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The Challenges of Down Syndrome Screening in Primary Healthcare for Pregnant Women in Iran in 2018

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Abstract

Background: This study aimed to evaluate the various aspects of the implementation phase, including an economic evaluation, of Iran's Down syndrome (DS) screening program.

Methods: Data were collected via phone interviews involving three random sample groups, with each group consisting of 1000 mothers who completed their pregnancies in 2018. To analyze the DS screening program from an economic aspect, we compared the costs related to the care of a DS individual in the country with that of finding and aborting a DS fetus based on the current screening program. In addition, to examine the financial expenses, we assessed the false positive rate (FPR) obtained from the tests and the status of pregnancy outcomes in terms of DS birth and the incidences of abortion complications in the interviewed samples.

Results: A total of 94.5% of pregnant mothers participated in the DS screening program. The calculated FPRs in the screening tests were in the range of 15.3% (95% confidence interval (CI): 12.7%–18.1%) to 16.5% (95% CI: 13.7%–19.5%) for mothers registered in Iran's Health Network and 12.5% (95% CI: 10.2%–15.2%) for all mothers. The results suggest the inefficiency of the current implementation of the DS screening program in Iran from an economic perspective and given the respective side effects, especially fetal loss.

Conclusions: The DS screening program in Iran necessitates urgent review and modification.

Keywords: down syndrome, health policy, Iran, maternal health

INTRODUCTION

Down syndrome (DS), a.k.a. trisomy-21, is the most prevalent nonlethal chromosomal abnormality, with an incidence of 1 out of 800–1200 live births.[1] At the global level, the prevalence of this disease accounts for 1 out of 1000–1100 births.[2] DS screening refers to the process of determining the probability of fetal DS in the first and second trimesters. The screening for DS can be achieved in several ways.[3,4]

Combined screenings in the first trimester, the most widely used screening protocol, combines Nuchal Translucency (NT) measurement and serum levels of human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein A (PAPP-A).[5] Through this protocol, the rate of diagnosis of DS in large prospective trials was in the range of 79%–88%, and that of false positive results was approximately 5%.[6] Mother's age affects combined screening;[7] in women who were older than 35 years at the time of delivery, the rate of diagnosis of DS was 90%–95%, which had a higher rate of false positive rate (FPR) (15%–22%).

Combined screening tests in the second trimester include the measurement of triple markers, including of unconjugated estriol (μE3), alpha-fetoprotein (AFP), and total β hCG, in the mother's serum in weeks 15–17 and Quadruple tests, including those for total β hCG, μE3, AFP, and dimeric inhibin-A (DIA), in weeks 15–17.[8] This triple test can diagnose 61%–70% of DS cases, and the false positive results reach 5%. The amount of the fourth marker, called DIA, increases in DS. The addition of this marker to the previous three markers enables the administration of a quadruple test, which, in the case of trisomy 21, is associated with a diagnosis rate of approximately 80% and an FPR of 5%.

Integrated screening tests, which include the following, increase the power of aneuploidy diagnosis. The integrated screening included NT + PAPP-A tests performed on weeks 11–14. The tests were conducted in consideration of the mother's age, a quadruple test in weeks 15–20, and a calculation of the final risk based on these seven parameters. Integrated screening shows an association with the highest rate of DS diagnosis (95%) and 5% of false positive results.[9] Sequential screening comprises two

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research methods.[3] The first one is Sequential.[10] This method includes the implementation of first-trimester tests and risk calculation. Based on the calculated risk, individuals who are at high risk (risk higher than 1.50) are determined, and counseling and diagnostic tests are suggested. Other lower-risk cases are referred to the quadruple test in the second trimester. The second one is Contingent sequential. This method includes the calculation of the risk of infection after the first trimester tests and allotment of women to three groups: high-, medium-, and low-risk groups. High-risk cases are referred for diagnostic tests. No further action is implemented for low-risk cases, and moderate-risk individuals, who account for 15%–20% of the population, are screened in the second trimester.

