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The Relationship between Thickness of Nuchal Translucency and Down Syndrome in the First Trimester of Pregnancy

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Abstract

***Background*:** Various anomalies, especially Down syndrome impose heavy emotional and financial burden on families and communities by development of mental and behavioral retardation. The purpose of this study is to assess the value of Nuchal Translucency **(**NT) to diagnose Down syndrome in the first trimester of pregnancy.

***Materials and Methods*:** This prospective study was conducted through evaluating 102 pregnant women of 17-44 years old with gestational age of 11 to 13 weeks and 3 days, in a private radiology clinic in Zahedan during May 2008 to June 2010. All embryos were ultra-sounded by a radiologist, their NT and crown-rump length were measured. After birth, all infants were examined by a pediatrician and cases suspected with Down syndrome were diagnosed through karyotype test.

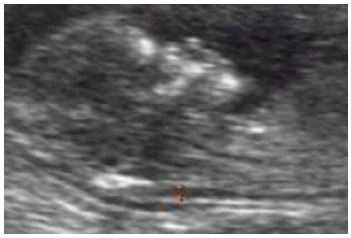
***Results*:** The mean of NT was 1.62 mm. NT was above 1.7 mm for women older than 35 years and it was 3.1 to 3.8 mm for women older than 40 years. 6 out of 7 cases diagnosed postnatal with Down syndrome, had above 95% normal NT and 4 out of 7 mothers who had baby with Down syndrome, were older than 35 years.

***Conclusion*:** Through measurement of NT during 11th to 13th weeks of pregnancy and consideration of base risk factors, the possibility of Down syndrome can be assessed and necessary diagnostic evaluations can be performed for risky cases.

Introduction

Trisomy is the most common chromosomal abnormality and the most common of which is trisomy 21 called Down syndrome [1]. Patients with Down syndrome typically have mental retardation [2]. The frequency of this syndrome in Iran is one out of 814 live births [3]. The patients with Down syndrome are recognized at birth with symptoms such as mental and developmental retardation and special facial features [4] and the definitive diagnosis will be done through examination of chromosomes [5]. Nowadays with the advancement of science, high-risk pregnancies can be first identified using noninvasive and inexpensive screening methods, and then infection or non-infection of the fetus can be detected using other diagnostic methods [6]. One of these methods is to measure nuchal translucency (NT) in the first trimester of pregnancy (Fig. 1).

Figure 1. Placement of fetus to calculate nuchal translucency thickness



Increased NT thickness is caused by fluid accumulation in this area. Although this increased thickness has been attributed to different reasons such as cardiac, anemia, or lymphoma problems, this scale is very close to chromosomal disorders.

NT is measured by measuring the transabdominal or in some cases, by measuring the trans-vaginal at sagittal section and neutral placement of fetus neck. NT can be normal up to 2 mm in 11th gestational week, and 1.7 mm in 12th to 13th gestational weeks and 2.8 mm in the 50% percentile and 95% percentile. If NT more than normal 95% higher than gestational age, with the help of other laboratory techniques and early diagnosis of Down syndrome, pregnancy can be terminated in the first trimester of pregnancy.

According to performed calculations, accuracy of NT to diagnose Down syndrome is 75% [7]. First trimester screening was first conducted in 1990 in London to diagnose Down syndrome [8]. Many studies indicate that the incidence of Down syndrome has a direct linear relationship with maternal age up to 30 years of age [9] and after that, its prevalence progressively increases and it is observed at 40 and above, more than any other age. Furthermore, Down syndrome is more seen in the infants born to mothers addicted to drugs and smoking. This

study aimed to assess NT value by ultrasound for screening and early detection of Down syndrome.

Materials and Methods

This prospective study was conducted through random sampling on 102 pregnant women with gestational age of 11 to 13 weeks and 3 days during October 2008 to July 2010, who referred to a private radiology clinic in Zahedan. Gestational age ranging from 11 weeks to 13 weeks and 6 days (based on crown-rump length scale) and informed consents were considered as inclusion criteria. 110 pregnant women with inclusion criteria and interested in participating in the study were randomly selected for participation in the study, among whom 8 cases were excluded for such reasons as abortion, delivery in another city and lack of access to mother and baby as well as lack of cooperation of subjects.

First, the conditions of research were explained to all participants in written and informed consent was obtained from them. In order to record information, a questionnaire was designed by the researcher in which the required information, such as maternal age, gestational age, and smoking of cigarettes, tobacco or drugs abuse were recorded. Then, all referred patients were examined by an ultrasound specialist and fetal NT and crown-rump length (CRL) were measured and recorded with My lab 40 ultrasound and probe 3.5 MHz. Cases in which gestational age by CRL was not in the range of Inclusion criteria, were evaluated by NT. NT thickness between the fetal superficial external skin texture and soft tissue covering the spine in the sagittal mode was calculated at the largest size so that the fetus of 3.4 diameter covers the monitor and cases larger than 2.8 mm were regarded as positive. It should be noted that ultrasound was performed freely for these mothers and according to the study type; the patients were explained that patient information remains confidential and results will be published collectively. After birth, the infants born to mothers participating in research were reviewed and examined by a pediatrician in order to diagnose Down syndrome and the infants suspected with Down syndrome were diagnosed decisively through karyotype test according to their physical and developmental problems.

