Congenital Hypothyroidism- Newborn Screening- The PIMS Experience

Objective: Screening programs for Congenital Hypothyroidism were established more than 30 years ago, the optimal screening strategy and particularly TSH threshold have not yet been satisfactorily defined. This was obvious in a survey, which outlined the status of neonatal screening in Europe in 2004.

Study Design: Prospective Study

Patients and Methods: Screening of Congenital Hypothyroidism was performed in newborns delivered in Maternal and Child Health center of Pakistan Institute of Medical sciences, Islamabad. This center has more than 1000 deliveries per month. Thyroid Stimulating Hormone (TSH) and T4 levels were done after 8th day of birth.

Results: During 03 years of study period, 1337 newborns were screened. 993 babies reported back with results in OPD. 962 babies had level of TSH \( \leq 10 \) mU/ml. Borderline levels were found in 31 babies, but on repeat test revealed only 03 babies with persistent high levels of TSH.

Conclusions: Screening for hypothyroidism must be offered to every newborn at birth.

Key words: Congenital Hypothyroidism, neonatal screening, TSH level

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Introduction

Hypothyroidism is a common endocrinal disorder. Its clinical presentation is variable but well established in developed countries. Screening programs for congenital hypothyroidism have virtually eradicated mental retardation and impaired somatic growth caused by thyroid hormone deficiency. This has been achieved by early diagnosis and treatment with L-thyroxin. Congenital hypothyroidism is the most common preventable cause of mental retardation. Severe developmental and physical morbidities may result from failure to diagnose this condition early. The disastrous consequences of congenital hypothyroidism occur as clinical features of this condition are subtle and easily missed or may not be evident in neonatal period. Most infants with this condition appear normal at birth in spite of deficiency of thyroid hormones. Screening for hypothyroidism were established more than 30 years ago, but in developing world the optimal screening strategy and particularly TSH threshold have not as yet satisfactorily been defined. This was obvious even in a survey, which outlined the status of neonatal screening in Europe in 2004. Screening TSH cutoff values ranging between 5 and 25 mU/ml were applied in 178 screening centers, using a variety of methods for TSH measurement and showed differences in the prevalence of congenital hypothyroidism.

In Pakistan exact incidence of congenital hypothyroidism is not known as no routine newborn screening is performed. In a study performed in a tertiary care hospital of Karachi, incidence reported as 1:1000. In another study conducted retrospectively in Islamabad also reported high frequency of congenital hypothyroidism in hospital deliveries. Apart from high expected incidence of congenital hypothyroidism, there is also controversy regarding cut off levels T4 and TSH. The newborn screening for congenital hypothyroidism was initiated in Greece as a pilot study in 1979 and was gradually generalized and covered the total newborn population 1990. A blood spot TSH value of 30 mU/ml was initially used as cutoff point, which was lowered to 20 mU/ml in 1990s, a value recommended by the Working group of the EUROPEAN society of pediatric endocrinology. Based on this criterion, an overall prevalence of congenital hypothyroidism 1:3000 screened newborns was found, a figure comparable with that in other European countries and the United States. In a local study conducted on hospital based data in Islamabad, normal reference values of TSH and T4 were determined but no national figures about cutoff levels of TSH and T4 are available.

We planned this study to know the magnitude of the problem and to determine cutoff of TSH level on newborn screening. Babies with borderline levels were recalled to eliminate error of TSH surge in immediate newborn period. In present study level of TSH<10 mU/ml was taken as cutoff normal level in newborn after 8 days of life.
Materials and Methods

The study was prospective and had been carried out between January 2009 and December 2011. Screening of congenital hypothyroidism was performed in newborns delivered in maternal and child health center of Pakistan Institute of Medical Sciences, Islamabad. This center has more than 1000 deliveries in a month. Screening was done in all babies delivered in this center irrespective of mode of delivery. Parents were informed and counseled for congenital hypothyroidism disease and screening. TSH and T4 levels were done after 8th day of life. All tests were sent to NORI, Hospital. Results were collected on follow-up visit to outpatient department. Cutoff value of TSH was set at 10 mU/ml. All babies with value of TSH in range of 10-20mU/ml were considered as borderline cases. They were advised to repeat test and labeled as case of congenital hypothyroidism if repeat test also showed persistent high levels (≥10mU/ml). Babies with level of TSH of more than 20mU/ml were labeled as congenital hypothyroidism and started with treatment and later-on followed up. Blood is taken by heel prick.