Cell-free fetal DNA,[11] extensive parallel sequencing or chromosomal selection sequencing, is used to isolate cell-free fetal DNA from maternal plasma to detect DS and other autosomal trisomies,[12] which can be diagnosed from the 10th week of pregnancy.[13] Recent experiments on high-risk pregnancies revealed a 95% detection rate for trisomies 13, 18, and 21 and a FPR of approximately 5%.[14,15]

In the case of a high-risk screening result, complementary and diagnostic tests are performed to confirm fetal DS. The Iranian Health System directs mothers carrying a DS fetus toward legal abortion. In 2011, Iran's Ministry of Health and Medical Education (MOHME) released a legally binding mandate requiring healthcare service providers to recommend to all pregnant women methods for fetal health diagnosis in terms of abnormalities. However, the latter instruction lacked details. Therefore, the MOHME released another document titled, "The Procedure for Screening and Diagnosis of Fetal Abnormalities" in 2013. This document defines the standards and frameworks for fetal screening. Subsequently, the National DS Screening Program was integrated into the Primary Healthcare Program for Pregnant Women in Iran's Health Network. The document has been revised and updated multiple times since 2013. This study was performed during the validation of the 2015 update titled, The National Guidelines for the Prevention of Fetal Chromosomal Disorders; Down Syndrome.[16]

In general, screening programs for a population are cost-effective only when implemented exclusively for high-risk groups, are optional, without substantial cost, and are conducted with careful continuous monitoring.[14,17] False positives and negatives are inevitable, and thus, screening programs can cause harm to people, specifically when they violate the abovementioned standards. Thus, careful evaluation should be conducted on the implementation phase of a national screening program in terms of costs, benefits, performance indicators of various agents, etc.[18]

Public and private sectors provide health services in Iran. The government renders free primary health care services. However, specialized tests related to prenatal screening are not covered by basic insurance and are mainly paid out of pocket. In Iran, approximately 10% of the gross domestic product (GDP) is allotted for health expenses, and from 2010 to 2018, on average, approximately 50% of health expenses comprised out-of-pocket payments.[19] Furthermore, families must directly shoulder DS screening tests. Moreover, as a legal obligation, all pregnant women are strongly advised to undergo DS screening. Therefore, the implementation of the DS screening program will likely result in adverse consequences.

Therefore, this study aimed to analyze the current DS screening program in Iran from a medical and economic point of view, i.e., to determine the mechanism underlying the program implementation medically and whether it is economically efficient. To attain such a goal, sub-objectives, such as the calculation of the cost burden of the DS screening program, the percentage of pregnant women undergoing such tests were set.

METHODS

This study received ethical approval from the Tehran University of Medical Sciences Research Ethics Board (IR.TUMS.MEDICINE.REC.1397.292). This study was a descriptive-analytical (cross-sectional) study performed in 2018. Research data were collected via phone interviews. The research sample comprised randomly selected pregnant women who had completed their pregnancies during the first quarter of 2018 and were registered in the SIB electronic system (SIB is the name of an integrated electronic health system used in Iran's Health Network). This system accounted for 85% of the country's entire population in 2018. The coverage has risen since 2018. It is almost 100% for villages and small cities but is lower for large cities.

This research included three randomly selected sample groups, with each group comprising 1000 women who had finished their pregnancy in the first quarter of 2018. The recruitment period and contact with samples lasted three months. The three sample groups were selected in accordance with the following logic: The DS screening program in Iran has two versions of declared guidelines which are routine and pilot. The pilot version, which has been implemented since 2014, was communicated to 11 medical science universities (in nine provinces). The routine version has been enforced in other provinces since 2012. Accordingly, two sample groups corresponded to the two versions of declared guidelines. However, these samples excluded mothers not covered by the Health Network during pregnancy.

To compensate for this shortcoming, we selected a third sample group that included mothers who had received vaccinations for their 2-month-old infants in April 2018. Unlike its coverage for pregnancy health services, the SIB contains records of almost 100% of the data regarding

infant vaccination. The selected samples in three separate classes were extracted from the SIB electronic system via simple random sampling. Thus, existing electronic system files were used in the initial selection of three separate groups of mothers based on the research objectives. The samples from each class were selected through simple random sampling. In consideration of the specificity of DS screening tests, this study required a minimum sample size of 245. This calculation used estimates of p = 0.9, d = 0.04, and z = 2.

