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PERMANENT AND TRANSIENT CONGENITAL HYPOTHYROIDISM (CH) AND THE RELEVANT FACTORS IN INFANTS BORN DURING 2011-13 IN HORMOZGAN PROVINCE

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ABSTRACT

Background and Purpose of the Study: Congenital hypothyroidism is among the most prevalent preventable causes of mental retardation among infants. A timely diagnosis and treatment can contribute greatly to the prevention of irreparable cerebral/auditory effects. Therefore, the present research aimed to investigate the occurrence of permanent and transient hypothyroidism and its underlying factors in infants born during 2011-13 in Hormozgan province.
Materials and Methods: The present descriptive, cross-sectional research was retrospective in type and was conducted in Hormozgan on 91,938 infants born from March 2011 to the end of February 2013. The occurrence rate of permanent and transient hypothyroidismwas estimated through thyroid tests and the data were analyzed statistically via SPSS v.21.
Results: The overall occurrence of congenital hypothyroidism in three years was estimated to be 1:574. In169 patients with CH, 107 patients were diagnosed with permanent CH (63.31%) and 48 with transient hypothyroidism(28.40%).14 patient were not referred to determining the permanency of CH. This study also revealed a statistically significant correlation between CH and geographical place of resdience.
Conclusion: The overall results indicated a higher rate of CH in south Iran and a higher rate of permanent CH than the global rate. It harshly requires meticulous tests upon childbirth so as to prevent mental retardation as far as possible and also cut down on the financial costs imposed on the healthcare system.

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Introduction

Hypothyroidism is among the most prevalent diseases of endocrine glands (1). The natural functioning of the thyroid is essential for infant's physical and mental growth (2). CH is among the most prevalent preventable causes of mental retardation in infants. It involves a series of clinical and biochemical disorders induced by disruptions in the production or functioning of the thyroid hormone in body tissues (3). The two types that can be conceived are permanent and transient (4).

85% of the permanent type is induced by disrupted thyroid structure such as thyroid ectopia or in situ hypoplasia. About 15% is induced by defective production of thyroid hormones. Another rare factor involved in permanent hypothyroidism is defective growth and unnatural transaction of thyroid hormones into the cell. Transient hypothyroidism can be induced by mother/child-

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related factors. The former includes mother's consumption of anti-thyroid medications, maternal inhibitors of TSH receptors and mother's hyperthyroidism. The latter includes pre- or post-natal increased iodine, congenital liver hemangioma, low birth weight (LBW) (<1500 g) or preterm birth. Transient CH can return to a normal state with or without any need for an alternative treatment. It is essential to diagnose transient CH so as to prevent unnecessary life-long treatments which have certain adverse effects (5).

The majority of infants lack anyclinical symptoms upon birth. These symptoms emerge gradually within 6-12 weeks of birth and is due to the passing of about one-third of mother's T4 which manages to maintain T4 level between 20 and 50% even in the case of full agenesis (6). If the diagnosis is merely based on clinical symptoms, irreparable side effects follow such as loss of hearing or mental retardation (7, 8).

Fortunately, in Iran a screening program was initiated since about 4 or 5 years ago and was incorporated as a national healthcare program. However, the research findings indicated that the national rate of CH was higher in Iran than the global rate and even that of Asia (about 1:1000 live infants born). As no research has been conducted so far with this concern in Hormozgan province and the prevalence of this disease is yet undetermined in this province, the present study was conducted. The aim was to estimate the prevalence of transient and permanent CH and the underlying factors in Hormozgan during 2011-13 so as to better manage to screen and cure the affected children and prevent adverse effects.

Materials and Methods:

In the present descriptive, cross-sectional and retrospective research, as regulated in a national screening program, all infants born in Hormozgan from March 2011 to the end of February 2013 went through a heel prick sampling.

Samples takenfrom the following counties were transferred in a cold box and protected from sunlight to the research center in Bandar Abbas for the required TSH testand were sent via ELISA: Bandar Abbas (the capital), Haji Abad (in the north), Qeshm, Kish, Hormoz, Abu Musa (in the south), Minab, Roudan, Sirik, Jask, Bashagard (in the east), Bastak, Khamir, Parsian, Bandar Lengeh (in the east).

