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# Down syndrome screening methods in Iranian pregnant women

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**ABSTRACT**

***Introduction:*** Down syndrome is one of the most prevalent genetic diseases. Screening methods for this syndrome are easy and safe and are recommended to all pregnant women particularly mothers over 35 years of age. This study aimed to review the status of Down syndrome screening and related factors in Iranian pregnant women. ***Methods:*** This descriptive analytical study was carried out in 2011. It included 400 women who were randomly selected from those referring to Alzahra Hospital (Tabriz, Iran) during their third trimester of pregnancy. Data was collected through a questionnaire whose reliability and validity have been approved. The data was analyzed by chi-square test in $SPSS_{13}$. ***Results:*** The results showed that while 28 and 26 women implemented screening tests during the first and second trimesters, respectively, only 5 subjects benefited from both (integrated test). Chi-square test showed significant correlations between the implementation of screening methods and age, education level, income, and the location of prenatal care ($p < 0.05$). ***Conclusion:*** The findings of the present study showed women to poorly implement Down syndrome screening methods. Therefore, the necessity of providing appropriate educational programs for health staff and mothers seems undeniable. Moreover, paying attention to the related factors such as income, educational level, and adequate training of mothers during pregnancy is essential.

## Introduction

Despite improvements in discovering the etiology and pathogenesis of abnormalities and malformations, 22% of neonatal deaths are due to major congenital malformations.[1] Down syndrome is the most prevalent congenital anomaly which occurs in one per 800 live births.[2,3] It can result from 3 separate mechanisms including non-separation of chromosomes, Robertsonian translocation, and mosaicism can happen.[4,5] The risk factors which increase the incidence of Down syndrome are increased age of mother and having a previous infant with Down syndrome.[2]

Patients with Down syndrome have specific facial characteristics such as flat nasal bridge, macroglossia, and mongoloid eyes.[6] They also experience retardation and many inabilities including cardiac diseases, gastrointestinal defects, eye and ear problems, hypothyroidism, Alzheimer's disease, severe learning disorder, and a 15 to 20-fold risk for leukemia.[2,5,7]

Having a fetus or child with Down syndrome is associated with a series of familial problems. In fact the inability of many families to adapt with such incapable children sometimes causes depression of women during pregnancy. In addition, birth of a child

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with Down syndrome would result in many problems in the relationships among the family members including the siblings.[8]

All research throughout the world has agreed that 70% of congenital abnormalities are preventable.[9] Screening tests such as double-, triple-, and quad-marker tests and ultrasound investigations,[10,11] which are pretty easy and safe for pregnant women,[12] are used for screening Down syndrome. Since many cases of Down syndrome as well as many fetal disorders occur in families with no history of birth defects,[12] prenatal assessment in high risk women (mothers over 35 years of age) would only detect 30% of risky fetuses. Many children with Down syndrome are born from mothers under 35 years old.[13] Therefore, American College of Obstetricians and Gynecologists strongly recommended all pregnant mothers to implement Down syndrome screening tests.[14]

Congenital malformations are among the most important causes of inability, disability, physical and mental problems, and mortality of infants and children. On the other hand, health care costs for infants with such anomalies have been estimated to be more than 6 million dollars per annum.[1] Down syndrome is the most common congenital anomaly whose treatment imposes a lot of costs on the families and related organizations and thus causes various socioeconomic problems. An epidemiologic study showed that the mean age of Iranian mothers with Down syndrome children is 6 years less than average ages in Western countries.[15] The importance of preventing congenital malformations is hence undoubtedly clear. It has been estimated that costs of screening methods and prevention from Down syndrome are much less than the mean costs of health care and training such children.[6] Moreover, the National Guidelines for Down Syndrome Control[16] and also the third paragraph of national executive guidelines for therapeutic abortion, i.e. physical and mental backwardness fault,[17] emphasize the necessity of screening for the syndrome and recommend abortion in proved cases.

Despite the high importance of Down syndrome screening, no extensive literature review studies have been conducted in Iran to explain the approaches to implement screening methods. This study thus aimed to evaluate the implementation of Down syndrome screening methods and their related factors among pregnant women who referred to Alzahra Hospital (Tabriz, Iran). The results of this study might be useful in developing health care programs to promote health level of mothers and prevent the incidence of anomalies in children.

## Materials and methods

This was a descriptive analytical study to review the implementation of Down syndrome screening methods and their related factors among pregnant women who referred to the Midwifery Clinic at Alzahra Hospital (Tabriz, Iran) during their third trimester of pregnancy. Most patients are referred from other hospitals and health care centers to Alzahra Hospital since it is located in the center of the city and provides services for risky pregnancies and also neonatal intensive care unit (NICU). Given that no study has ever been conducted in this regard, the sample size was calculated as 400 subjects using the formula to estimate a proportion ($n = z^2pq/d^2$) where $p = 0.5$, $q = 0.5$, $d$ (maximum acceptable error) $= 0.05$, and $Z = 1.96$. After calculating the total number of pregnant women who referred to the clinic during a 3-month period, *www.randomizer.com* website was used to randomly select 400 study subjects.