Prompted by the concerns regard missing data, the researcher decided to increase the sample size to increase the power of the study. As the interviews were conducted through phone communication from the university call center, no substantial cost was incurred for the research team. Therefore, the sample size for each group increased to 1000. The Clopper–Pearson exact method was used to calculate the 95% confidence interval (CI) for the selected proportions.

The interviews were fully structured and based on a predefined questionnaire containing 14–16 questions. The same questionnaire was administered to first and second sample groups, and all screening steps were explored to determine whether each step was undertaken, the outcome of each step, and the due costs the interviewees had paid. The questionnaires also explored the pregnancy outcome determining fetal loss and live birth condition in terms of DS. Each person completed the questionnaire for 15–20 min. The direct costs related to screening were inquired in the interviews, and the expenses related to caring for an affected person in other countries were obtained from the literature.

Two trained medical students performed the interviews, heeding the following points: (1) Interviewees were contacted through phone calls using the 5-digit phone number of the Health Department of Tehran University of Medical Sciences (TUMS), (2) prior to asking questions, the interviewers introduced the organization behind the study and elaborated its objectives, (3) interviewees were informed that participating in the study was optional, moreover, they were excluded if they did not want to participate in the study, and (4) interviewees were informed that in case they forgot any information, they could call back the same number and express the complementary points.

We used the phone numbers registered in the Ministry of Health's SIB system to communicate with the samples. Each number was called up to three times. If we failed to communicate with the person during these three attempts a result of calling the wrong number, changing phone numbers, etc., that participant was removed from our interview list and considered missing data. A period of less than one year elapsed between interviews and screening tests. Thus, the probability of recall bias was low. In addition, in Iran, these tests are unusually expensive and not covered by basic insurance. Therefore, they still pose a concern among people. Notably, recall bias is one of this study's limitations.

IBM SPSS Statistics 21 was used in data analysis, including the calculation of the actual variables of interest, i.e., the false positive value (FPV) and positive predictive value (PPV) of the DS screening system and other variables, such as the sensitivity and specificity ratios, and financial calculations. Economic analysis was performed by comparing the total cost of detecting a DS fetus through the current procedure in Iran with the cost of caring for a DS individual heeding US standards. This step was performed in three different scenarios

RESULTS

Overall, 2,096 individuals out of 3,000 who were eligible participated in the study, i.e., the response rate equaled 69.9%. The remaining 30.1% (those who did not answer) comprised individuals whose phones were switched off (23.4%), those with wrong numbers (4.5%), and individuals who refused to participate in the study (2.2%). Table 1 presents the response rate and age distribution of participants in this study. The average age of the participants was 25 years old, and the overall response rate was 69.9%.

A total of 94.5% of mothers in the third sample underwent DS screening tests (Table 1). The FPRs of DS screening tests were 15.3% (95% CI: 12.7%–18.1%), 16.5% (95% CI: 13.7%–19.5%), and 12.5% (95% CI: 10.2%–15.2%) for the first, second, and third sample groups, respectively.

TABLE 1. Phone interview participation in each sample group and their corresponding age distribution

No.	Description of the Sample Group	Number of Participants	Response Rate	Min. Age	Max. Age	Average Age
1	Pregnant mothers under care in the National Health Network, in the pilot program	719	71.9	16	50	23
2	Pregnant mothers under care in the National Health Network, in the routine program	651	65.1	15	46	24
3	All Pregnant mothers (whether covered by the National Health Network or not)	726	72.6	15	57	29

TABLE 2. Primary description and analysis of data gathered through phone interviews

