distribution represents Khulna division.

Table-I: Distribution of Newborn on locality & gender.

Residence	Male	Female	Total (%)
Khulna	651	542	1193 (88.2)
Neighboring districts	86	74	160 (11.8)
Total	737	616	1353 (100)

Profile of the mothers and newborn are shown in Table II). Majority (57.5%) of mothers belonged to the age group of 15 to 25 years and only 8 (0.6%) mothers were below 15 years of age. Regarding the newborn 452 were low birth weight and among these 19 were very low birth weight. Low age group mothers delivered more VLBW baby in comparison to higher age group.

TSH level were divided into three categories. Higher levels (10-20) were found in thirty five babies and all were recalled for thyroid function. Twenty four (68.6%) of them eventually turned up and one child (TSH-17.6) was found hypothyroid. Since he was a member of the twin, other sibling (TSH-8.1) was also tested and hypothyroidism was detected as well. No baby was found to have TSH level above 20.

Table-IV: Profile of Congenital Hypothyroidism cases

Home district	Date of Birth	Mothers name & age	Sex	Wt (Kg)	TSH screen	Thy Func text (Norm) T3- (1.5-3.5 nm/L) T4- (54-173 nm/L) TSH- (0.3-5 MIU/L)
Bagerhat	01/06/02	Jahera (24yrs)	F	2.2	8.7	T3-1.9 T4-32.8 TSH-9.5
Bagerhat	01/06/02	Jahera (24yrs)	M	2.3	17.6	T3-1.5 T4-27.5 TSH-17.8

Discussion

Congenital hypothyroidism identified by newborn screening has favorable outcome but IQ reduction and persistent cognitive deficit are reported in many studies. Their specific deficits reflects when the disease began in utero, etiology of the disease and starting dose of hormone therapy.⁹

In UK, screening for CH was introduced in 1981 and the program has been successful in identifying infants before irreversible neurological damage

Table-II: Birth weight of the baby in relation to mothers age

Age	<1.5kg	1.5-2.5kg	2.5-3.5kg	>3.5kg	Total (%)
Up to 15yrs	04	02	02	00	08 (0.6)
15+-25yrs	09	249	473	46	777 (57.5)
25+-35yrs	06	173	331	31	541 (40.0)
>35yrs	00	09	16	02	27 (1.9)
Total (%)	19(1.5)	433(31.9)	822(60.7)	79(5.9)	1353(100)

Table-III: TSH level among the Newborn

TSH level	Number	Percent	Mean± SD (Range- 0.3- 17.6MIU/L)	CH
Upto 10 MIU/L	1318	97.4	3.1 ± 2.4	1
> 10-20	35	2.5		1
>20	0	0		0

Two out of 1953 newborn were detected as a sufferer of congenital hypothyroidism (0.15%) Twins were hailing from Bagerhat, the adjacent district of Khulna. The mother was 24 years of age having no sign or drug history of hypo or hypothyroidism. Both the case was low birth weight (LBW) babies. At birth, no abnormal sign was noted. All the children had good drug tolerance and at the end of one year their physical and mental development was well.

has occurred thereby preventing lifelong disability.¹⁰ Transient hypothyroxinemia occurs up to 6 months in infants who are born to mothers with poorly controlled graves disease. The central hypothyroidism may develop in three different ways by way of short term hypothyroidism as a result of passively transferred thyroxin, by was of long term hypothyroidism as a result of passively transferred thyroid antibody and directly after birth. Therefore thyroxin supplementation during a

period of central hypothyroidism is of importance. However TSH based neonatal screening can not detect central hypothyroidism.¹¹

During fetal life, secretion of thyroid hormone starts at 12 weeks, the level of which increases up to term. Throughout gestation, maternal T₄ crosses the placenta in limited amounts but in third trimester, this plays a critical role in central nervous system development. In areas of endemic iodine deficiency, iodine supplementation to mother in pregnancy protects the fetal brain. From the second trimester the continued transfer of T₄ from mother to fetus remains important for their babies with primary thyroid abnormalities. Despite cord blood reaching only 40%, neurological developments occur near normal if replacement is started promptly¹². In premature babies thyroxin level is low and cause is multifactorial. These are loss of maternal T₄ contribution, immaturity of the hypothalamic pituitary axis, unresponsiveness of thyroid gland to TSH and immaturity of peripheral tissue deiodination¹².