In order to collect data, a questionnaire was designed based on the study objectives and according to available information in books and articles. While the first part of the questionnaire included demographic characteristics, the second part covered midwifery and labor information as well as factors affecting screening methods, e.g. history of having a child with Down syndrome in the family and relatives, consanguinity of the parents, and location of prenatal care. The third part assessed the use of Down syn-

 

drome screening methods, including biochemical serum measurements such as free beta human chorionic gonadotropin (B-HCG), pregnancy-associated plasma protein-A (PAPP-A), and sonographic evaluation of nuchal translucency (NT), during the first trimester. It also included screening methods, such as biochemical serum measurements through quad-marker tests (alpha-fetoprotein, estriol, B-HCG, and inhibin A) and triple-marker tests (alpha-fetoprotein, estriol, and B-HCG), used in the second trimester. We also considered nuchal fold ultrasound, measurements of humerus and femur, and assessments of fetal hyperechogenic bowel, minor hydronephrosis, choroid cysts, short fifth middle phalanx, and nasal bone.

After explaining about the study and its objectives and ensuring the confidentiality of the collected information, consents were obtained from the participants. The questionnaires were then distributed and completed according to health records and documents regarding screening.

Content validity was used to validate the questionnaire. Therefore, it was evaluated by 8 faculty members of Tabriz University of Medical Sciences (Tabriz, Iran). Employing test-retest, a correlation coefficient of 0.83 was calculated and the reliability of the questionnaire was confirmed.

The obtained data was analyzed by descriptive and inferential statistics in $SPSS_{13}$. P values more than 0.05 were considered as significant.

## Results

The results of the study showed the mean (SD) age of the mothers and fathers to be 27.85 (5.66) and 32.51 (6.69) years, respectively. Most mothers (27%) had junior high school education. In addition, they were most (98%) housewives. Primiparous women constituted 41.8% of the participants. Consanguineous marriage was reported by 7% of the women. Most of the subjects were urban residents (85.8%), had planned pregnancy (70%), and had only referred to health care centers to receive prenatal care (40.3%). While 28 and 26 women implemented screening methods only during the first and second trimesters, respectively, no more than 5 women conducted screening methods in both trimesters (Tables 1 and 2).

**Table 1.** Frequency distribution of the study subjects based on implementing screening during the first trimester of pregnancy (n = 400)

| Screening during the first trimester | YES | NO |
|---|---|---|
| Ultrasound indicators (without biochemical indicators)* | 30 (7.25) | 370 (92.75) |
| Biochemical indicators (without ultrasound indicators)** | 13 (3.25) | 387 (96.75) |
| Ultrasound and biochemical indicators*** | 28 (7) | 372 (93) |

Values are expressed as n (%).
* Nuchal translucency (NT); ** Pregnancy-associated plasma protein-A (PAPP-A) and free beta human chorionic gonadotropin (B-HCG); *** PAPP-A, free B-HCG, and NT

**Table 2.** Frequency distribution of the study subjects based on implementing screening during the second trimester of pregnancy (n = 400)

| Screening during the second trimester | YES | NO |
|---|---|---|
| Only ultrasound indicators* | 34 (8.5) | 366 (91.5) |
| Quad-marker test** | 15 (3.75) | 385 (96.25) |
| Triple-marker test*** | 11 (2.75) | 389 (97.25) |

Values are expressed as n (%).
* Nuchal fold (NF); ** Alpha-fetoprotein, estriol, beta human chorionic gonadotropin (B-HCG), and inhibin A; *** Alpha-fetoprotein, estriol and B-HCG

Implementing the screening methods during the first trimester was significantly correlated with mothers' age and education, family income, location of prenatal care, and consanguineous marriage. In other words, the highest frequency of using screening methods in the first trimester was observed among mothers who aged 36-40 years, had an academic degree, adequate income, or consanguineous marriage, or referred to the physician for prenatal care. On the other hand, there was no significant correlation between implementing screening methods during the first trimester and mothers' employment status or place of residence. More importantly, the results showed that 18 out of 34 mothers who aged over 35 years implemented the first trimester screening test while the other 16 did not receive any form of screening (Table 3).