A second blood sample was taken from the following cases2 weeks after the first pricks: the premature (<2500 g), those of a high birth weight (HBW) (>4500), twins or more, those with a history of hospitalization, with a history of blood transfusion, consumption of particular pediatric medications and those with a TSH level≥5-9.9. A TSH level of <5 and <4 were respectively taken as normal for 3-7 day and 8 day infants. Those whose TSH exceeded the above-mentioned levels, the final diagnosis was based on a venal blood sample to measure T4, TSH and T3RU through electrochemiluminescence. It needs to be reminded that if an infant's TSH exceeded 20 in the first screening phase, a treatment procedure was initiated and continued at the same time as the serum test. Once a natural test result was obtained, the treatment was stopped. CH was to be proven by a T4<6/5 µgr/dl, a TSH≥10mu/L and a T3Ru:%25-35 in the venal sample.

The treatment would go on up until the age of three, if a child was diagnosed with CH. Afterwards, the treatment was supposed to be stopped for four weeks followed by a series of t4 and TSH tests. Abnormal T4 and TSH levels would then be a proof for permanent CH while a normal level of the two variables showed a transient type.

According to the existing documents in Hormozgan healthcare center, a checklist was developed comprised of demographic information including infant's sex, birth weight and height (9), place of residence and mother's history of thyroids (10).

The data entered SPSS ver21 for the required statistical analyses. Mann-Whitney U-test was run for the quantitative data and Chi-squared test was employed for the qualitative. The significance level was set at $p<.05$.

Findings:

From among the 96,938 infants screened, 515 were male and 49% were female. 31,985 were screened in 2011, 32,903 in 2012 and 32,050 in 2013.

169 infants were diagnosed with a high TSH in their heel sampling. The mean TSH level of 42% ranged between 5 and 9.9. In 11% of infants, it ranged from 10 to 19.9 and in 26% it was 20 or higher.

Once TSH, T4 and T3RU were measured, the 160 infants diagnosed with CH were treated. A number of 14 (4 in 2011, 3 in 2012 and 7 in 2013) were excluded from the research due to immigration, unwillingness to participate, parents' lack of follow-up and quit on the tests that distinguished permanent and transient CH.

63% of the infants were screened 3-5 days of birth and 37% were screened after 5 days of birth. The mean rate of serum T4 was 29.1±48.47 while the mean TSH was 30.7±33.3. The average age of the infants at the outset of the treatment was 32±23.6 days.

The occurrence rate of transient and permanent CH during 2011-13 is summarized in table 1. Figure 1 casts a comparative look at the occurrence of this disorder within the target years. The overall occurrence rate of CH during these years was 1:574. The overall occurrence rate of permanent CH was estimated at 1:906 and that of the transient was 1:2020.

Table 1: Distribution of infants screened in terms of transient and permanent CH type

Occurrence of permanent CH	Occurrence of transient CH	Total n. of infants with CH	Year span
30(1:1066)	16(1:1999)	46	1390
39(1:844)	20(1:1645)	59	1391
38(1:843)	12(1:2671)	50	1392

