



Cost-Effectiveness analysis of ultrasound scans during pregnancy in Iran

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Abstract

Background & Aims: There is limited evidence in Iran regarding the costs, effectiveness, and cost-effectiveness ratios of ultrasound screening scenarios. The aim of this study was to address these knowledge gaps

Materials & Methods: We used the cost-effectiveness analysis of one-time pregnancy ultrasound screening (OTPUS) and two-time pregnancy ultrasound screening (TTPUS) strategies from the societal perspective. We applied a Monte Carlo Simulation model including 1000 pregnant mothers and calculated each scenario's cost, effectiveness, and cost-effectiveness ratios based on 2020 data. We took the direct medical (obstetrician's visits, ultrasound tariffs, and confirmatory tests) and non-medical costs (travel costs) into account to calculate the costs based on the bottom-up approach. Moreover, we estimated the number of detected fetal anomalies as an effectiveness factor by considering the sensitivity and specificity of the screening methods. The average and incremental cost-effectiveness ratios determine the cost-effectiveness of each screening scenario. The data on costs were extracted from the official Iranian public sector tariffs in 2020. Moreover, the epidemiological and diagnostic accuracy data were extracted from the published evidence. We applied the one-way sensitivity analysis to determine the effects of data uncertainty on the study's findings.

Results: The screening costs per pregnant mother in the OTPUS and TTPUS models were \$12.08 and \$17.35, and the effectiveness of these approaches was 8 and 17 detected fetal anomalies per 1000 pregnant mothers, respectively. The average cost-effectiveness ratios were \$1509.50 for OTPUS and \$1020.35 for TTPUS. Finally, the cost of diagnosing an additional anomaly in the two-time ultrasound approach was \$585.56.

Conclusion: The OTPUS model imposes 43.6% lower costs on pregnant mothers, but also detects a significantly lower number of fetal anomalies. TTPUS policy needs \$585.56 more to find an extra case.

Keywords: Congenital Abnormalities, Cost-effectiveness, Iran, Pregnancy, Ultrasound

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Introduction

Congenital anomalies are a leading cause of death in early childhood in developed and developing countries and are considered chronic illnesses and lifelong disabilities. According to the World Health Organization's (WHO) definition, these disorders include single or several structural, functional or biochemical, and molecular anomalies before birth and are diagnosable. The term "congenital anomalies" is often used synonymously with "birth defects" or "congenital malformations".

In Iran, similar to the developed countries, about 3-5% of live births have at least one congenital anomaly. Moreover, about half of these anomalies have a severe condition (1). However, the anomalies point prevalence ranges from 2% in the west to 3.2% in the east of the country, based on lifestyle and accessibility to maternal and neonatal care services (2). The most prevalent types of abnormalities include musculoskeletal, genitourinary tract, and limb abnormalities (2). Congenital anomalies lead to a significant reduction in the individuals' quality of life during their lifetime, impose high financial costs on their family and the health system, and reduce their household incomes (3-7). These anomalies are classified into two categories including minor and major anomalies. Major abnormalities, which include anatomical anomalies, impose severe mobility limitations on the individual and impair his/her quality of life. Consequently, their prompt diagnosis and treatment are absolutely vital. However, minor anomalies, which include structural changes in the organs of the body, do not require treatment and are less likely to affect the patient's quality of life (8).

Therefore, diagnosing fetal disorders in the prenatal stage provides pregnant women with a range of informed choices and prepares them to give birth to children despite these disorders (9, 10). Sonography is a diagnostic imaging technique based on ultrasound and is used to visualize the size and structure of most of the internal organs and various tissues of the human body and determine the different kinds of pathological lesions (11). A pregnancy ultrasound is carried out to diagnose normal and abnormal pregnancy, bleeding during

pregnancy, abdominal pain in pregnant women, determine the gestational age, and specify the location of the gestational sac and the placenta (12).

Ultrasound plays a significant role in the diagnosis of diseases and fetal anomalies. Nonetheless, it may produce unreliable positive and negative results. Moreover, there is no information on the long-term effects of exposure to ultrasound on its detection effectiveness. Furthermore, hospitals or physicians have no unanimous policy regarding the optimal number and timing of ultrasound scans during pregnancy (3, 12, 13). According to the American Institute of Ultrasound in Medicine (AIUM), during pregnancy, ultrasound scans should be carried out only in cases where their medical use is vital. In these situations, there is a need to carry out the ultrasound scans with the least possible contact to obtain the necessary diagnostic information (3).