Most North American programs used a two tiered laboratory approach. An initial filter paper blood spot T₄ measurement is followed by a measurement of TSH in the filter paper specimen with low T₄ values. This can identify thyroxin binding globulin deficiency, hypothalamic pituitary hypothyroidism but recall rate in this approach (0.30%) is quite high. A majority of European and Japanese program favors screening by means of primary TSH measurement supplemented by T₄ determination for those infants with elevated TSH values. With these approach infants with TBG deficiency, hypothalamic pituitary hypothyroidism and hypothyroxinemia with delayed TSH elevation will be missed however the recall rate is less {0.05%}. Combined T₄ & TSH estimation is the best method but until its availabilities there are limitations of each method. Even in the absence of technical and human error studies suggested that 5-10% of newborn with CH have normal screening hormone concentration regardless of the type of approach used^{2,3}.

Present study was done on the basis of primary TSH measurement by radioimmunoassay because of its greater sensitivity and lesser recall rate.

Standard cut off level at the beginning of the study was 20 MIU/L which again depends on the time of taking the sample. After six months the cut off values were reviewed and majority was below 5, therefore the cut off value of recall were lowered down to 10, which resulted in recall of 35 babies (2.6%). Among the twenty-four respondents two (twin) were diagnosed as CH.

KMCH drains people from all walks of life, mostly from in and around the college within a radius of 20 km. But higher number of peoples from neighboring districts has also attended this tertiary care hospital seeking safe delivery. Pregnant mothers from neighboring district were 11.8%. Thus the total cases represent the division as a whole. Regarding the characteristics of mother and babies it was observed that 33.4% of babies were low birth weight which was much lower than national figure (45-47%)¹³. Few young mothers (0.6% were below 15 years of age, but the number of premature babies has not been estimated which could reveal the relationship between TSH and gestational age.

Congenital causes of hypothyroidism are numerous. Majority of the problem are thyroid dysgenesis (70-80%), thyroid dyshormonogenesis (10-20%) and thyroid hormone unresponsiveness (1-2%). Central hypothyroidism and transient hypothyroidism may occur in small number of newborn due to fetal exposure to antithyroid drugs, maternal antibodies and endemic iodine deficiency¹⁴. In contrast to screening costly investigations are necessary to find out the cause of CH.

The incidence of CH in our study (0.15%) is 1.5 in 1000 which is quite high in comparison to global standard. Both the cases were low birth weight although the mothers were of normal age group. Among all the mothers 15 mothers were found in 9 and 6 cases respectively. But none of their babies revealed hypothyroidism.

In America (USA-1995), CH is 1:4,000 but it is more prevalent in native American infants and less in black Africans and females are affected twice as common as males. In Europe (England-1991) it is 1:2500. In the opposite side of the globe

(Australia-1992) it is 1:3,500 and in Asia (Malaysia-1995) it is 1:3000³. No major community based studies has been done before in Bangladesh but prevalence of cretinism was found as 0.6% in hyperendemic zone⁵.

The principle limitation of our study was the population which should have been much higher for focusing the true incidence of hypothyroidism since the global incidence is 1 in 4,000. The hospital delivery rate of in KMCH is much higher but lack of manpower and financial support were the deterrent for collecting large number of samples. The doctors who gave their voluntary service were trained to take the sample but only one at a time was available during the office time. Moreover, while sample collection was easy at birth table, mother refused to give blood on the next day to avoid further prick thus many a babies were missed as our study cases. It is probably too simplistic to classify CH into mild, moderate and severe in relation to brain architecture. From the available clinical evidence it appears that starting dose of levothyroxin should be higher (10-16 µg/kg) than lower dose (8-10 µg/mg) for better outcome without any long term overdose effect.^{15,16} A moderate dose treatment was used in our cases with good outcome.

In conclusion, the incidence of congenital hypothyroidism in southern part of Bangladesh is quite high and screening for CH could be highly cost effective. A nation wide survey program is necessary before initiating this screening program.

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