

ANNUAL INCIDENCE OF CONGENITAL HYPOTHYROIDISM IN SULAIMANI CITY-KURDISTAN REGION/IRAQ

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Submitted 14/1/2017; accepted 31/12/2017

ABSTRACT

Background: Congenital hypothyroidism is one of the most common preventable causes of intellectual disability. Most neonates born with congenital hypothyroidism are normal on clinical examination. Hypothyroidism in the newborn period is almost always overlooked, and as a result delay in management will cause profound neurological insult and mental retardation. Neonatal screening in Sulaimani city (center of Sulaimani governorate in north of Iraq) had started in 2013 for screening of Phenylketonuria, congenital hypothyroidism and glucose 6 phosphatase deficiency.

Subject and Method: All neonates born in Sulaimani city including all hospital deliveries (both private and public governmental hospitals) in addition to the home deliveries that were referred to (Registration Bureau of Births and Deaths) during the period from January 1st to December 31st 2014 were included. Thyroid stimulating hormone was measured from heel prick blood samples obtained from neonates aged between 3 and 10 days. Neonates showing a TSH level of $\geq 5\text{mIU/L}$ were recalled to Sulaimani pediatric teaching hospital for confirmation of diagnosis. Aim of our study was to determine annual incidence of congenital hypothyroidism in the city.

Results: Among 13050 neonates screened for congenital hypothyroidism, 75 (0.5%) were recalled (TSH, $\geq 5\text{mIU/L}$). Congenital hypothyroidism was detected in 11 (14.6%) recalled neonates (incidence of congenital hypothyroidism in our study 1 in 1186 live births).

Conclusions: According to this result, we concluded that Sulaimani city have high incidence of congenital hypothyroidism and in future, all newborn should be screened in this region including district areas.

Duhok Med J 2017; 11 (2): 27-36.

Keywords: Congenital Hypothyroidism; Sulaimani city; Newborn screening programs.

Thyroid hormone has a key role for normal development of the nervous system¹. Since fetal life till 2 years after birth is deemed as a critical period for central nervous system which depends on thyroid hormone for its development². Congenital hypothyroidism (CH) is the result of hypothalamus–pituitary–thyroid axis dysfunction, which leads to reduction of thyroxin secretion, and consequently causes severe insult to the brain. Congenital hypothyroidism is categorized

as either permanent or transient CH (PCH/TCH), 2 main etiologies suggested for PCH, the first one (85%) is linked to dysgenesis, including atrophy, athyreosis, and ectopic, and the second one (15%) has hereditary basis (major cause is inborn errors of thyroid hormone (TH) synthesis), nevertheless the TCH is unknown. According to related investigations, TCH is resulted from a set of factors including; multiplicity (triple and quadruple), prematurity, low birth weight, and iodine

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deficiency or excessive use of antithyroid drugs. As well as, TCH may also be affected by interaction between genes and the environmental factors^{3, 4, 5, 6}.

Central hypothyroidism — screening programs that utilize the initial T4-blood level and follow-up TSH approach are introduced for diagnosis of Infants with central (hypothalamic or pituitary) hypothyroidism. Central hypothyroidism occurs in 1:25,000 to 1:100,000 newborns⁷.

The high percentage (more than 95 %) of infants with CH do not show clinical manifestations of hypothyroidism at birth⁸. Birth length and weight typically are within the normal range although birth weight can be increased, head circumference also may be increased. Absence of knee epiphyses are more likely to take place among males in comparison with the females (40 versus 28 percent, respectively)^{9, 10}.

Lethargy, slow movement, hoarse cry, feeding problems, constipation, macroglossia, umbilical hernia, large fontanels, hypotonia, dry skin, hypothermia, and prolonged jaundice may be considered as early symptoms and signs of CH¹¹.

An inverse relationship between age of diagnosis and future intelligence quotient (IQ) is observed, so that the delay in diagnosis of CH leads to lower IQ in future¹². Since there is no significant clinical manifestations of thyroid deficiency at birth and the majority of cases are sporadic, it is impossible to predict which infants are likely to be affected. Thus, newborn screening programs (NSP) which was developed in the mid-1970s, is a process that either

thyroxine (T4) or thyroprotein (TSH) are measured in heel-stick blood samples to detect this condition as soon as possible¹³.

Before practicing of screening in 1970, one third of congenital hypothyroidism cases were not diagnosed until 3 months after birth when irreversible mental retardation had been developed^{13, 14}. By five or six months delay in management of CH cases, the IQ could be affected significantly in comparison with those who were detected at birth¹⁶.