Nowadays, physicians are very interested in ultrasound screening to identify fetal anomalies, fetal growth restriction, placenta, and gestational age. Moreover, most women want to have at least one ultrasound image as their first baby photo (3, 14, 15). The detection efficiency of the ultrasound varies according to the kind of disease. More specifically, its diagnosis efficiency is 80%, 70-60%, and 70-75% regarding Spina bifida anomalies, congenital heart disease, and Down syndrome, respectively (16). The ultrasound has many potential benefits for pregnant women, but its high cost, especially for low-income families, has raised doubts about its cost-effectiveness for the Iranian health system. Therefore, this study is the first study that aims to measure the costs, effectiveness, and cost-effectiveness ratios of prenatal ultrasound screening scenarios, including One-Time Prenatal Ultrasound Screening (OTPUS) and Two-Time Prenatal Ultrasound Screening (TTPUS) in Iran.

Materials & Methods

Setting

To achieve the United Nations Millennium Development Goals, Iran's healthcare system has designed a national program of Safe Mother in integrated maternal healthcare and organized the referral

system in three levels of first, second, and third service providing. This program aims to improve the quality of maternal and child care during pregnancy and after delivery and intends to reduce the mortality of infants and children less than one year old. Carrying out the pregnant women's Sonography is prenatal care at the first level of healthcare services. The first ultrasound scan is carried out in rural areas free of charge in the reference hospitals. Upon request for more ultrasounds, rural mothers, like mothers living in non-rural areas, can receive services from contracted public and private centers by paying 15% of the government-approved tariff. According to the defined service package, the health system is committed to providing plain radiographs and abdominal ultrasounds in two sessions of 16-20 weeks and 31-34 weeks of pregnancy at the first level of healthcare delivery. Of course, ultrasound of fetal anomalies is not part of the free ultrasound examination.

Ultrasound at the secondary level of healthcare is provided to pregnant mothers based on the share of insurance organizations and franchises approved by the Cabinet in the contracted centers, both public and private. In general, imaging services should be provided in the program's reference centers with a maximum distance of half an hour by car from the mother's living place. If a patient is referred to a radiology and laboratory unit other than the contracted centers, the recipient will bear all costs (12).

Model

This investigation is an economic evaluation conducted from a societal perspective, encompassing pregnant women aged 20–35 years who are referred to public hospitals in Urmia, Iran, over a one-year time horizon. This study analyzed two screening scenarios of performing pregnancy ultrasounds once in the first trimester and twice in the first and second trimesters to diagnose the most common congenital anomalies. Although ultrasound screening of pregnant women is often prescribed in conjunction with other methods of serum testing in the mother's bloodstream such as alpha phytoprotein (AFP), unconjugated sterol (uE3), and

(Free β -HCG), this study focused only on ultrasound screening of pregnant women to obtain an understanding of costs, effectiveness, and cost-effective ratios of the technology available to detect fetal abnormalities. However, only amniocentesis, MRI, and fetal heart echo were used as confirmatory tests and included in the model associated with the positively diagnosed mothers. The sensitivity and specificity of these complementary tests are more accurate than the ultrasound alone, but the combined accuracy of these tests is highly dependent on the type of ultrasound technology used in the first stage. To simplify the study's complexity, which arose from the multiplicity and variety of anomalies studied, we turned all anomalies into one by taking the weighted average of epidemiological and cost values. According to the theory, this type of calculation does not have a significant effect on the results of the study. In this study, we did not include abortion cases in the model due to its legal limitations. We utilized the average NIMA (NIMAI) exchange rate for 2020 (140,000 IRR) as the exchange rate of the Iranian rial versus the US dollar.

Study scenarios

Two alternative and available ultrasound strategies in Iran to diagnose common fetal abnormalities are defined as follows:

OTPUS: First-trimester screening ultrasound with measurement of nuchal translucency with or without nasal bone, which is essential in diagnosing anomalies in the early stages of pregnancy, can be requested for all pregnancies and carried out once from 11 weeks to 13 weeks and six days.