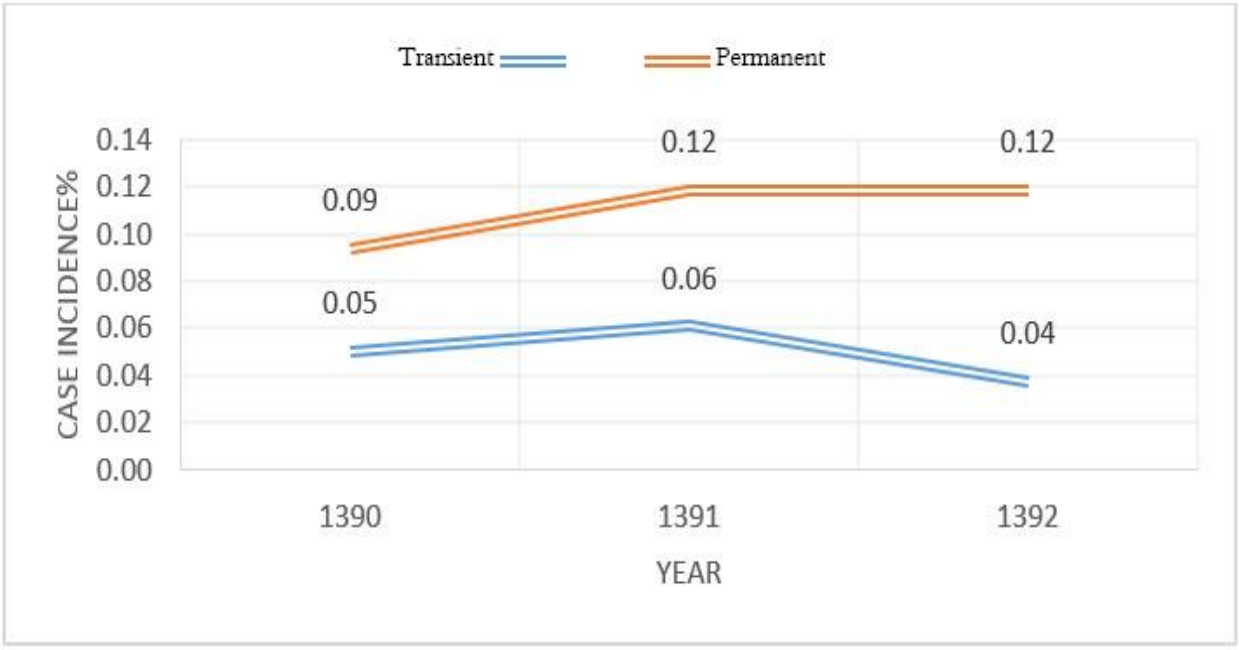

Figure 1: Comparison of the occurrence of CH in 2011-13

The highest prevalence of CH in Hormozgan province was found in Bandar Abbas (29.6%) while the lowest prevalence was in Parsian (1.2%). 72 cases had consanguineous parents. *In 50 cases*,the parents were third cousins; in 22 cases, they were fourth cousins. In 68 cases, the parents were not consanguineous and in 15 cases, whether the parents were relatives or not was evident.

Table 2: indicates patients' with permanent or transient CH demographic information

variable	Transient CH	Permanent CH	P-value
Weight mean(SD)	2920.00(803.06)	2941.65(550.20)	0.658
Height mean(SD)	47.09(4.33)	48.69(2.59)	0.124
Percentage(%)			
2011	12(24.0)	38(76.0)	0.430
2012	20(33.9)	39(66.1)	
2013	16(34.8)	30(65.2)	
Sex(%)			
female	25(32.9)	51(67.1)	0.611
male	23(29.1)	56(70.9)	
Consanguineous parents(%)			
Yes			
No			
Mother's history of thyroids(%)	22(30.6)	50(69.4)	
Yes	26(38.2)	42(61.8)	0.339
No			
	3(37.5)	5(62.5)	1.000
Geographical place of residence (%)	45(32.8)	92(67.2)	
Center			
provincial north			
Provincial south			
Provincial east			
Provincial wet	2(4.3)	44(95.7)	<0.001*
	0(0.0)	3(100.0)	
	10(71.4)	4(28.6)	
	25(37.3)	42(62.7)	
	11(44.0)	14(56.0)	

Discussion and Conclusion:

Hypothyroidism is among the most prevalent endocrine gland diseases in children that can lead to mental retardation but can be prevented and controlled (11).

As the present findings revealed the occurrence rate f this disease in Hormozgan was estimated at 1:574. Similar investigations in Isfahan (12), South Khorasan (13) and Tehran (14) estimated this rate respectively at 1:357, 1:549 and 1:914 which is high in all three cases. The occurrence of this disease was, however, found to be lower in Shiraz (15), Egypt (16) and Thailand (17) reported as 1:1465, 1:2941 and 1:1800 respectively.