Infants with abnormal screening results are recalled for further testing. At this session, the infants are examined and a blood specimens are obtained by venipuncture to support hypothyroidism detection. If the diagnosis of hypothyroidism is confirmed, other sophisticated investigations (such as thyroid radionuclide uptake and imaging, ultrasonography, tests for thyroid autoantibodies, serum thyroglobulin assay or urinary iodine excretion) may be performed to identify the final diagnosis.

Prematurity is suggested as another cause for low serum total and free T4 and normal serum TSH concentration¹⁷.

As the main purpose of treatment; a normal growth and development and similar psychometric outcome to genetic potential should be obtained by normalizing the serum T4 concentration rapidly followed by continuous clinical and biochemical euthyroidism. Oral levothyroxine (L-T4) is the treatment of CH cases. Dose of L-T4 — Both dose of TH replacement and timing are important^{18, 19, 20}. The American Academy of Pediatrics (AAP) recommends a starting L-T4 dose of 10 to 15 mcg/kg/day²¹. The initial aim of management should be to restore the serum T4 concentration to more

than 10 mcg/dL (>129 nmol/L) or a serum free T4 in the upper half of the normal range for age as soon as possible, and keep the serum T4 or free T4 (fT4) concentration in the upper half of the normal range in the first year of life.

In the past 40 years, neonatal screening programs for CH decreased incidences of severe MR in those infants who were diagnosed and treated early in infancy. The neuropsychological evaluation of children with CH detected early has shown normal mental development in almost all cases, although, a certain percentage of infants albeit treated early, show mild anomalies of mental development.

The aim of this study was to find out the incidence of congenital CH in Sulaimaniya city.

PATIENTS AND METHODS

We did a retrospective study in Sulaimani Pediatric Teaching Hospital which started neonatal screening for all life births inside Sulaiamni city (which is center of Sulaimani Governorate) in June 2013. From the total of 32055 neonates who were born inside Sulaimani Governorate and referred to (Chwarbakh Bureau for Births and Deaths) in Chwarbakh Street, 40.7% of newborns (13050 neonate) were from Sulaimani city and included in this study which extended from January 1st 2014 to January 1st 2015. Birth certificate are only issued from this Bureau after the completion of screening tests, so one can be certain that almost all newborn babies during this period were included in the study except for small number of children who were discussed latter in exclusion criteria. Demographic information, including data for age,

weight, sex, maturity, parental consanguinity were recorded in a questionnaire. Thyroid stimulating hormone concentrations were measured from blood sample taken from heel-prick by trained nurses for all newborn aged between 3 and 10 days (all children included and no family registered to refuse this test. The specimen were subjected to enzyme linked immunosorbent assay (ELISA).

Babies were not included in the screening program:

- Refugee babies from other provinces of the country, Syrians and Iranians.
- Sick babies who remain in hospital the first 2 weeks of life.
- Babies from districts and towns outside of Sulaimani city (target group was babies from Sulaimani city).

At registration bureau Blood specimen were collected on a collection card (we used Whatman 903 to collect the infant's blood on the pre-printed circles on the sample card) and all collected sample for that day were transferred to screening department in pediatric teaching hospital in a special container. In hospital using Neo-PKU Kit: Quantitative enzymatic assay of TSH in dried blood spots were performed. Blood TSH level of 5 mIU/L is considered as the cutoff point. Neonates with TSH levels of less than 5 mIU/L were excluded from further evaluation. However, neonates with TSH levels greater than 5 mIU/L in filter-paper blood samples were recalled within 1 week for confirmation of CH by radioimmunoassay for TSH and T4 levels from venous serum samples.

Primary CH was diagnosed if T4 levels were less than 111.11nmol/L and TSH levels were more than 10mIU/L.

RESULTS

A Total of 0 13050 newborns who were included in our study, 6690 were male (51.26%) and 6360 were female (48.74%), which mean male: female ratio of (1.1:1).

Thyroid stimulating hormone value of 5mIU/L was considered as cut value for recall for further investigation in hospital, From all screened newborn 75 (0.5%) of them have a TSH of >5mIU/l, of which 42 were females, and 33 males giving a female to male ratio of 1.3:1.

Distribution of the TSH level in these 75 cases were as follows:

64 cases (85.33%) from 5-10 mIU/L

4 cases (5.33%) from 10.1-20 mIU/L

2 cases (2.66%) from 20.1-60 mIU/L

5 cases (6.66%) more than 60 mIU/L

Only 70 patients recalled (5 cases were lost because of not responding after recalling, their TSH level were between 5-10 mIU/L). Second heel prick blood sample results revealed that only 11 patients had TSH level more than 10mul/l and diagnosed as CH, of which 6 were females, and 5 males giving a female to male ratio of 1.2:1.