TTPUS: In this combined option, all fetal organs are examined according to ISOUc-AIUM standards during first and second-trimester anomaly ultrasounds. These organs include the head, thorax, abdomen, upper and lower limbs, heart, placenta and amniotic fluid, spine, urogenital tract, gastrointestinal tract, and markers of chromosomal abnormalities. In general, this ultrasound is recommended in all pregnancies at 16-20 weeks. In mothers with diabetes, heart disease, taking various

medications, and having a birth history with an abnormal baby, it may be necessary to repeat the ultrasound if the first result is abnormal. Obstetricians and midwives are qualified people in the Iranian referral system to prescribe the relevant service.

Study data

The secondary data required for this study are generally defined in three categories of cost, epidemiological, and diagnostic accuracy data. We extracted the number and prevalence of congenital anomalies from Iranian population-based studies and accuracy data, including sensitivity and specificity of diagnostic interventions, from published international evidence for ultrasound in the first and second trimesters. We used the "1-specificity" formula to estimate the number of women diagnosed with false positives. The study hypotheses were that all mothers who had a positive diagnostic test received a package of complementary tests, and all women who had a false positive test received a negative test in the complementary tests and continued their pregnancies.

We considered only direct medical and direct non-medical costs to calculate the cost of each screening method for pregnant women. In these calculations, we defined and measured the cost units for each Sonography case based on the official 2020 tariffs in the public sector. We did not calculate capital and staff costs because the infrastructure of pregnant women's ultrasound centers was available and active in almost all public hospital centers. Direct medical costs include the cost of visits of obstetricians, ultrasound tariffs, and confirmatory tests, and direct non-medical costs include patients' travel costs. To calculate the travel costs, we assumed that the average time interval between mothers' living place with the public hospitals using a taxi is about half an hour, the cost of which is equal to 3.04 USD (95% confidence interval: 2.17-3.91 USD). Therefore, in this study, we used secondary data, and pregnant women were not directly involved in the study. The input data used in the cost-effectiveness analysis considering their upper and lower ranges based on the 95% confidence intervals are presented in Table 1.

Table 1. Inputs of the decision tree model for cost-effectiveness analysis of the ultrasound screening scenarios

Inputs	Values	Sensitivity analysis		Ref.
		LL	UL	
Prevalence of congenital anomalies	0.018	0.01 ^o 6	0.02 ^o o	(17)
Accuracy of Sonography				
Sensitivity of the 1 st trimester Sonography	0.425	0.384	0.521	(18)
Specificity of the 1 st trimester Sonography	0.999	0.999	1	(18)
Sensitivity of the 2 nd trimester Sonography	0.510	0.135	0.853	(12)
Specificity of the 2 nd trimester Sonography	0.999	0.999	1	(12)
Costs – USD				
Sonography of 1 st trimester	7.240	6.516	7.964	
Sonography of 2 nd trimester	5.095	4.586	5.605	
Visit	1.617	1.455	1.779	
Travel	3.043	2.174	3.913	2020 Tariffs
Amniocenteses	53.943	48.549	59.337	
Echocardiography	19.325	17.393	21.256	
MRI	29.478	26.530	32.426	
Effectiveness (probability of detection)				
OTPUS	0.008	0.007	0.009	This study
TTPUS	0.017	0.015	0.019	This study

OTPUS; One-time pregnancy ultrasound strategy, TTPUS; Two-time pregnancy ultrasound strategy

Data Analysis

We designed a decision tree (Figure 1) to do a cost-effectiveness analysis that reflects the screening scenarios, costs, and outcomes for 1000 pregnant mothers using the Monte Carlo Simulation model. The alternative approaches can identify fetuses with at least one musculoskeletal, urogenital, organ, neurological, cervical, cardiovascular, gastrointestinal, or chromosomal abnormalities. These eight fetal malformations are the most common in Iran, constituting more than 90% of all abnormalities. There were three possible outcomes in the model; no abnormalities, detected abnormalities, and missing abnormalities. The effective detection probability of the

studied anomalies was calculated as a prevalence-weighted average, incorporating diagnostic sensitivity across both scenarios. The outcome was the actual number of fetal abnormalities detected through prenatal ultrasound screening.

The study results were calculated as the Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER). In the ACER analysis, each of the two scenarios studied is compared with their non-performance, with zero cost and zero effectiveness. In ICER analysis, the TTPUS was compared with the scenario of single ultrasound. We applied the TreeAge Pro 2012 software (TreeAge Software) to analyze the data.