Sample Group No.	1 (N = 719)	2 (N = 651)	3 (N = 726)
1st Trimester Test	711	557	551
NT Sonography (1st-trimester screening)	690	617	602
Sonography + Test (1st-trimester screening)	714	642	647
Quadri Marker Test (2nd Trimester)	335	242	341
% of Compliance with Screening	100%	100%	94.5%
Amniocentesis or CVS	39	41	32
% of Compliance with Amniocentesis or CVS	5.4%	6.3%	4.4%
NIPT	24	27	27
% of Compliance with NIPT	3.3%	4.1%	3.7%
false positive rate (FPR)	15.3 (110/719)	16.4 (107/651)	12.5 (86/726)
SPE (95% CI)*	84.7 (81.9–87.3)	83.5 (80.6–86.3)	87.5 (85.6–90.4)
PPV	1.79 (0.22–6.30)	Indeterminable	Indeterminable
NPV	99.8	99.8 (99.1–99.9)	-
No. of 2nd Trimester Abortions	19	18	0

* Clopper–Pearson exact method

TABLE 3. Average direct clinical costs corresponding to the current DS screening program (US$) in the 3rd sample group who had undertaken each screening stage

Description	1st trimester screening		2nd trimester screening	Invasive complementary tests		
	Double Marker Test (N = 551)	NT Sonography (N = 602)	Quadri Marker Test (N = 341)	Amniocentesis (N = 32)	NIPT (N = 27)	Total (N = 726)
Mean unit cost	30.68	34.09	38.64	363.64	363.64	-
Total costs	16,906	20,522	13,175	11,636	9,818	**72,058**

TABLE 4. Number and percentage of abortions in the first and second sample groups

Sample group no.	No. of participants	No. of abortions by normal mothers	No. of abortions by high-risk mothers	No. of abortions following amniocentesis	Total 2nd trimester abortions (N)	Total 2nd trimester abortions (%)
1	719	5	13	1	19	2.6
2	651	6	12	0	18	2.7

The percentage of invasive diagnostic tests, including amniocentesis and chorionic villus sampling (CVS) was 5.4% (95% CI: 3.8–7.1%), 6.3% (95% CI: 4.4–8.2%) and 4.4% (95% CI: 2.9%–5.9%) for the first, second, and third sample group, respectively. Moreover, for the 3 sample groups, 3.3% (95% CI: 2.0%–4.7%), 4.1% (95% CI: 2.6%–5.7%), and 3.7% (95% CI: 2.3%–5.1%) of participants went through the complementary genetic test on cell-free DNA. The results indicate that 8%–10% of pregnant women were referred for complementary diagnostic tests, including noninvasive prenatal test (NIPT), amniocentesis, and CVS.

The calculated specificity of DS screening tests in the current program were in the range of 83.5–87.5. In addition, the PPV and NPV were 1.79 (95% CI: 0.22%–6.30 %) and 99.8 (95% CI: 99.1%–99.9%), respectively (Table 2). Table 3 provides the direct clinical costs of various DS screening tests in USD. The raw data were in rial, and the exchange rate at the time of the study was 44,000 rial for 1 USD. The direct clinical cost of DS screening for one pregnant woman was estimated at $99.3. Table 4 presents the abortion statistics, which indicate that 2.6%–2.7% of pregnancies ended in the second trimester.

DISCUSSION

Studies on DS screening experiences in other countries revealed compliance rates considerably lower than 94.5%, e.g., 33.6% in Canada, 33% in Sweden, and 30% in the Netherlands.[15,20,21] This finding was due to the restriction of DS screening of high-risk groups (ages higher than 35–40 in different countries), and honoring the right of mothers to inhibit from undergoing DS screening.[20,22,23]

The FPR of DS screening tests ranges 1.8%–5% in countries with firm standards that set an upper bound for the FPR and implement careful monitoring of the process to minimize fetal loss.[14,24–26] This study revealed a large difference between this rate in Iran (12.5%–16.5% for different samples) and 1.4%–5%.

One of the most important reasons for such differences is the implementation of several screening tests in Iran. In addition, any mother with at least one positive result from each test is considered a "positive" case. Thus, the FPR increases with the use of an "OR" operator between various results. In regard to the low specificity of these

tests in Iran, a sequential algorithm has been suggested for DS screening. However, in practice, complementary screening tests are recommended and performed for most mothers, regardless of the results of previous tests.