**Table 3.** Factors affecting the implementation of Down syndrome screening methods during the first trimester of pregnancy

| Factors | Implementing screening methods | | Statistical Indicators |
|---|---|---|---|
| | YES | NO | |
| **Mother's Age (years)** | | | |
| < 21 | 5 (10.6) | 42 (89.4) | |
| 21-25 | 9 (9.5) | 86 (90.5) | $\chi2 = 50.209$ |
| 26-30 | 22 (15.6) | 119 (84.4) | P < 0.001 |
| 31-35 | 32 (37.6) | 51 (61.4) | df = 5 |
| 36-40 | 16 (57.1) | 12 (42.9) | |
| > 40 | 2 (33.3) | 6 (66.7) | |
| **Mother's Education** | | | |
| Illiterate | 4 (15.4) | 22 (84.6) | $\chi2 = 17.95$ |
| Elementary | 21 (24.4) | 86 (80.4) | P = 0.01 |
| Junior high school | 20 (18.20) | 90 (81.8) | df = 4 |
| High school | 17 (16.8) | 84 (83.2) | |
| University | 24 (42.9) | 32 (57.1) | |
| **Family Income** | | | |
| Inadequate | 14 (15.4) | 77 (84.6) | $\chi2 = 29.01$ |
| Average | 46 (17.9) | 211 (82.1) | P < 0.001 |
| Adequate | 26 (50) | 26 (50) | df = 2 |
| **Location of Prenatal Care** | | | |
| Physician's Office | 63 (44.1) | 80 (55.9) | $\chi2 = 72.20$ |
| Midwifes' Office | 3 (15) | 17 (85) | P < 0.001 |
| Hospital | 4 (33.3) | 8 (66.7) | df = 3 |
| Health Center | 16 (7.1) | 209 (92.9) | |
| **Consanguineous Marriage** | | | $\chi2 = 11.08$ |
| YES | 13 (46.4) | 15 (53.6) | P = 0.01 |
| NO | 73 (19.6) | 299 (80.4) | df = 1 |
| **Employment Status** | | | |
| Housewife | 2 (0.5) | 390 (99.4) | Fisher's exact test = 0.41 |
| Work at home | 0 (0) | 0 (0) | P = 1.0 |
| Work outside | 0 (0) | 8 (100) | df = 1 |
| **Place of Residence** | | | |
| Urban | 2 (5.5) | 341 (94.4) | Fisher's exact test = 0.33 |
| Rural | 0 (0) | 57 (100) | P = 1.0 |
| | | | df = 1 |

Values are expressed as n (%).

As Table 4 shows, implementing screening methods during the second trimester had significant correlations with mother's age and income and location of prenatal care. In fact, the highest frequency of implementing second trimester screening methods was seen among the age group of 40 year-olds, parents with adequate income, and those who re-

 

ferred to physicians for prenatal care. However, there were no significant correlations between the implementing second trimester screening methods and mother's employment status and education, place of residence, or consanguineous marriage. Furthermore, only 10 out of 34 mothers over 35 years of age referred for the second trimester screening methods and no screening has been performed for 24 women.

**Table 4.** Factors affecting the implementation of Down syndrome screening methods during the second trimester of pregnancy

| Factors | Implementing screening methods | | Statistical Indicators |
|---|---|---|---|
| | YES | NO | |
| **Mother's Age (years)** | | | |
| < 21 | 3 (6.4) | 44 (93.6) | |
| 21-25 | 3 (3.2) | 92 (96.8) | $\chi2 = 25.37$ |
| 26-30 | 20 (14.20) | 121 (85.8) | $P < 0.001$ |
| 31-35 | 20 (24.1) | 64 (75.9) | df = 5 |
| 36-40 | 8 (28.6) | 20 (71.4) | |
| > 40 | 2 (33.3) | 4 (66.7) | |
| **Mother's Education** | | | |
| Illiterate | 1 (3.8) | 25 (96.1) | |
| Elementary | 5 (4.6) | 102 (95.3) | $\chi2 = 9.2$ |
| Junior high school | 1 (0.9) | 109 (99.09) | P = 0.56 |
| High school | 0 (0) | 101 (100) | df = 4 |
| University | 0 (0) | 56 (100) | |
| **Family Income** | | | |
| Inadequate | 11 (12.1) | 80 (87.9) | $\chi2 = 8.29$ |
| Average | 31 (12.1) | 226 (87.9) | P = 0.01 |
| Adequate | 14 (26.9) | 38 (73.1) | df = 2 |
| **Location of Prenatal Care** | | | |
| Physician's Office | 33 (23.1) | 110 (76.9) | $\chi2 = 19.12$ |
| Midwifes' Office | 0 (0) | 20 (100) | P = 0.01 |
| Hospital | 3 (25) | 9 (75) | df = 3 |
| Health Center | 20 (8.9) | 205 (91.1) | |
| **Consanguineous Marriage** | | | Fisher's exact |
| YES | 2 (7.1) | 26 (92.8) | test = 0.41 |
| NO | 5 (1.3) | 367 (98.6) | P = 0.08 |
| | | | df = 1 |
| **Employment Status** | | | Fisher's exact |
| Housewife | 7 (1.7) | 385 (98.2) | test = 0.14 |
| Work at home | 0 (0) | 0 (0) | P = 1.0 |
| Work outside | 7 (46.7) | 8 (53.3) | df = 1 |
| **Place of Residence** | | | Fisher's exact |
| Urban | 7 (2.0) | 336 (97.9) | test = 0.1.18 |
| Rural | 0 (0) | 57 (100) | P = 0.6 |
| | | | df = 1 |

Values are expressed as n (%).