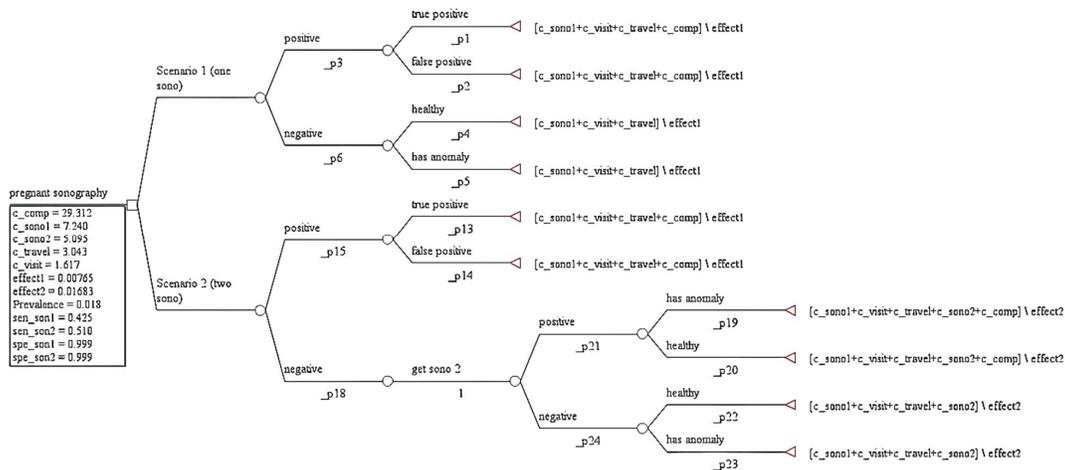


Fig. 1. Decision tree for the congenital anomaly screening during pregnancy with the one-time and two-time pregnancy ultrasound scenarios

Sensitivity Analysis

We applied one-way sensitivity analysis to consider the uncertainty related to the variables and determine their effects on the study results. In this analysis, we used a 95% confidence interval for each parameter.

Results

Findings on cost, effectiveness, and cost-effectiveness of OTPUS and TTPUS in Iran to identify

fetuses with the most common congenital anomalies are presented in Table 2. The average cost of OTPUS and TTPUS is 12,076 USD and 17,346 USD, respectively. The probability of identifying common congenital anomalies in one and twice Sonography is estimated to be 8 and 17 cases per 1000 pregnancies, respectively. The findings show that the average cost for identifying each congenital anomaly in the OTPUS in the first trimester of pregnancy is 1509.50 USD and for the

TTPUS in the first and second trimesters of pregnancy is 1,020.35 USD. The incremental cost of identifying

one more abnormality in a TTPUS is 585.56 USD compared to a single ultrasound.

Table 2. Results of ACER and ICER compared to one-time pregnancy ultrasound screening in Iran

Screening scenarios	Mean per woman (Standard deviation)		Mean per woman (95% Confidence Interval)	
	Costs (USD)	Effectiveness (Detected anomaly number)	ACER (USD)	ICER (Detected anomaly number)
OTPUS	12.076 (2.264)	0.008 (0.001)	1509.50 (1226.51-1792.53)	585.56 (496.22-674.89)
TTPUS	17.346 (3.068)	0.017 (0.001)	1020.35 (839.88-1200.82)	

OTPUS; One-time pregnancy ultrasound strategy, TTPUS; Two-time pregnancy ultrasound strategy.

Figure 2 shows the cost-effectiveness plan for the two Sonographic screening scenarios. In this plan, the TTPUS has a higher cost and effectiveness than the OTPUS.

