Clinical and Experimental Obstetrics & Gynecology

*Clin. Exp. Obstet. Gynecol.* **2023**; 50(10): 220
https://doi.org/10.31083/j.ceog5010220

*Original Research*

# Knowledge and Attitude Regarding Non-Invasive Prenatal Testing (NIPT) among Women: A Cross-Sectional Study in Saudi Arabia

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Academic Editor: Michael H. Dahan
Submitted: 11 July 2023 Revised: 22 August 2023 Accepted: 1 September 2023 Published: 20 October 2023

**Abstract**

**Background**: The most prevalent type of inherited intellectual disability worldwide is Down syndrome. Prenatal testing can determine the possibility of a pregnant woman giving birth to an infant with Down's. Many invasive interventions help with early diagnosis of Down's. Although high-risk pregnancies should be offered invasive prenatal diagnosis, the International Society for Prenatal Diagnosis encourages non-invasive prenatal screening testing (NIPT) as a primary screening test for all pregnant women, regardless of risk. The present study aimed to determine the knowledge and attitude regarding NIPT among Saudi Arabian women. **Methods**: This cross-sectional study involving 1028 participants living in Saudi Arabia was conducted from February to March 2023, using a re-designed questionnaire shared among women with pregnancy history. The questionnaire assessed their knowledge, attitudes, and beliefs regarding NIPT. **Results**: Only 14.8% of our respondents had undergone NIPT; the most common indication was a recommendation from their healthcare provider (41.7%). About 3.4% of the respondents had given birth to a child with Down syndrome, and 22% had relatives with chromosomal abnormalities or genetic diseases. Surprisingly, only 22.3% of the respondents had previously heard about NIPT. The mean knowledge score about NIPT was 2.82 $\pm$ 1.89. The mean knowledge score was found to be significantly higher among females who had undergone NIPT, were aged $<$30, and had high school education. **Conclusions**: Most Saudi Arabian women have poor knowledge about NIPT and a positive attitude toward it. Thus, the suggestion is to raise awareness about NIPT use, indications, prices, and possible complications.

**Keywords:** noninvasive prenatal testing; prenatal investigations; maternal fetal health; Down syndrome

## 1. Introduction

Non-invasive prenatal testing (NIPT) is a relatively recent and highly accurate prenatal screening tool for chromosomal abnormalities, such as Down syndrome, that can be performed as early as at 9–10 weeks of gestation. NIPT analyzes cell-free fetal DNA (cffDNA) fragments circulating in the maternal bloodstream, which can be extracted and sequenced to detect extra or missing chromosomes. This method offers various advantages over invasive standard prenatal diagnostic methods, such as amniocentesis and chorionic villus sampling (CVS). Down syndrome is the most common form of inherited intellectual disability, and the most prevalent non-inherited disease caused by an imbalance of genes on chromosome 21 [1]. Prenatal screening assesses pregnant women's risk of giving birth to a child with Down syndrome. Two types of screening are available, which includes maternal serum screening of first- and second-trimester serum, and a combination of nuchal translucency measurement, human chorionic gonadotropin (hCG) or serum free-hCG, and pregnancy-associated plasma protein-hCG. Analytical levels are assessed during prenatal screening in addition to ultrasonography [2]. If the screening tests are positive, an invasive prenatal testing is recommended for confirmation, such as CVS or amniocentesis [3]. As a screening test, NIPT for Down's, Patau's, and Edwards' syndromes is also available [4]. Sensitivity, specificity, and negative predictive value (NPV) are crucial statistical measures to assess the performance of medical tests, including prenatal tests. Sensitivity measures how well a prenatal test can correctly identify fetuses with a particular condition, while specificity measures how well the test can correctly identify fetuses without the condition. NPV measures the probability that a negative test result accurately indicates the absence of the tested condition. For trisomy 21, the sensitivity, specificity, and NPV of this method are all $>$99%, with a slightly lower interpretation for trisomy 13 and 18. A prenatal test with high sensitivity and specificity is desirable, as it accurately identifies fetuses with the condition, and rules out those without it [5]. It is based on the ability to test the cffDNA in the maternal blood [4]. After delivery, the cffDNA that increased with gestational age in the mother's blood is eliminated [6]. As claimed by the American College of Medical Genetics, NIPT is not considered a diagnostic tool as it does not di-

rectly analyze fetal DNA. NIPT instead looks at the proportion of cffDNA fragments with certain chromosomal abnormalities in maternal blood, which can suggest an elevated risk of those fetal abnormalities. Yet, it can replace conventional screening for Down's, Patau's, and Edwards' syndromes, beginning at 9–10 weeks of gestation [7]. The International Society for Prenatal Diagnosis advocates NIPT as a primary screening test for all pregnant women, regardless of risk; even high-risk pregnancies that should be offered invasive prenatal diagnosis should be given NIPT first [8].