The following issues also contribute to the above differences in the FPRs: (1) most physicians and laboratories disobey the standards set by the MOHME. As for the side findings of this work, in a survey that was conducted on 40 subspecialists of perinatology, the Ministry of Health set a 1/250 cutoff for determining high-risk cases for referral to additional tests (including invasive tests or NIPT); however, contrary to the national guidelines, according to more than 75% of these specialists, their experts' opinion was to refer a pregnant mother within a cutoff of 1.1100–1500 for additional tests (mainly invasive tests, such as amniocentesis). At the time of conducting the study, one referral laboratory, which performs approximately 70% of prenatal screening tests in Iran, recommended that mothers with a screening risk of more than 1.2000 be referred for NIPT testing, which is contrary to the standards announced by the Ministry of Health on its official website. This approach was reflected in the screening result report sheet presented to the mothers. (2) DS screening's not being limited to high-risk groups. According to the national guidelines at the time of the conduct of the study, health personnel were required to screen all pregnant mothers of any age, even if they were under 20 years old regardless of a positive family history of DS birth or having insurance to support expensive tests. Screening was seriously recommended in this regard. In addition, if a pregnant mother refuses the test, health personnel are obliged to obtain a written waiver from the mother and indicate in her health care file that "if I give birth to a child with Down syndrome, I will take responsibility for the consequences." (3) Conflict of interest. As the private sector mainly provides these specialized tests, and once this issue becomes clearer, any action aimed at improving the current process and raising it closer to national and international standards will be met with resistance by interested groups. A total of 8%–10% of pregnant women in Iran are referred for complementary diagnostic tests, including NIPT, amniocentesis, and CVS. Moreover, the DS screening tests in the current program in Iran have a specificity of 83.5–87.5. In addition, the PPV and NPV reach 0.017 and 99.8, respectively. Notably, the program lacks acceptable PPV and NPV, which indicates the lack of accurate test quality and high false positive and negative results. This condition implies the need to modify and standardize the program.

As noted previously, complementary diagnostic tests in Iran are not covered by insurance coverage nor provided with another form of financial support. However, some developed countries offer complementary diagnostic tests for pregnant mothers for free.[23] From an economic point of view, we compared the following costs to analyze the DS screening program: how much is the cost burden of caring for a DS individual for the country and how much is the cost burden of finding and aborting a DS fetus for the country based on the current DS screening program.

Regarding the first question, in 2002, the cost of raising a DS individual was $677,692 in the US.[27] Based on the US Consumer Price Index for 2018, the abovementioned cost can be updated to $1,148,745 for the timeframe of this study. The abovementioned cost for Iran can be estimated by multiplying the estimated cost for the US by the ratio of Iran's nominal GDP per capita to that of the US.[28,29] Accordingly, considering the US standards, the cost burden of raising one DS individual in Iran was estimated to be 104,431$ in this study's timeframe.

Regarding the second question, i.e., the cost burden of finding and aborting a DS fetus, at least two types of costs must be considered: 1) the costs of required DS screening tests and 2) costs due fetal loss. For estimation of the first type, the probability of DS occurrence in Iran must be determined. In consideration of the maternal age range of births that occurred in the year of study (the last three quarters of 2017 and the first quarter of 2018) and the corresponding DS risk for each range, the DS occurrence for this study had a probability of 1 out of 885. On the other hand, the direct clinical cost of DS screening tests was 3,180 million rials for the third sample group (726 participants), i.e., 3,870 million rials for a population of 885 participants. Considering the exchange rate of 44,000 rials to 1 US$ in the first quarter of 2018, the total cost of DS screening tests for detecting a DS fetus would be $89,000.

Estimation of the second type of cost necessitated investigation of due abortions. Abortions that occurred in the DS screening process are categorized into the following three groups: 1) DS fetuses discovered during the process and were aborted legally; 2) complications of invasive complementary tests; 3) illegal abortions. The third group of abortions can be attributed to the high FPR of DS screening tests, the unaffordable cost burden of complementary diagnostic tests for an average family in Iran, and the lack of financial support and insurance coverage.