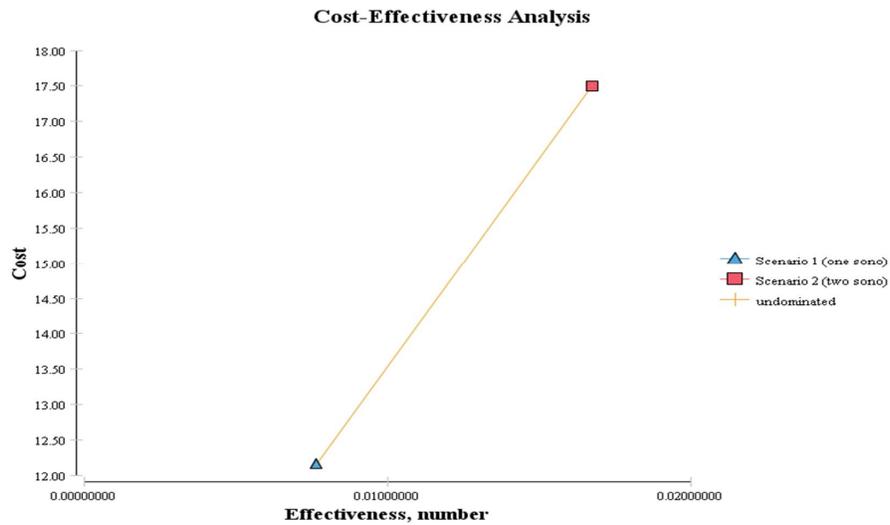


Fig. 2. Cost-effectiveness plan of the pregnancy ultrasound screening scenarios in Iran

The findings of sensitivity analysis in Table 3 showed that the uncertainty about the studied

parameters did not affect the study findings and ICER values varied in the range of 733.76-532.01.

Table 3. Results of one-way sensitivity analysis of ICER for twice versus one-time pregnancy ultrasound screening.

Parameters	Sensitivity analysis		Resulted ICER	
	Lower limit	Upper limit	Minimum	Maximum
Prevalence	0.0156	0.0205	580.31	594.97
Sensitivity of the first-trimester ultrasound	0.384	0.521	585.12	593.07

Parameters	Sensitivity analysis		Resulted ICER	
	Lower limit	Upper limit	Minimum	Maximum
Sensitivity of the second-trimester ultrasound	0.014	0.853	565.94	607.21
Cost of the first-trimester ultrasound	6.52	7.96	587.49	587.49
Cost of the second-trimester ultrasound	4.59	5.61	532.01	643.01
Effectiveness of the first-trimester ultrasound	0.007	0.009	548.64	688.78
Effectiveness of the second-trimester ultrasound	0.015	0.019	576.81	733.77

Discussion

This study evaluates the economics of two pregnancy ultrasound screening approaches, OTPUS and TTPUS, to diagnose the most common fetal abnormalities. The study results showed that the cost of screening in the TTPUS during the first and the second trimesters was about 43.6% more than the cost of screening in the OTPUS (\$17.35 vs. \$12.08). Nonetheless, the cost of diagnosing a congenital anomaly in the TTPUS was about 47.9% less than this ratio in the OTPUS (\$1020.35 vs. \$1509.50). This superiority stems from the double effectiveness of the TTPUS over the other scenario. More specifically, the dual strategy can identify 17 congenital anomalies cases per thousand ultrasound scans compared with only eight cases in the OTPUS. Consequently, the TTPUS was much more cost-effective than the OTPUS and had 50% more economic efficiency. The results of the ICER analysis supported this claim and showed that the TTPUS imposes only 585.56 USD for detecting an additional congenital anomaly that significantly decreases the costs.

The sensitivity analysis showed that the effectiveness ratio of the TTPUS and cost of the OTPUS scenario had the most significant and negligible impact on ICER results, respectively. Nonetheless, the results generally had acceptable validity since the current uncertainty about the input parameters did not significantly influence these results.

This study provided precise cost, effectiveness, and cost-effectiveness information for health policymakers. Despite this, there was no criterion for measuring the cost-effectiveness of the examined interventions since the effectiveness index of the study was the number of diagnosed cases. Consequently, the decision-makers

must decide on applying the pregnancy ultrasound screening scenarios by considering the issue's importance, policies and goals of the health system, upstream laws, and the available budget. Nonetheless, considerable price fluctuations in the Iranian market harm the generalizability of the obtained results in the coming years. The policymakers should pay attention to the fact that the analysis of this study must be updated if there is a significant change in medical tariffs, including the tariffs on visits, ultrasounds, and complementary tests.

According to the Single Article Act of therapeutic abortion, which was approved in June of 2005 in Iran, a legal therapeutic abortion permit will be issued only if there is a definite diagnosis of fetal anomaly or life-threatening maternal disease, which is confirmed by three trusted physicians of the Forensic Medicine Organization and has the mother's consent before the 19th week of pregnancy. Consequently, both examined ultrasound scenarios can help mothers decide about legal abortion before the legal deadline.