Since NIPT is a new screening test, the attitudes and knowledge of women and their families toward it have been studied in various settings, revealing that women's attitudes toward it as a favorable screening test differ across countries [5]. Alsulaiman and Hewison *et al.* [9] discovered that Saudi Arabian parents warmly accepted prenatal diagnosis when King Faisal Specialist Hospital and Research Center in Riyadh introduced the NIPT as a screening test in 2013. A study was conducted in China to better understand the impact of billing strategies on NIPT acceptability and satisfaction, as well as providing some recommendations for NIPT promotion, based on a cross-sectional questionnaire among 622 nonpregnant women and 1201 pregnant women from Shenzhen and Zhengzhou. This study found that 83% of Shenzhen women and 54% of Zhengzhou women who had taken NIPT to screen for fetal aneuploidy were satisfied and accepted NIPT in clinical practice [10]. More than 98% of pregnant women in this study were satisfied and underwent NIPT in clinical practice [10]. A study conducted in Saudi Arabia limited to one hospital in Riyadh collected 150 responses via a survey to assess women's knowledge and attitudes toward NIPT and the factors influencing their decision to undergo the test, revealing that only 38% of women had prior experience with NIPT, 54% understood the test's purpose, and 93% would agree to the test if they were ordered to do it [11].

NIPT has been added recently to the Antenatal Care Program in Saudi Arabia, which will provide a variety of screening options for pregnant women to examine the health of the mother and fetus, involving testing for chromosomal abnormalities and genetic diseases. The Saudi Antenatal Care Program also provides a variety of other services to support the health of mothers and newborns, such as nutrition counseling, breastfeeding and infant care education, and support for maternal mental health.

Few studies have explored NIPT knowledge in Saudi Arabia, and a limited number of genetic counselors are available in the country. Thus, the present study aimed to assess the knowledge and attitude regarding NIPT among women in Saudi Arabia.

## 2. Materials and Methods

Study setting and participants: This cross-sectional study was conducted among women in Saudi Arabia from February 2023 to March 2023. A questionnaire was randomly given to women in obstetrics and gynecology clinics. Women who were pregnant or who had a pregnancy history were included in the study, and those who did not have any pregnancy history were excluded. The study aimed to determine the knowledge and attitude regarding NIPT. A total of 1028 participants living in Saudi Arabia were accepted for the study, and their data were analyzed. Informed consent was obtained for all patients.

**Table 1. Distribution of the participants according to their demographic characters.**

| Variable | No. (%) |
|---|---|
| Age (years) | |
| <30 | 270 (26.3) |
| 30–39 | 328 (31.9) |
| 40–49 | 288 (28) |
| >50 | 142 (13.8) |
| Educational level | |
| Elementary | 25 (2.4) |
| Intermediate | 65 (6.3) |
| High school | 219 (21.3) |
| Graduate | 605 (58.9) |
| Postgraduate | 114 (11.1) |
| Occupation | |
| Employee | 433 (42.1) |
| Student | 76 (7.4) |
| Unemployed | 519 (50.5) |
| Region of Saudi Arabia | |
| Central Region | 174 (16.9) |
| Eastern Province | 151 (14.7) |
| Northern Region | 77 (7.5) |
| Southern Region | 57 (5.5) |
| Western Region | 569 (55.4) |
| Do you have medical insurance? | |
| No | 552 (53.7) |
| Yes | 476 (46.3) |
| Number of family members | |
| 3 | 273 (26.6) |
| 4 | 219 (21.3) |
| 5 | 211 (20.5) |
| 6 | 153 (14.9) |
| 7 or more | 172 (16.7) |
| Monthly income | |
| <1332.99 USD | 180 (17.5) |
| 1332.99–2665.97 USD | 399 (38.8) |
| >2665.97 USD | 449 (43.7) |

USD, United states dollar.