Considering 1.5 million births in Iran during the year of study and the probability of DS occurrence (1 out of 885 pregnancies), we expected to deliver 1,695 DS infants if no screening program were implemented. According to the Iranian Legal Medicine Organization, 1371 pregnant mothers obtained a legal abortion license for their DS fetuses within the abovementioned timeframe.

A considerable portion of abortions in the second trimester are related to non-DS fetuses. Thus, some non-DS fetuses were eliminated to discover one DS fetus. These unwanted abortions fell under two groups: iatrogenic abortions and illegal abortions. Iatrogenic

abortions result from the DS screening procedure. According to the literature on obstetrics and gynecology, invasive diagnostic tests incur a 0.5%–1% probability of abortion.[30–32] This study revealed that 4.4%–6.3% of all pregnant women in Iran are referred for either amniocentesis or CVS. In addition, 94.5% of Iranian mothers underwent DS screening tests. Given this information and considering 1.5 million annual births in the year of study, the number of iatrogenic yearly abortions caused by the DS screening procedure in Iran were either 312–893 or 624–1786, depending on the invasive tests' referral rates (4.4%–6.3%) and the selected probabilities (0.5%–1%). (312 = 1.5 million * 94.5% * 4.4% * 0.5%; and 893 = 1.5 million * 94.5% * 6.3% * 1).

Illegal abortions are induced after DS screening. According to the literature on obstetrics and gynecology, apart from fetal or maternal disorders that result in spontaneous abortions in the second trimester, a considerable and often neglected part of second-trimester abortions is due to screening procedures and aneuploidy diagnosis.[30,31] Spontaneous abortions account for 0.5% of the total pregnancies in Ireland, where no screening program is implemented, and elective-induced abortion is illegal.

A total of 2.1%–2.2% more second-trimester abortions were documented in Iran. As for the reasons, we cannot offer explicit judgment as the differentiation between elective and spontaneous abortions was not possible via interviews due to legal considerations. Therefore, limitations were encountered regarding the estimation of the number of illegal abortions after DS screening tests. However, given the high FPR of the current DS screening program in Iran (12.5%–16.4%), which is higher than the standard threshold in developed countries (2%–5%), and the lack of financial support to the cost burden of complementary diagnostic tests, induced abortion remains the exclusive means for families to terminate a DS fetus.

We can investigate the causes of non-spontaneous abortions in the second trimester in three scenarios. The first one is the best scenario. This scenario indicates the absence of illegal abortions (the second group mentioned above). In this case, 312–1786 iatrogenic abortions occur in the second trimester, i.e., 0.19–1.11 normal fetus abortions for each discovery of one DS fetus. The second one is the intermediate scenario. This scenario entails abortions related to high-risk mothers referred for invasive complementary tests, which all illegal, and subsequent to DS screening. This setting assumes that mothers have opted to abort their fetuses to avoid giving birth to a DS infant before undertaking the complementary tests (probably prompted by due cost burden). In this case, illegally induced abortions after DS screening tests range within 1.3%–1.8% of the annual pregnancies. Two extreme states exist in this scenario: 1) lower bound: all spontaneous abortions are abortions related to high-risk mothers; and 2) upper bound: all abortions related to high-risk mothers are induced and illegal. The ranges are equal to illegal yearly abortions of 19,500–27,000. Iatrogenic abortions shall be also accounted for.

The third one is the worst scenario. All 2.1%–2.2% of abortions that occur in the second trimester (after deducting the 0.5% spontaneous abortions) are illegal abortions subsequent to DS screening, i.e., mothers have selected to abort their DS-suspected fetus. This finding means 31,500–33,000 illegal abortions, i.e., 18.5–19.4 normal fetuses for the discovery of one DS fetus, to which we should add iatrogenic abortions.