The type, timing, and the number of ultrasounds are not the same in the other similar studies. Therefore, their findings are not necessarily comparable to ours. However, the present study results are in line with the results of the studies by et al. (13) and Bricker et al. (12) in England and also Levio (19) in Finland regarding the cost-effectiveness of ultrasound screening during the second trimester. It should be mentioned that there were differences between the examined scenarios of the present study and the scenarios in the mentioned studies. In a study by Roberts et al., the ultrasound screening during the second trimester was more cost-effective than the other 11 different options consisting of four types of ultrasound scans that were carried out to diagnose four

major fetal anomalies, including cardiac anomalies, spina bifida, Down syndrome, and fatal anomalies. The cost of finding each target anomaly in these programs ranged from £5000 to £109000. However, the screening scenarios could not diagnose more than 3.6-4.7 anomalies per 1000 pregnant women.

Similarly, in a systematic review study, Bricker et al. argued that the ultrasound program was a very cost-effective option during the third trimester. The incremental cost of this program to diagnose an additional anomaly ranged from £271-477 compared to a pregnancy ultrasound scan in the second trimester period. Likewise, compared to the OTPUS during the second trimester, the TTPUS during the second and the third trimesters imposed an incremental cost ranging from £7369 to £5809 for detecting one additional fetal anomaly.

Study strengths and weaknesses

The study has limitations requiring cautious interpretation. We focused only on direct medical costs, excluding indirect costs like production losses for mothers and caregivers, which could reduce cost-effectiveness. We assumed fixed government tariffs, lower than private sector rates; using private tariffs might render screening uneconomical in Iran. Costs and effectiveness were set to zero in the non-screening scenario due to data gaps, though some mothers access services informally, potentially causing inequity favoring higher-income families—a topic for further study. Finally, we used foreign accuracy data for ultrasound sensitivity and specificity, which may differ in Iran due to equipment overuse, suggesting that local validation is needed. Despite these, the study's strengths include a robust Monte Carlo Simulation model for cost-effectiveness analysis of OTPUS and TTPUS, integrating local (2020 tariffs, Iranian data) and international evidence for validity. It also provides reliable policy insights via precise ACER/ICER calculations and sensitivity analysis, showing TTPUS's cost-effectiveness with minimal uncertainty (\$532.01–\$733.77 ICER range), enhancing its relevance for Iran's health system.

Conclusion

Taking care of pregnant women is an essential part of any primary healthcare system and is regarded as a high priority in all health systems because it focuses on both the mother and the fetus. Due to limited resources in developing countries, such as Iran, screening pregnant mothers to identify fetal abnormalities is limited. Nonetheless, our findings showed that these services would be efficient and economical if provided with government tariffs in the public sector. Compared with the OTPUS scenario during the first trimester, the TTPUS during the first and second trimesters imposes about 43.6% higher costs on the health system and pregnant mothers. TTPUS is a more efficient policy since it increases the effectiveness by 122.5% and results in the identification of 17 cases of fetal anomalies per one thousand ultrasounds compared to eight cases in the one-time approach. Consequently, we recommend that the TTPUS be given priority over the OTPUS and be allocated the budget needed to implement it.

Acknowledgments

Not applicable.

Author's Contributions

Cyrus Alinia and Sima Ahmadpoor conceived the idea of the study. Cyrus Alinia, Sima Ahmadpoor, and Hasan Yusefzadeh contributed to the study design. Cyrus Alinia performed the statistical analysis. Cyrus Alinia, Sima Ahmadpoor, Hamidreza Farrokh-Eslamlou, and Hasan Yusefzadeh took part in the interpretation of the results. Cyrus Alinia, Sima Ahmadpoor, Hamidreza Farrokh-Eslamlou, and Hasan Yusefzadeh critically revised the manuscript.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available for confidentiality reasons since individual privacy could be compromised, but are available from the corresponding author on reasonable request.

Conflict of Interest

The authors have no conflict of interest in this study.