Study instrument: a questionnaire re-designed from two studies in Hong Kong and Saudi Arabia was translated into Arabic and used in the current study [12,13]. Once completed, the questionnaire was written in an online Google form and sent to all targeted participants.

The questionnaire was divided into three sections. The first one was about the demographics of the participants (including age, educational level, number of family members,

**Table 2. Distribution of the participants according to amniocentesis, CVS, NIPT, having a child with Down syndrome, and relatives with chromosomal or genetic problems.**

| Variable | No. (%) |
|---|---|
| Do you use any birth control (contraception) method? | |
| No | 506 (49.2) |
| Yes | 522 (50.8) |
| Previous experience with amniocentesis? | |
| No | 925 (90) |
| Yes | 103 (10) |
| Previous experience with CVS? | |
| No | 963 (93.7) |
| Yes | 65 (6.3) |
| Previous experience with NIPT? | |
| No | 876 (85.2) |
| Yes | 152 (14.8) |
| If yes, why did you undergo a non-invasive prenatal test (NIPT)? (Indication of NIPT): | |
| Family history (own child) | 14 (9.2) |
| Family history (relative) | 14 (9.2) |
| Maternal age | 21 (13.8) |
| Recommendation from a relative | 12 (7.8) |
| Recommendation of the doctor | 63 (41.7) |
| Serum marker | 8 (5.2) |
| Ultrasound results | 20 (13.1) |
| Have you ever had an abortion? (Experience with miscarriage) | |
| No | 621 (60.4) |
| Yes | 407 (39.6) |
| Do you have a child with Down syndrome? | |
| No | 993 (96.6) |
| Yes | 35 (3.4) |
| Do you have relatives with chromosomal abnormalities or genetic diseases? | |
| No | 802 (78) |
| Yes | 226 (22) |

CVS, chorionic villus sampling; NIPT, non-invasive prenatal screening testing.

medical insurance, and income); usage of any method to prevent pregnancy or any *in-vitro* fertilization; and whether they had undergone amniocentesis, CVS, and NIPT (if they underwent NIPT, then why). The second part assessed the data about the pregnancies and deliveries of the participants, including parity, gravidity, abortion, and whether they had given birth to a child with Down syndrome or any genetic defect. The last part assessed the details about the knowledge and attitude of the participants toward NIPT. The knowledge score was statistically obtained based on their responses to the questions in the previous section.

Data analysis: once all participant responses were collected, the responses were analyzed using SPSS Statistics version 21 (IBM Corp., Armonk, NY, USA). Continuous variables showed mean and standard deviation, while categorical variables showed counts and percentages. Significance was determined using a *t*-test and chi-square test. A *p*-value of $<0.05$ was considered statistically significant.

## 3. Results

A total of 1028 participants were analyzed. The demographical data of the participants are presented in Table 1. Of the participants, 10% had undergone amniocentesis, 6.3% reported previous CVS, and only 14.8% had undergone NIPT. The most common indication of it was a recommendation from their healthcare provider (41.7%), as shown in Table 2. About 39.6% of the participants had a previous abortion. 3.4% had a child with Down syndrome, and 22% had relatives with chromosomal abnormalities or genetic diseases.

The knowledge of the respondents is revealed in Table 3. About 34.6% of the respondents knew that the anticipated condition included common chromosomal abnormalities (trisomies, monosomies, and sex chromosomes), and 34.5% knew that NIPT could be undertaken from the 10th week of pregnancy.

Factors affecting the participants' decision-making about NIPT are displayed in Table 4. The most important was the worry about the baby's safety (91.1%), quality of

**Table 3. Participants' response to knowledge items regarding NIPT.**

| What is the correct information about NIPT in your opinion? | I don't know | No | Yes |
|---|---|---|---|
| | No. (%) | No. (%) | No. (%) |
| Test is carried out by taking blood from the mother | 477 (46.4) | 99 (9.6) | 452 (44) |
| Used to screen for Down syndrome in fetus | 457 (44.5) | 89 (8.7) | 482 (46.9) |
| If a positive test result is returned from the NIPT, it is necessary to undergo invasive testing (amniocentesis or CVS) | 565 (55) | 88 (8.6) | 375 (36.5) |
| The accuracy of a positive test result can be affected by the age of the mother | 512 (47.8) | 141 (13.7) | 375 (36.5) |
| The test can be carried out from the 10th week of pregnancy | 570 (55.4) | 103 (10) | 355 (34.5) |
| At present, the anticipated condition includes common chromosomal abnormalities (trisomies, monosomies and sex chromosomes) | 594 (57.9) | 77 (7.5) | 356 (34.6) |

CVS, chorionic villus sampling; NIPT, non-invasive prenatal screening testing.