Statistical analysis: The SPSS (version 10.0) statistical software was used to analyze the data.

Results

During three years of study 1337 newborns were screened. Out of them, 993 babies reported back in OPD with reports. Rest of babies were considered as loss to follow-up. Out of 993 babies, 962 babies had TSH levels ≤10 mU/ml. Rest of results are as follows:

<table>
<thead>
<tr>
<th>Table I: Babies screened for Congenital Hypothyroidism:</th>
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<tbody>
<tr>
<td>Total babies screened</td>
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<tr>
<td>TSH ≤ 10mU/ml</td>
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<tr>
<td>TSH 10-20 mU/ml</td>
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<td>TSH ≥ 20mU/ml</td>
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<table>
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<tr>
<th>Table II: Sex Distribution in Screened babies</th>
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<tbody>
<tr>
<td>TSH level</td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>≤ 10mU/ml</td>
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<tr>
<td>10-20 mU/ml</td>
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<td>≥ 20mU/ml</td>
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<th>Table III: Levels of TSH in Repeat cases:</th>
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<tr>
<td>TSH level</td>
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<td>----------------</td>
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<tr>
<td>10-20 mU/ml</td>
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<td>≥ 20mU/ml</td>
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Only one baby had clinical goiter, other two were asymptomatic. All babies were full term except one baby who was preterm. This baby had TSH level 20 mU/ml, repeat results were normal. None of the babies had maternal history of thyroid disease. Congenital hypothyroidism was found in three babies of 1337 screened.

Discussion

The characteristic sign and symptoms of Congenital hypothyroidism are rarely seen in the neonatal period. This explains why, before the advent of mass screening approximately 10% of infants were diagnosed clinically in the first month and 35% within three months. The age at which treatment for congenital hypothyroidism is started is determinant of success of screening program. Treatment of congenital Hypothyroidism if started before age of 03 months conduces to satisfactory physical and mental development in affected infants. The sign and symptoms such as jaundice, umbilical hernia, macroglossia, enlarged anterior fontanelle, coarse facial features are rarely seen. In Finland, Virtanen found prolonged neonatal jaundice in 57% of congenital hypothyroidism infants within one month. This is in contrast to our study, as we did not find any significant sign/symptoms in affected patients. Only one baby had Goiter at time of presentation.

Screening programs based on measurement of TSH in blood captures 97% of infants. This has been proved by review of literature. Screening in neonatal age is most significant modality of diagnosing Congenital Hypothyroidism. However, no screening program is 100% sensitive or specific in diagnosing Hypothyroidism. Compared with prescreening period, worldwide reported incidence has more than doubled and is now estimated to be between 1:2000 and 1:4000 newborns. Our Study has revealed very high number of cases (3 cases in 1337 screened). This high level may be because of limited study population. But even in limited data these high numbers of cases suggest the need to screen every newborn for this preventable cause of mental retardation.

Another problem in screening of congenital Hypothyroidism is cut off TSH levels. It’s difficult to compare results of different studies because cut off levels are different. If level of TSH≥30 mU/ml is taken as reference, there is a chance to miss many cases. In multicenter trials it has been proved to keep cut off level of TSH as low as 10mU/ml. This approach is suggested to avoid missing cases with initial borderline levels but later has persistent high levels of TSH. It is now recommended to recall babies with borderline levels of TSH, for a repeat test. This is recommended to avoid over diagnosis and over treating this lethal condition. In our study we used the same method of recalling babies. But contrary to other studies, our study...
showed only two babies with borderline TSH values on initial test that later on had persistent high levels. Surprisingly, our results showed 12 babies to have normal results, although their initial TSH values were more than 20mU/ml. Due to limited sample size our findings suggest need of mass level newborn screening program to have national figures of prevalence and cut off TSH levels to avoid element of over/under diagnosis.

**Conclusion**

Screening for hypothyroidism must be offered to every newborn at birth.

**References**