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Hearing outcome in infants following correction of maternal hypothyroidism during pregnancy

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ABSTRACT

Purpose: There is significant prevalence of overt and subclinical hypothyroidism in pregnant women in rural areas. Maternal hypothyroidism is known to cause congenital hypothyroidism resulting in sensorineural hearing loss. Anti-Thyroperoxidase antibodies are known to cross placental barrier. There is no literature on hearing assessment in infants born to women whose hypothyroidism was corrected during pregnancy. Do these infants suffer hearing loss? Our study addresses this question.

Methods: 140 infants born to women on treatment for hypothyroidism during pregnancy and 140 infants born to euthyroid women were evaluated for hearing by Brainstem Evoked Response Audiometrry at 1 and 4 months age. Anti-TPO antibodies were estimated at 4 months of age.

Results: There was no clinical hearing deficit or delay in neurological development in infants born to women undergoing treatment for hypothyroidism during pregnancy. However wave V latency on BERA was slightly prolonged in them compared to infants born to euthyroid women. There was absence of wave V when maternal subclinical hypothyroidism persisted till parturition. However within 6–8months of age the wave V latencies corrected to normal. Anti-TPO antibodies were within normal range at 4months age.

Conclusion: Maternal hypothyroidism when corrected before parturition does not affect hearing in the infants clinically. The mild delay in wave V on BERA corrects within first year of life. However larger studies to assess hearing in infants born to women having overt hypothyroidism during first trimester of pregnancy may be desirable to assess whether hearing is adversely affected in them.

1. Introduction

Hypothyroidism is the most common endocrinological disorder in women in the reproductive age group. It is often subclinical and is noticed only during pregnancy [1]. In our region, 11% of pregnant women were found to be hypothyroid and the most common cause was autoimmune thyroiditis [2]. Iodine deficiency is common cause for hypothyroidism and goiter in our region. Maternal hypothyroidism can be associated with congenital hypothyroidism. Congenital hypothyroidism results in sensorineural hearing loss in infants [3]. There is also evidence of antibodies to Thyroperoxidase crossing the placental barrier [4]. Very few studies have evaluated the hearing in infants born to women whose hypothyroidism was corrected during pregnancy. We therefore performed this observational study to assess the hearing by Brain Stem Evoked Response Audiometry in 140 infants born to women whose hypothyroidism was corrected during pregnancy. This was compared with hearing assessment done by Brain Stem Evoked Response Audiometry on 140 infants born to euthyroid women.

2. Aim

The aim of this observational study was to compare the hearing

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acuity in infants born to women whose hypothyroidism was corrected during pregnancy with the hearing acuity in infants born to euthyroid women.

3. Materials and methods

This is an observational study done in a rural tertiary care hospital from December 2016 to April 2018. The Institutional Ethics Committee approval (IRB) has been taken before starting the study and the patients have been screened for the study.

The sample size was calculated with the prevalence of hearing loss in infants born to hypothyroid women (10%) and euthyroid women (2%) from a previous study conducted in Northwest India by Dayal D et al., in 2016 [8] and the formula Sample size = $\{2pq\ (Z_a + Z_b)^2\}/(p1\text{-}p2)^2$ was used to arrive at a sample size of 140 infants born to women whose hypothyroid was corrected during pregnancy and 140 infants born to euthyroid women.

3.1. Inclusion criteria

This study included 140 infants who were born to women with documented overt or subclinical hypothyroidism which was corrected during pregnancy and 140 infants born to euthyroid women. Initially 157 hypothyroid women were screened and treated with Thyroxine supplements during pregnancy. However, 17 women continued to be hypothyroid at the time of parturition. 2 women had marginally raised TSH with normal free T4 levels and were clinically euthyroid. They were included in the study and termed as subclinically hypothyroid at the time of parturition.

3.2. Exclusion criteria

Infants with evidence of otitis media, hyperbilirubinemia requiring phototherapy, birth weight less than 1 Kg, birth asphyxia requiring ventilator support, and craniofacial dysmorphism were excluded from the study. Infants born to women with overt or gestational diabetes mellitus, familial hearing loss or syndromic hearing loss were also excluded from the study.

3.3. Methodology

Pregnant women presenting to the department of Obstetrics in our hospital were screened clinically for hypothyroidism and confirmed by estimating serum Thyroxine and Thyroid stimulating Hormone levels. The pregnant women with documented evidence of hypothyroidism were counselled to attend antenatal clinic regularly and informed written consent was obtained from them to evaluate the hearing of their child after delivery. The hypothyroidism in these women was corrected during pregnancy.