**Table 4. Distribution of the participants regarding factors affecting their decision making about NIPT.**

| Which of these factors might affect your decision to undergo a NIPT? (Decision making factors) | Important | Not important |
|---|---|---|
| | No. (%) | No. (%) |
| Wanting to know as much information as possible about the baby | 906 (88.1) | 122 (11.9) |
| Worry about the baby's safety | 937 (91.1) | 91 (8.9) |
| The quality of life of a baby with a chromosomal abnormality | 893 (86.9) | 135 (13.1) |
| Fear of not being able to cope with a baby with a chromosomal abnormality | 798 (77.6) | 230 (22.4) |
| My family's support and attitude toward having a baby with a chromosomal abnormality | 789 (76.8) | 239 (23.2) |
| The support available in the society for a child with a chromosomal abnormality | 74 (77.2) | 234 (22.8) |
| Knowing relatives or people who have a child with a chromosomal abnormality | 764 (74.3) | 264 (25.7) |

NIPT, non-invasive prenatal screening testing.

**Table 5. Participants' attitude towards NIPT.**

| What do you think are the disadvantages of NIPT? | No | Yes |
|---|---|---|
| | No. (%) | No. (%) |
| Too expensive | 249 (24.2) | 779 (75.8) |
| Only detect few aneuploidy disorders | 358 (34.8) | 670 (65.2) |
| It may harm the fetus | 395 (38.4) | 633 (61.6) |
| It needs local anesthesia | 444 (43.2) | 584 (56.8) |
| Painful to the mother | 412 (40.1) | 616 (59.9) |

NIPT, non-invasive prenatal screening testing.

life of a baby with a chromosomal abnormality (86.9%), and wanting to know as much information as possible about the fetus's health (88.1%). Regarding their attitude toward NIPT, the most reported disadvantage was expensiveness (75.8%), as presented in Table 5.

The mean knowledge score about NIPT was 2.82 $\pm$ 1.89; mean knowledge scores represent a summary measure of the overall level of knowledge about a topic within a group of participants. Table 6 shows that the mean knowledge score about NIPT was significantly higher among the participants aged <30 (3.23 $\pm$ 1.9, $p < 0.001$), postgraduates (3.25 $\pm$ 1.98, $p = 0.009$), students (3.25 $\pm$ 1.93, $p = 0.006$), and from the Western region of Saudi Arabia (3.04 $\pm$ 1.88, $p < 0.001$). Additionally, Table 7 demonstrates that the mean knowledge score about NIPT was significantly higher among females using birth control (3.05 $\pm$ 1.98, $p < 0.001$). The participants who had undergone amniocentesis (3.62 $\pm$ 1.88, $p < 0.001$), CVS (3.52 $\pm$ 1.76, $p = 0.001$), had a child with Down syndrome (3.77 $\pm$ 1.71, $p = 0.002$), or relatives with chromosomal or genetic problems (3.16 $\pm$ 2, $p = 0.007$) also had a significantly higher mean knowledge score ($p \leq 0.05$).

## 4. Discussion

This study aimed to assess the knowledge and attitude regarding NIPT among women in Saudi Arabia. The mean knowledge score about NIPT was found to be 2.82 $\pm$ 1.89. Less than half of the respondents were knowledgeable about NIPT, as claimed in a previous single-center Saudi Arabian study [13]. Our results showed that the mean age of the participants was between the ages of 30 and 39, and more than half had a high school education. These results were similar to those in many previous studies by Yotsumoto *et al.* [14], Abdo *et al.* [15], and Ogamba *et al.* [16]. Only 14.8% of our respondents had performed NIPT. The most common indications were a recommendation from their healthcare