## Discussion

As indicated from the results, 28 women implemented the first trimester screening (7%), 26 women implemented the second trimester screening (6.5%). In fact, 15 (3.75%) and 11 (2.75%) women underwent quad- and triple-marker tests. However, only 5 women conducted screening (integrated) tests during

both the first and second trimesters which indicates the weakness of screening status. No other Iranian study has evaluated the frequency of implementing screening methods.

Although the only advantage of quad-marker test over the triple-marker test is including inhibin A, its diagnostic power (75%) is higher than the triple-marker test (66%).[11,12]

The standard health care protocol for pregnant women in Australia includes serum screening during the first and second trimesters and also NT assessment.[13] Similarly, in England, all pregnant women are recommended to undergo NT evaluation and screening during the first and second trimesters through a series of methods which can diagnose over 60% of the cases and indicate false positive results in lower than 5% of individuals.[13]

In the present study, NT was evaluated in 30 cases (7.25%) without using biochemical screening methods. Although NT assessments in the first trimester can detect less than half of all Down syndrome cases, its use in combination with an algorithm including serum indicators and age-related risk factors would significantly increase the efficiency of screening.[12] According to the literature, the best results would be obtained by employing an integrated test[8,12] which has a diagnostic power over 95%.[5,6] In the present study however, only 1.25% of the subjects underwent the integrated test.

We found higher rates of using screening tests among women with higher age, educational level, and income and also those who referred to the physician's office for receiving prenatal care. Therefore, it seems that physicians had often encouraged women over 35 years of age to undergo screening. However, performing evaluations solely based on higher age would result in diagnosing only 30% of all cases.[13]

Among our 34 participants (8.5%) who aged over 35 years old, 3 (8.8%), 9 (26.4%), and 2 (5.8%) women had received quad-marker test, double-marker plus NT tests, and integrated test, respectively. The 20-year screening program in England, which only considered mother's age, failed to efficiently reduce the prevalence of Down syndrome. Therefore, national institutions announced that screening for Down syndrome should be recommended to all women.[13] In New Zealand, an official screening program has not yet been established. Screening is thus only suggested to older women or to families with a history of a child with Down syndrome. Nevertheless, even women who are not at risk are recommended to be informed about such screening tests.[13] Scotland had stated that integrated screening tests should be available for all women by 2011.[14]

In the present study, amniocentesis was only conducted on 1.5% of all subjects due to positive screening tests. The results were found to be false positive in all 6 subjects. American College of Obstetricians and Gynecologists has suggested invasive tests for women with positive screening.[13] Although the risk of abortion is 0.5-1%[5] in amniocentesis and 1.5% in chorionic villus sampling,[6] the chance of having a sick child is higher than losing a healthy one which approves the usefulness of diagnostic tests.[14]

## Conclusion

The results of this study indicated poor performance of women toward screening methods, particularly the integrated test, for Down syndrome during both the first and second trimesters. This by itself raises the necessity of developing and providing educational and executive programs concerning the primary prevention of Down syndrome. Therefore, presenting the required educations in this regard by the health staff seems fully essential during prenatal period and the first and second trimesters. As mentioned earlier, the factors related with the implementation of screening included age, education level, income, and location of prenatal care. However, the Down Syndrome Control Project (approved by the Ministry of Health and Medical Education, Iran) has recommended to train all pregnant women regardless of what age they are at.[16] In addition, the status of Down syn-

 

drome screening method should be developed by emphasizing all pregnant women about the benefits of diagnosis at initial stages. Since our results highlighted a relation between using screening methods and family income, a major issue about Down syndrome screening is the related costs. The government is thus suggested to make policies to reduce the screening costs and to provide affordable services for all women with any level of income. In addition, considering the poor performance of women, it is suggested to review the status of implementing screening methods again after a public educational program.

The limitations of the present study were not reviewing the barriers of implementing screening and also attitude and knowledge of women toward Down syndrome screening methods. Further studies are hence required to evaluate screening obstacles and knowledge and attitude of staff members and mothers toward screening.

## Ethical issues

None to be declared.

## Conflict of interest

The authors declare no conflict of interest in this study.

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