Ethical Statement

This study protocol was reviewed and approved by the Research Ethics Committee at the Deputy of Research and Technology, Urmia University of Medical Sciences with the Code of Ethics IR.UMSU.REC.1399.286 and was found to comply with ethical standards. This study was in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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References

- Behrman RE, Kliegman RM, Jenson H. Nelson textbook of pediatrics. 16th editions. Washington: WB Saunders Company. 2000.
- Irani M, Khadivzadeh T, Asghari Nekah SM, Ebrahimipour H, Tara F. The prevalence of congenital anomalies in Iran: A Systematic Review and Meta-analysis. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2018;21(Supple):29-41.
- Sharami S, Faraji R, Khoramnia S, Dalile Heyrati S. Survey the reason of maternal request for prenatal ultrasound in low risk pregnancy. *Journal of Guilan University of Medical Sciences*. 2011;20(78):49-55.
- Šamáněk M. Congenital heart malformations: prevalence, severity, survival, and quality of life. *Cardiology in the young*. 2000;10(3):179-85. <https://doi.org/10.1017/S1047951100009082>
- Faal G, Abbasi R, Bijari B. The prevalence of major congenital anomalies among live births in Birjand, Iran. *Modern Care Journal*. 2018;15(2). <https://doi.org/10.5812/modernc.81084>
- Carvalho M, Brizot M, Lopes L, Chiba C, Miyadahira S, Zugaib M. Detection of fetal structural abnormalities at the 11-14 week ultrasound scan. *Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis*. 2002;22(1):1-4. <https://doi.org/10.1002/pd.200>
- Abbaszadeh F, Bagheri A, Mehran N. Quality of life among pregnant women. *Hayat*. 2009;15(1).
- Hematyar M, Khajouie P. Prevalence of congenital anomalies in 1000 live births in Javaheri Hospital, Tehran, 2004. *Medical Science Journal of Islamic Azad University-Tehran Medical Branch*. 2005;15(2):75-8.
- Kavoosi ES, Younessi S, Farhud DD. Screening of fetal chromosome aneuploidies in the first and second trimester of 125,170 Iranian pregnant women. *Iranian journal of public health*. 2015;44(6):791.
- Aryan Z, Bahadori A, Farhud D. Prenatal diagnostic tests of genetic disorders. *Tehran University Medical Journal*. 2019;77(1):8-12.
- Novelline RA, Squire LF. Squire's fundamentals of radiology. La Editorial, UPR. 2004.
- Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, et al. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]*. 2000. <https://doi.org/10.3310/hta4160>
- Roberts T, Mugford M, Piercy J. Choosing options for ultrasound screening in pregnancy and comparing cost effectiveness: a decision analysis approach. *BJOG. An International Journal of Obstetrics & Gynaecology*. 1998;105(9):960-70. <https://doi.org/10.1111/j.1471-0528.1998.tb10258.x>
- Ewigman BG, Crane JP, Frigoletto FD, LeFevre ML, Bain RP, McNellis D, et al. Effect of prenatal ultrasound screening on perinatal outcome. *New England journal of medicine*. 1993;329(12):821-7. <https://doi.org/10.1056/NEJM199309163291201>
- Brezinka C. Training, certification and CME in obstetric ultrasound scan in Europe. *European Clinics in Obstetrics and Gynaecology*. 2006;1(4):223-6. <https://doi.org/10.1007/s11296-006-0015-z>
- Kagan KO, Wright D, Valencia C, Maiz N, Nicolaides KH. Screening for trisomies 21, 18 and 13 by maternal age, fetal nuchal translucency, fetal heart rate, free β -hCG and pregnancy-associated plasma protein-A. *Human reproduction*. 2008;23(9):1968-75. <https://doi.org/10.1093/humrep/den224>
- Daliri S, Sayehmiri K, Asadollahi K, Rezaei N, Saroukhani D. Prevalence of congenital anomalies in

- Iran: a systematic review and meta-analysis. *Iranian Journal of Neonatology IJN*. 2018;9(2):21-32.
<https://doi.org/10.1080/14767058.2018.1465917>
18. Karim JN, Roberts NW, Salomon LJ, Papageorghiou AT. Systematic review of first-trimester ultrasound screening for detection of fetal structural anomalies and factors that affect screening performance. *Ultrasound in Obstetrics & Gynecology*. 2017;50(4):429-41.
<https://doi.org/10.1002/uog.17246>
19. Leivo T, Tuominen R, Saari-Kemppainen A, Ylöstalo P, Karjalainen O, Heinonen O. Cost-effectiveness of one-stage ultrasound screening in pregnancy: a report from the Helsinki ultrasound trial. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 1996;7(5):309-14.
<https://doi.org/10.1046/j.1469-0705.1996.07050309.x>