Taking 140 infants born to women whose hypothyroidism was corrected during pregnancy, satisfying the inclusion and exclusion criteria (study subjects) underwent a detailed ENT examination and audiological evaluation with Brain stem Evoked Response Audiometry at 1st and 4th month of life. The serum TSH and T4 levels were estimated in these infants within one week after birth. Thyroperoxidase antibodies titre was estimated in these infants. 140 infants born to euthyroid women (controls) also were included and they also underwent detailed ENT examination, estimation of serum T4 and TSH levels and audiological evaluation with Brain stem Evoked Response Audiometry at 1st and 4th month of life after getting an informed written consent from the parents/caregivers. A 2 channel Smart EP by Intelligent hearing Systems (IHS) was used for ABR testing. The replicability of Wave V in BERA at 30dBnHL was noted and their latency period in milliseconds was documented. The developmental milestones (attainment of social smile and head control) in both the subjects and controls were documented. A comparison was done between the hearing results among study subjects and the controls.

Two infants born to hypothyroid women were followed up to 6th and 8th month of life due to absence of wave V replicability at 1st and 4th month.

Statistical analysis was done using SPSS 22 version software. Individual *t*-test was used as a test of significance and Fischers exact *t*-test for p value of and <0.05 was taken statistically significant.

4. Results

In our study, 83 pregnant women had overt hypothyroidism and were on treatment with Thyroxine supplements. Their serum thyroxine levels were corrected during pregnancy. 35 women were found to have subclinical hypothyroidism during the first trimester of pregnancy which was corrected with Thyroxine supplements. 22 women presented after first trimester of pregnancy and were found to have subclinical hypothyroidism. 18 of these subclinically hypothyroid women were compliant with treatment and their hypothyroidism was corrected before the third trimester. However in 4 women the subclinical hypothyroidism persisted till the postpartum period. Among these 4 women 2 were found to have Hashimoto's Thyroiditis (as shown in Table 1).

The infants born to these 140 women whose hypothyroidism was corrected during pregnancy and infants born to 140 euthyroid women underwent a detailed general physical examination to rule out features of hypothyroidism in infants. All infants (study and control group) had a good APGAR score (average 7 at 1 min after birth and 9 at 5 min after birth). A detailed otological examination was also done. All these infants were found to be clinically normal. The serum T4 and TSH in all the infants in both study and control groups were found to be normal. However it was observed that in the study group, infants had birth weight of 2.52 ± 0.47 kg and in control group was 2.63 ± 0.40 kg, which was not clinically significant. The level of Anti-TPO antibodies were checked in the infants at the 4th month of life and were below 60uI/mL which was in the normal range. All infants (both study and control group) attained social smile at 2 months of age and good head control at the 4th month of life which corresponds to normal developmental milestones and no global developmental delay was noticed in any infants.

All infants underwent BERA at 1st and 4th month of life. The presence of replicable wave V at 30dBnHL was checked in all the infants. All infants in the control group had replicable Vth peak at 30dBnHL. However, in the study group 2 infants had absent wave V at 30dBnHL in the study group at 1st and 4th month of life. However they showed appearance of replicable wave V at 30dBnHL at 6th month and at 8th month age at 7.32 and 7.43milliseconds. Among these 2 infants, one was born to a woman with subclinical hypothyroidism at the time of delivery and the other infant was born to a woman with Hashimoto's Thyroiditis whose Thyroxine levels were corrected late in pregnancy (third trimester).

It was observed that the latency of wave V on BERA in 50% (66 infants) was slightly prolonged in the study group when compared to the control group at the first month of life. However this minimum delay in wave V in the study group was not statistically significant and later corrected by 4th month of life. The average latency of wave V in the study group was 8.03 ± 0.60 ms at 1st month of life compared to average latency in wave V of 7.76 ± 0.2 ms in the control group. At 4th month of life, the average wave V latency in the study group was 7.9 ± 0.45 ms

Table 1
Showing the types of hypothyroidism in the study group.

TYPES OF HYPOTHYROIDISM DETECTED DURING PREGNANCY	N (%)
Overt	83 (59.3)
Subclinical hypothyroidism	
Early pregnancy	35 (25.0)
Late pregnancy	22 (15.7)

compared to 7.6 ± 0.01 ms in the control group. It was also observed that the minimum delay in wave V latency in 66 infants in the study group involved those infants who were born to women whose hypothyroidism was corrected only during late pregnancy. The average latencies of wave V at 1st and 4th month of life for both study and control group are shown in Table 2. However, on comparing between the groups, it was found that the difference was not statistically significant (p = 0.498, not less than 0.05) (as shown in Table 3).

5. Discussion

In this observational study, infants born to 140 women whose hypothyroidism was corrected during pregnancy and 140 infants born to euthyroid women underwent hearing assessment by Brain Stem Evoked Response Audiometry. 83 out of 140 women were found to have overt hypothyroidism inspite of being on treatment with Levothyroxine supplements and 57 women were found to be subclinically hypothyroid. The high prevalence of overt hypothyroidism inspite of treatment can be attributed to the poor economic conditions, irregular antenatal check-up, lack of awareness and stress on the thyroid gland during pregnancy [5]. The prevalence of Iodine deficiency also contributes to hypothyroidism and goiter in our region.