Results

102 pregnant women with gestational age of 11-13 weeks and 5 days participated in this study. Pregnant mothers aged 17-44. After birth of infants and their examination by a pediatrician and additional reviews, 7 cases of Down syndrome were diagnosed, 6 of which had increased NT in the first three months of pregnancy. 4 infants with Down syndrome were born to mothers over 35 and 3 infants were born to mothers below 35. Table 1 represents the number and percentage of participants in research. Maximum number of subjects was in the age group of 20-24. In addition, the results of the measurement of variable NT has been determined in terms of age groups, NT value was 2.1-3.8 mm with an average rate of 1.6 mm. Maximum values of NT and most cases of Down syndrome were observed in the age groups over 35.

Table 1. Distribution of nuchal translucency and down syndrome cases by maternal age groups

NT (mm) Mean±SD	Down syndrome cases	Numbers of participants	Age groups (year)
1.40±0.18	1	11	Under 20
1.45±0.15	0	28	20-24
1.46±0.17	0	23	25-29
1.58±0.16	2	21	30-34
1.73±0.18	3	12	35-39
3.2±0.20	1	7	40-44
1.62±0.18	7	102	Total

* Nuchal Translucency

The average gestational age in these samples is 12.35±0.74 weeks and the average measured crown-rump length (CRL) was 60.95±13.26 mm. In this study, about 60% of mothers had a history of tobacco use, and 6 out of 7 mothers who had infants with Down syndrome, had a history of tobacco use. It should be noted that every 4 mothers who had infants with Down syndrome and were over 35, had a history of tobacco use. Also, 2 out of 3 mothers under 35 who had babies with Down syndrome also had a history of tobacco use. The sensitivity of this method in the diagnosis of Down syndrome cases in the subjects was 86% with a specificity of 100%.

Discussion

According to the results of this study, a high risk of fetal Down syndrome can be accurately predicted by measurement of NT in the first trimester. In addition, there is a direct relationship between increasing maternal age and smoking by mother and fetus's size of NT. In this study, 7 cases of Down syndrome were diagnosed among which 86 percent increased NT in the first trimester of pregnancy. 57% of mothers of infants with Down syndrome were over 35 and 43% of these infants were born to mothers under 35. 6 out of 7 mothers with infants with Down syndrome (86%) had a history of tobacco use. Diagnostic sensitivity of NT in this study to identify cases of Down syndrome was 86% with a specificity of 100%.

Children with congenital anomalies impose economic, social and cultural burden on family and community [10]. About 20% of embryos that are formed and about 0.5 to 1 percent of infants are also affected by chromosomal abnormalities. One of the most common of these abnormalities is Down syndrome with a frequency of one in every 650-700 infants [11]. Although there is a direct correlation between maternal age during pregnancy and Down syndrome in fetus, 60% of infected infants are born to mothers under 35. Therefore, all pregnant women should be considered for early diagnosis of congenital diseases [9].In his study in 2004, Nicolaides has discussed NT and other ultrasound markers of the first trimester to identify chromosomal disorders. This study shows that NT size alone is able to diagnose 76.8% of trisomy cases [7]. Schuchter et al in 2001 managed to diagnose 57.9%

of Down syndrome cases through NT measurement alone in pregnant women with gestational age of 10 to 13 weeks and to diagnose 94/7% of Down syndrome cases [12] through measurement of NT and serum factors. Although it is better to use ultrasonography measurements and serum markers together to detect chromosomal abnormalities, several studies have shown that NT measurement alone is also effective in diagnosis of Down syndrome. Wayda et al studied NT transvaginal in pregnant women with gestational age of 10-12 weeks. In that study, considering the maximum normal of 2.5 mm and 3 mm, the sensitivity of NT in the detection of Down syndrome was respectively 96% and 85% [13]. Comas et al studied NT size in pregnant women with gestational age of 10-16 weeks. They intended to study the diagnostic value of NT size alone compared with the calculation of NT and serum markers to diagnose Down syndrome. NT sensitivity in diagnosis of Down syndrome cases was alone 92.3% with a specificity of 95.4%. The researchers concluded that NT value is very high to diagnose Down syndrome and there is no need to calculate other serum markers [14]. Panburana et al could diagnose all Down syndrome cases (2 cases) through NT measurement in pregnant women of 10 to 13 weeks [15].

Chasen et al managed to diagnose 83.3% of Down syndrome cases in an extensive research project, through combined measurement of fetal NT and maternal age in 2, 131 pregnant women with gestational age of 11-14 weeks [16]. Whitlow et al managed to diagnose 65.2% of Down syndrome cases through NT measurement in pregnant women with gestational age of 11-14 weeks [17]. Thus, it can be argued that NT measurement can be very useful to diagnose the cases suspected with Down syndrome. However, skills of the sonographer along with good quality of ultrasound machine can be very effective in promoting this approach.

Based on this study, it can be concluded that Down syndrome can be screened in a very high accuracy in the first trimester through the precise measurement of NT and considering maternal age, gestational age, smoking and tobacco use history. Given that most deprived areas of Iran lack adequate laboratory facilities, and most people living in these areas do not afford to pay for specialized tests, ultrasonography of fetal NT is recommended as a useful and efficient, yet simple, inexpensive and applicable tool for screening of pregnant mothers in these areas.

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