Distribution of the TSH level in these 11 cases were as follows:

2 cases (18.18%) from 10-15 mIU/L

3 cases (27.27%) from 15.1-20 mIU/L

1 case (9%) from 20.1-60 mIU/L

5 cases (45.45%) more than 60 mIU/L

Regarding parents of cases which were diagnosed as a case of CH: three of them had consanguinity positive, no one had history of drug use during pregnancy or exposure to radiation.

One premature and ten full term, one had family history of CH, the annual incidence of CH in our study was 1 in 1186.

DISCUSSION

The annual incidence of CH among neonates in Sulaimania city has not been determined in past , but this study shows that the estimated incidence is 1 in 1186 live births which is considered high incidence region compared to other countries as the incidence of CH varies throughout the world, but the worldwide reported incidence is 1 in 3000-4000 live births^{22,23}. It has been reported to be 1:2097 in Saudi Arabia ²⁴ and another study which was performed in between 1997 and 2001 in Tehran and Damavand by Ordookhani, et al.²⁵ showed an incidence of 1:914, although it was reported to be 1:1433 in the study of Amirhakimi et al from Shiraz in 1990²⁶, and another study showed incidence of 1:370 which was done by Hashemipour et al from Isfahan²⁷. We think that similarity in incidence of CH between our city and Iranian province is a result of similar consanguinity marriage rate in the community and screening kits used were manufactured by the same country.

In Baghdad, a study which was performed from Dec. 1st 2001 to Dec. 31st.2002 on a total of 6949 neonates were screened for CH, three neonates were proved to have Congenital hypothyroidism (incidence of 1: 2275)²⁸.

The CH re-call rates also vary from 0.16% to 3.3% among different countries in which the screening programs were performed between 3 and 5 days after birth^{29, 30, 31}. In the present study, the recall rate was 0.57%, the recall rates in other

countries, after primary TSH level assessment in neonates aged 3–5 days, varied from 0.16% to 3.3%. The recall rates were 0.16% in the Philippines, 0.3% in Greece, 2.3% in Turkey, 0.35% in Austria, 0.28–0.29% in Hungary, and 3.3% in Estonia^{24, 30, 32-37}. In contrast, in some studies conducted in Italy, the recall rate measured on the basis of T4 levels was 2.5%, while that measured on the basis of both T4 and TSH levels was 0.11%³⁸, these huge differences in recall rate for newborn screened for congenital hypothyroidism mainly depends on either T4 level or both T4 and TSH measurement done for screening and also depend on time of taking blood sample as in studies in which most of samples are taken during 3rd and 4th days of life will have a high recall rate because of larger number of newborns with transient hypothyroidism will be recalled. In addition the cutoff point for recall is detrimental, the lower the cutoff point of TSH level; the higher the recall rate.

The female: male ratio for CH varies in different countries and is reported as 6:1 in Estonia, 3:1 in Saudi Arabia, 1.2:1 in Japan and as 1.4:1 in the eastern part of Iran^{39,40,41, 42}. Results of most screening programs also suggest a female preponderance for CH, approaching a 2:1 female to male ratio⁴³. In our study female to male ratio was 1.2:1. The differences in prevalence and in female/male ratios may be due to differences in prevalence of consanguineous marriages and to differences in frequency of undiagnosed family history of CH, as reported also by Castanet et al⁴³. Again, the preponderance of CH in females might be due to undiscovered genetic factors, perhaps

linked to autoimmunity, which is usually more common in females⁴⁴.

Several studies have shown that CH is more prevalent among Asians than among non-Asians. Rosenthal et al. performed a study on the prevalence of CH among different races, nationalities, and small communities, particularly Muslims and Asians, in the United Kingdom⁴⁵. They found that the incidence rate of CH among Asians was 1 in 918 live births; our results were closer to this value than they were to the incidence of CH in non-Asians (1 in 3391 live births). They attributed this high prevalence of CH among Asians to increased rates of parental consanguinity⁴³. In conclusion, the annual incidence of CH in the present study is similar to the incidence in the nearby countries. This study might be used as a Pilot for introducing a national neonatal screening program for CH in Iraq as it can be conducted in hospitals following an intensive training course for doctors, nurses and laboratory personnel.