**Table 6. Relationship between the participants' mean knowledge score and their demographic characters.**

| Variable | Knowledge score (Mean ± SD) | Test | *p*-value |
|---|---|---|---|
| Age (years) | | | |
| <30 | 3.23 ± 1.9 | 3* | <0.001 |
| 30–39 | 2.8 ± 1.84 | | |
| 40–49 | 2.67 ± 1.8 | | |
| >50 | 2.4 ± 1.91 | | |
| Educational level | | | |
| Elementary | 1.92 ± 2.01 | 4* | 0.009 |
| Intermediate | 2.7 ± 1.92 | | |
| High school | 2.79 ± 1.96 | | |
| Graduate | 2.8 ± 1.83 | | |
| Postgraduate | 3.25 ± 1.98 | | |
| Occupation | | | |
| Employee | 2.98 ± 2.01 | 2* | 0.006 |
| Student | 3.25 ± 1.93 | | |
| Unemployed | 2.63 ± 1.76 | | |
| Region of Saudi Arabia | | | |
| Central Region | 2.35 ± 1.67 | 4* | <0.001 |
| Eastern Province | 2.861 ± 1.99 | | |
| Northern Region | 2.68 ± 2.02 | | |
| Southern Region | 2.24 ± 1.81 | | |
| Western Region | 3.04 ± 1.88 | | |
| Do you have medical insurance? | | | |
| No | 2.72 ± 1.9 | 2.12** | 0.033 |
| Yes | 2.94 ± 1.88 | | |
| Number of family members | | | |
| 3 | 3.01 ± 1.92 | 4* | <0.001 |
| 4 | 3.05 ± 1.91 | | |
| 5 | 3.04 ± 1.91 | | |
| 6 | 2.47 ± 1.72 | | |
| 7 or more | 2.29 ± 1.79 | | |
| Monthly Income | | | |
| <1332.99 USD | 2.53 ± 1.77 | 2* | 0.07 |
| 1332.99–2665.97 USD | 2.91 ± 1.87 | | |
| >2665.97 USD | 2.86 ± 1.94 | | |

Note: * = Kruskal Wallis test; ** = Mann Whitney test.

USD, United states dollar; SD, Standard deviation.

provider (41.7%), followed by maternal age (13.8%), which is relatively similar to a Chinese study which reported that 54.93% of their sample chose to undergo NIPT because of its high accuracy, followed by a recommendation from doctors (39.85%) [10]. A study published in Japan also showed that maternal age is the most common indication for undergoing NIPT [14].

As evidenced by the results of our study and previous research, healthcare providers most significantly influence a pregnant woman's decision to undergo NIPT, which makes it essential for them to clarify this procedure and its benefits toward increasing the knowledge and providing the correct information about the procedure in the first place. Nevertheless, consistent with a previous study by Akiel *et al.* [13], most women assessed in our study had never heard about NIPT before. On the other hand, published research in Jordan concluded that 74% of the Jordanian women who participated in their study were aware of NIPT and its procedure [15]. This might be related to the fact that NIPT has been added recently to the Antenatal Care Program in Saudi Arabia, thus participants awareness and knowledge regarding NIPT and its application is still relatively low. Antenatal Care Program in Saudi Arabia provides a variety of screening options for pregnant women to examine the health of the mother and fetus, involving testing for chromosomal abnormalities and genetic diseases. Starting in the first-trimester of pregnancy, the program recommends regular antenatal care visits, and screening options include first-trimester combined screening, second-trimester maternal serum screening, NIPT, and diagnostic testing, such as

**Table 7. Relationship between the participants' mean knowledge score and birth control, amniocentesis, CVS, abortion, having a child with Down syndrome and relatives with chromosomal or genetic problems.**

| Variable | Knowledge score (Mean ± SD) | Test | *p*-value |
|---|---|---|---|
| Do you use any birth control (contraception) method? | | | |
| No | 2.59 ± 1.761 | 3.58** | <0.001 |
| Yes | 3.05 ± 1.98 | | |
| Previous experience with amniocentesis? | | | |
| No | 2.73 ± 1.87 | 4.55** | <0.001 |
| Yes | 3.62 ± 1.88 | | |
| Previous experience with CVS? | | | |
| No | 2.78 ± 1.89 | 4.98** | 0.001 |
| Yes | 3.52 ± 1.76 | | |
| Have you ever had an abortion? (Experience with miscarriage) | | | |
| No | 2.91 ± 1.88 | 2.19** | 0.028 |
| Yes | 2.69± 1.9 | | |
| Do you have a child with Down syndrome? | | | |
| No | 2.79 ± 1.89 | 3.07** | 0.002 |
| Yes | 3.77 ± 1.71 | | |
| Do you have relatives with chromosomal abnormalities or genetic diseases? | | | |
| No | 2.73 ± 1.85 | 2.72** | 0.007 |
| Yes | 3.16 ± 2 | | |

Note: ** = Mann Whitney test.