In other studies hypothyroidism during pregnancy in this part of the country was found to be 11% [2]. Similarly global prevalence of hypothyroidism during pregnancy is 13%. The prevalence of subclinical hypothyroidism in our country is significant. This is because routine evaluation of thyroid function is not done in this rural area. There is lack of awareness particularly among the women [6].

The most common cause of hypothyroidism in our study was autoimmune thyroiditis. Other studies done in this area and neighboring countries also found autoimmune thyroiditis is the most common cause of hypothyroidism [6].

The use of iodized salt and evaluation of thyroid function during pregnancy have decreased the prevalence of severe maternal hypothyroidism and complications like congenital hypothyroidism or miscarriages. However adequate correction of thyroxine levels in these women is not always possible due to irregular follow up and poor compliance in this region. There are very few studies in literature which have evaluated the impact of treatment of hypothyroidism and subclinical hypothyroidism during pregnancy. However literature has shown infants with congenital hypothyroidism have hearing impairment and cognitive dysfunction due to lag in Central auditory processing [7]. A meta-analysis showed that there is no significant difference on the outcome of pregnancy in subclinically hypothyroid and euthyroid women [8]. Therefore treatment of subclinical hypothyroidism during pregnancy is not mandatory. However some studies have shown that Anti Thyroperoxidase antibodies can cross the placental barrier and were found to be high in the cord blood of infants born to hypothyroid women. These anti-TPO antibodies were found to be raised in children with congenital hypothyroidism thereby affecting the development of the child [4]. None of the studies in the literature have evaluated hearing in infants born to women whose hypothyroidism was corrected during pregnancy. It is not clear whether the timing of correction of serum thyroxine levels during pregnancy affects the development of the fetus. Therefore evaluation of hearing in children born to women treated for hypothyroidism during pregnancy is important. This requires objective and sensitive testing by Brainstem Evoked Response Audiometry [9,10].

Table 2
Showing the mean latency of replicability of Vthpeak at 30dBnHL.

The mean latency of replicability of Vthpeak at 30dBnHl		Study group (N = 140)	Control group (N = 140)
1st month	BERA (Mean ± SD)	8.03 ± 0.60	7.76 ± 0.2
4th month	BERA (Mean ± SD)	7.9 ± 0.45	7.6 ± 0.01

Table 3
Showing the inference of the study and control group.

Group	INFERENCE		p value
	Within Normal Limits N (%)	Delayed N (%)	
Study group	138 (98.6)	2 (1.4)	0.498 *
Control group	140 (100)	0	

In our study all the cases (subjects and controls) were found to be clinically normal and were found to have normal serum levels of thyroxine and TSH. This is similar to the results seen in a meta-analysis involving children born to subclinically hypothyroid women. This can be explained by the fact that almost all overt and subclinically hypothyroid women in our study were adequately treated and were almost euthyroid at the time of parturition.

However on evaluation with BERA there was a mild delay in wave V latency in infants born to hypothyroid women on treatment when compared to infants born to euthyroid women at the 1st month of life. However this delay in wave V was minimal. At 4 months age this delay in wave V had reduced. Two infants in the study group had absence of replicable wave V on BERA even at 4months age. This however corrected by 6 and 8 months respectively. Both these infants were born to women who had persistent subclinical hypothyroidism till parturition inspite of Thyroxine supplements. One among these 2 women had Hashimoto's Thyroiditis.

The anti-TPO antibodies estimated for study subjects at 4months age were within normal limits. This indicates that the anti-TPO antibodies transferred to the fetus through cord blood probably declined by 4months of age. Therefore none of the subjects in this study had clinically detectable hearing loss.

There was no clinical handicap in hearing in infants born to hypothyroid women treated with Thyroxine during pregnancy. This correlates with other studies were there was no delay in milestones and neurological development in infants born to women with subclinical hypothyroidism [8,11].

6. Conclusion

There is a significant prevalence of overt as well as subclinical hypothyroidism in pregnant women in rural areas. The infants born to women whose hypothyroidism was corrected during pregnancy had clinically normal hearing. However on Brainstem Evoked Response Audiometry there is minimum delay in wave V latency among these infants which corrects by 4months of age. There can be absence of replicable wave V in such infants if maternal subclinical hypothyroidism persists till parturition. This also returns to normal within 8months of age.

Ethical clearance

The institutional ethical clearance was obtained from our institution both for start of the study as well as for publishing it. Copy of the Ethics committee certificate is attached.

Declaration of competing interest

There is no conflict of interest among the authors. This study was not funded by any institution or agency.

The study did not involve any animal experiments.

There were no experiments on humans. As part of the study, the hearing of the subjects and the controls was evaluated by BERA and their Thyroxine (T4), Thyroid Stimulating Hormone and Anti-

Thyroperoxidase antibodies were estimated.

An informed written consent was obtained from the parents of every infant (subjects and controls) before enrolling them for the study. Their participation in the study, its benefits to science, the investigations involved in the study were explained in detail. There was no expenditure incurred by the subjects or controls for being part of the study nor they were given any financial renumeration.

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