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ثوختة

ريذةي سالانتي ئو منالانتي لة شاري سليمان لة داك نعين وة توشى كمي رذيني دةرقي زطماكي بوون

نيشةكي: كمي رذيني دةرقي زكماكي يتيكة لة هوارة سقرةكيةكاني نةخوشي دواكوتني طةشةي ميشكي منال كة لة توانادا هتية خوي ليبثايزريت , زوربةي ئو منالانتي بقم نةخوشيةوة لة دايم نعين لة سقرةتايي ديانيدا ئاسايين وة نةخوشيةكيةان ثبوة ديار نيبوة وة زوربةي كات ئو منالانتي لة لايقن ثريشكوة نةخوشيةكيةان تةشخيص ناكريت وة نقم دواكوتني لة ديار لة ديار كرندي نةخوشيةكية دةبيتة هوي زيان ئيطتشتني مشيسكي منال و دواكوتني طةشةي ميشكي منال وة ئيفليجي منالكة , ثروطرامي تشكنيني منالي تازة لة داك بووي لة شاري سليمان لة سالي 2013 دةستي ثيكرد بو ديار كرندي ئو منالانتي كة كمي رذيني دةرقي و نةخوشي كمي نةنزيمي (G6PD) زطماكيان هتيةو ئو منالانتي نةخوشي PKU هتية.

ريكين ظكولينى: هتموو ئو منالانتي لة ناو شاري سليمان لة داك بوون وة لة نوسينطةي ضوارباخ بو لة داكبوون و مردن تومار كراون لة نيوان 2014\1\1 تا 2014\12\31 وة نقم منالانتي لة ربي وقررتني خوين لة قاضى منالكةوة تشكيرون وة ئو منالانتي ئنجامي تشكينينةكيةان ئاسايي نةبووة , ئو منالانتي نيردراون بو نةخوشخانتي منالان تا تشكنيني تريان بو بكريت تا نةخوشيةكية ديار بكريت.

ننجام ودةرنةنجام: ئنجامي تشكنيني كوتايي دةرختوة كة نةخوشي كمي رذيني دةرقي زكماكي لة شاري سليمان بريتية لة 1 منال لة هتموو 1186 منالدا وة نمةش ريذةتيكي بقرزة وة وا ئيوس نةكات هتموو مناليك لة هتريمى كوردستان نقم تشكينيتي بو بكري لة داهاتودا.

الخلاصة

المعدل السنوي لقصور الغدة الدرقية الخلقي في المدينة السليمانية

الخلفية والأهداف: قصور الغدة الدرقية الخلقي، هو واحد من أسباب الأكثر شيوعاً للإعاقة الفكرية و الذي يمكن يمكن الوقاية منها. معظم الأطفال حديثي الولادة الذين عندهم هذه مرض يبدون طبيعيين في الفحص السريري. قصور الغدة الدرقية في فترة الولادة يتم تجاهله غالباً ، و تأخير تشخيص يسبب إعاقة العصبية دائمة والتخلف العقلي. وفحص الأطفال حديثي الولادة في مدينة السليمانية (مركز محافظة السليمانية في شمال العراق) بدأت في عام 2013 لفحص قصور الغدة الدرقية الخلقي ونقص انزيم G6PD و مرض PKU.

طرق البحث: شملت جميع حديثي الولادة ولد في مدينة السليمانية بما في ذلك جميع الولادات في المستشفى (كل من المستشفيات الحكومية العامة والخاصة) بالإضافة إلى الولادات المنزلية التي تم تسجيلهم في (مكتب تسجيل ولادات والوفيات) خلال الفترة 1 كانون الثاني - 31 كانون الاول لعام 2014. وقد تم اخذ عينات الدم من خلال وخز الكعب و تم فحص كل حديثي الولادة الذين تتراوح أعمارهم بين 3 و 10 أيام أطفال الذين عندهم مستوى TSH أكثر من 5 $\mu\text{IU/L}$ تم إحالتهم إلى مستشفى الأطفال التعليمي للتأكيد تشخيص.

النتائج: من بين 13050 طفل تم فحصهم خلال هذه المدة 75% (0.5) تم إحالتهم (TSH أكثر 5 $\mu\text{IU/L}$ قصور الغدة الدرقية الخلقي تم تشخيصها عند 11 (14.6) طفل , نسبة قصور الغدة الدرقية الخلقي في دراستنا كان 1 من 1186 طفل حي عند الولادة.

الاستنتاجات: ووفقاً لهذه النتيجة التي خلصت إلى أن مدينة السليمانية لديهم نسبة عالية من قصور الغدة الدرقية الخلقي وفي المستقبل يجب فحص جميع الأطفال حديثي الولادة في هذه المنطقة بما في ذلك المناطق منطقة.