SD, Standard deviation; CVS, chorionic villus sampling.

CVS and amniocentesis. These screening options provide valuable information about pregnancy. The Saudi Antenatal Care Program also provides a variety of other services to support the health of mothers and newborns, such as nutrition counseling, breastfeeding and infant care education, and support for maternal mental health.

As for knowledge and attitude regarding NIPT, 46.9% of the participants in our study were aware that NIPT is used to screen fetal Down syndrome, 44% knew that it is performed by collecting blood from the mother, 36.5% knew that the age of the mother can affect the accuracy of a positive test result, and 36.5% were familiar that a NIPT positive result indicates the need for invasive testing (amniocentesis or CVS). These outcomes are consistent with the results of previous Jordanian and Japanese studies [14,15]. Knowing about the possible screening tests for Down syndrome was highly anticipated, given the disease prevalence in our country, recently reported to be 8 per 10,000 live births [17]. Additionally, the participants in our study were asked about the main approaches to obtaining NIPT-related information, which were mainly physicians (62.3%), medical lectures (18.2%), and websites (10.7%). This knowledge emphasizes the significance of providing patients with relevant and beneficial information from a reliable source, typically their healthcare professional, either in the clinic or through medical lectures. The most substantial factors that influenced the participants to undergo NIPT were their worry about their baby's safety (91.1%), the quality of life of a baby with a chromosomal abnormality (86.9%), and wanting to know as much information as possible about the fetus's health (88.1%). The results aligned with the findings reported by Akiel *et al*. [13], who concluded that the most significant factors were related to the infant's health, followed by the desire to acquire as much knowledge as possible about the baby.

As for the association between knowledge and multiple demographic factors, the knowledge score about NIPT was found to be significantly higher among participants aged <30 and postgraduates which is consistently agreed upon in some previous studies [12,13]. The score was also significantly higher among those with medical insurance herein, which is similarly reported in another published study [15]. Additionally, the mean knowledge score about NIPT was significantly higher among females who had undergone NIPT or who had heard about it before. These results were similar to those of a study conducted by Sylvia *et al*. [12], which found that women who had heard about NIPT scored higher, on average, on the knowledge score compared to those who had not. These results were logically expected because women who had undergone the procedure before, certainly had some prior information about it. The limitation of our study was that it is similar to any cross-sectional study, limited by time and recall bias. Additionally, the nature of our sample, comprising only women with a pregnancy history, might affect the knowledge level.

## 5. Conclusions

This study investigated women's knowledge and attitude regarding NIPT in Saudi Arabia. The major conclusion was that most women had poor knowledge about NIPT. Moreover, most women present knowledge that NIPT is used to screen fetal Down syndrome and knew that it is carried out by drawing blood from the mother. Furthermore, participants knew that a positive NIPT test indicates undergoing invasive testing (amniocentesis or CVS), and that the anticipated condition includes common chromosomal abnormalities (trisomies, monosomies, and sex chromosomes).

Furthermore, researchers recommend raising awareness about NIPT uses, indications, prices, and possible complications through antenatal clinics or medical lectures. Healthcare workers, including physicians, nurses, and midwives, should provide the necessary knowledge about NIPT to every pregnant woman who may need to undergo the test. To broaden their knowledge and influence their decision on whether to take the test, it is advised to offer them alternate information sources, such as brochures and videos. The results of the current study will contribute to the field of knowledge regarding NIPT. They can be utilized to develop ways to educate pregnant women about the advantages, disadvantages, and complications of NIPT. Lastly, the study provides data for helping future research.

## Abbreviations

NIPT, Non-invasive prenatal testing; cffDNA, cell-free fetal DNA; CVS, chorionic villus sampling; USD, United states dollar; SD, Standard deviation.

## Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Author Contributions

NMB and DMB designed the research study. GAE, AMBS and AMS collected the data and wrote the manuscript. All authors analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki and the protocol was approved by the Ethics Committee of King Abdul-aziz University Hospital (approval number: 88-23).


## Acknowledgment

We would like to express our gratitude to all those who participated in our research. Thanks to all the peer reviewers for their opinions and suggestions.

## Funding

This research received no external funding.


## Conflict of Interest

The authors declare no conflict of interest.

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