Fetal loss due to the current implementation of the DS screening program was determined by estimating an individual's economic production at the time of this study. Such a goal was accomplished based on Iran's Gross National Income per capita in the year of study, i.e., $21,050.[24] Multiplying this number by 50, i.e., an individual's productive life period (15–64 years), we obtained a value of $1,052,500.[33]
Next, we identified the loss incurred in each of the above scenarios by multiplying the individual's economic production during their lifetime by the number of fetal losses in each scenario:

1) Best scenario: Loss is only due to iatrogenic abortions:
$$1{,}052{,}500 \times [0.19, 1.11] = [199{,}975, 1{,}168{,}275]\$$$

2) Intermediate scenario: Loss is due to iatrogenic plus induced abortions, and abortions by high-risk mothers are assumed to be induced:
$$\begin{cases} iatrogenic\ abortion\ loss = [199{,}975, 1{,}168{,}275]\$ \\ induced\ abortion\ loss = 1{,}052{,}500 \times [11.5, 16] = [12{,}103{,}750, 16{,}840{,}00]\$ \\ Total\ loss = [12{,}303{,}725, 18{,}008{,}275]\$ \end{cases}$$

3) Worst scenario: Loss is due to iatrogenic plus induced abortions, and all second-trimester abortions are either iatrogenic or illegally induced ones:
$$\begin{cases} iatrogenic\ abortion\ loss = [199{,}975, 1{,}168{,}275]\$ \\ induced\ abortion\ loss = 1{,}052{,}500 \times [18.5, 19.4] = [19{,}471{,}250, 20{,}418{,}500]\$ \\ Total\ loss = [19{,}671{,}225, 21{,}586{,}775]\$ \end{cases}$$

The above costs were added to the total direct clinical costs of DS screening tests to discover one DS fetus, i.e., $89,000. The total cost of finding one DS fetus in the best scenario was $288,975 – $1,257,275. The total cost of finding one DS fetus in the intermediate scenario was $12,103,750 – $18,097,275. And the total cost of finding one DS fetus in the worst scenario was $19,760,225 – $21,665,250.

A comparison of the costs of raising 1 DS child, i.e., $104,431, with the costs of finding one DS fetus in the current DS screening program in Iran, revealed that none of the three scenarios is economically justified. Therefore, if no DS screening were implemented, and the government accepted all DS children and the costs of caring for them, based on US standards, the expenditures would be reduced by 2.7–12 times in the best scenario, by 118–173 times in the intermediate scenario, and by 189–207 times in the worst scenario, compared with the current situation.

Finally, the most critically problematic factors underlying the implementation of the DS screening program in Iran can be summarized as (1) compelling the public to undergo DS screening tests, merging them into the Primary Healthcare Program for Pregnant Women, minus the differentiation of potentially high- and low-risk individuals in the target population; (2) poor consultation programs for pregnant women inform them properly about the various aspects of the DS screening program, i.e., the aim (determining whether their fetus is a DS fetus and helping them abort it rather than curing the anomaly), steps, the meaning of results, and so on; (3) financial support in the form of insurance coverage for DS screening tests, especially the expensive complementary ones, is lacking; (4) conflicts of interest for DS screening service providers that lead to excessive tests; and (5) weaknesses in monitoring key standard indicators can be used to evaluate the performances of laboratories, gynecologists, and radiologists at various stages of the DS screening program.

The limitations encountered in this work comprise incorrect phone numbers and lack of response, which we attempted to solve by increasing the sample size; the interviewee's lack of trust in the interviewer, whom we contacted by calling the special line phone number of the Health Center of TUMS, which is a well-known phone number, and people trusted it more easily; and noncooperation and consent of interviewees to participate in the interview. We attempted to encourage the interviewees to participate in the discussion by expressing data confidentiality and the importance of this study for the health of mothers and children of the country.

CONCLUSIONS

As observed, the cost of screening and discovering fetuses with DS was costly in any scenario compared with the cost of caring for individuals with DS. Therefore, laboratory tests should be revised and standardized due to their low PPV and high FPV. In addition, as screening of low-risk groups, where the chance of disease occurrence is less than that in false positive tests, is practically useless, mandatory screening should be removed in low-risk groups.

CONFLICT OF INTEREST

None declared.

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