Moreover, 69% of infants in the present study whose type of CH was determined showed to suffer from permanent and 31% from transient CH. In other investigations, Hashemipour et al. (12) as well as Bekhitet al. (16) came up with similar results. Those afflicted with permanent CH were respectively 59.8% and 82.3% which was higher than the transient type. Nevertheless, Ghasemi et al. (18) observed a higher rate of transient CH (79.4%) which was inconsistent with the present findings.

Different results across different studies worldwide can be explained by a number of intervening factors:

- the mere employment of T4 or TSH for screening
- different criteria set for a definite diagnosis of CH in infants
- different ethnic and racial characteristics
- contextual, hereditary and familial factors in particular populations (7)
- iodine deficiency in several parts of the world
- excessive use of iodine-containing antiseptics in C-sections especially the case of preterm infants or infants hospitalized in ICU (probably involved in a low prevalence of transient CH) (19).

As it can be observed in figure 1, the less occurrence of permanent CH in 2011 and 2012 followed an increasing trend. Later on, however, this trend was stopped. In 2012, the prevalence of transient CH also followed a decreasing trend. This could be due to the raised awareness of people and a more effective execution of the screening program.

The *optimal* age for initiating the treatment process is not later than 28 days of birth and the *acceptable* age is up until 40 days of infant's life (20). The mean age of treatment initiation in Hormozgan was estimated at 32±23.6 days of age which is acceptable. It showed to be more optimal than the mean age estimated for the total country (until 2010) which was in 92.9% of cases the age of 40 days (21). In some other research in Isfahan (22), the age of treatment initiation was reported to be 22.9±13.2 days. This value was estimated at 17 in the U.K. (23) which appears to be more optimal than that of Hormozgan in the present research. Part of the reason for this difference can be delayed test taking and test results in Hormozgan.

According to the present findings, the mean neonatal T4 level was29.1±48.47. The same value was estimated at 13.82±18.9 and 8.3±2.42 respectively in Siami et al.'s (19) and Hashemipour et al.'s (24) works of research. Concerning TSH level, whereas in the present research this value was30.7±33.31, in the two works of research just mentioned, it was estimated at 35.33±36.05 and 36.85±45.05.

According to the results reported in table 3, the occurrence rate of permanent and transient CH in male newborn infants (50.96%) was much higher than the female. This finding was consistent with that of Ismail Nasab et al. (25). An extensive body of research on CH found sex as a risk factor for this disease. Several studies especially those conducted in Italy (26) and the U.S. (27) reported a higher prevalence of this disease in female than the male population. On the contrary, Ismail Nasab et al. reported a reversed prevalence pattern (25).

Ismail Nasab et al. estimated a statistically significant correlation between affliction with CH and a history of thyroids in family (26). However, what the present findings revealed was a higher rate of CH in infants whose mother had no history of thyroids. This divergence can be explained by preeclampsia in pregnant women and limitation on salt consumption which, in turn,decreases iodine provision for mother's body and the child, as a result.

One particularly interesting finding in the present research was the correlation of geographicalplace of residence and the occurrence of permanent or transient CH in this region. In fact, this disease showed to be more prevalent in certain parts of the province. As an instance, about half of the afflicted population resided in the east while only 1.93% resided in the north. Such factors as iodine deficiency or low quality, ethnic/racial differences, public awareness, authorities' and families' follow-up and reception of screening programs, contextual, hereditary and familial factors can all contribute to the heterogeneous distribution of this disorder within the province.

Among the limitations of this research mention can be made of incomplete or defective medical files, occasional lack of collaboration and follow-up, immigration and, therefore, inaccessibility of several patients in the mid work.

It can be concluded that though the neonatal screening contributed to a timely diagnosis and treatment of the disease, this disease is still threateningly prevalent in Hormozgan. It harshly requires meticulous tests upon childbirth so as to prevent mental retardation as far as possible and also cut down on the financial costs imposed on the healthcare system.

It is further suggested that more retrospective investigations be conducted in longer year spans to clearly manifest the changing trend of the disease in Hormozgan. Regular checks on iodine provision for mothers are also recommended to obtain better results and generalizations to the population.

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Conflict of Interest: None declared

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