

The Impact of COVID-19 Vaccine on Menstrual Cycle in Saudi Females in Jeddah City

Nedaa Mohammed Bahkali, MD* Dana Suhail Sawan, MD* Razan Saleh Alsayed, MD** Eman Yahya Hazazi, MD** Maha Hani Alenazi, MD** Reham Ahmad Alsharif, MD** Maisam Hamed Alhammadi, MD** Nabeel Salem Bondagji, FRCSC*

ABSTRACT

Background and Objectives: There have been reports on changes in the menstrual period in the course of the COVID-19 pandemic. This research specifically seeks to determine the impact of COVID-19 vaccine on the menstrual cycle in Saudi females in Jeddah City.

Design: Cross-sectional

Settings: Jeddah City, Saudi Arabia

Methods: We conduct a total of 421 online surveys and phone call interviews with participants who are between 20 to 40 years old, living in Jeddah City, not pregnant, and have no gynecological problems or abnormalities for this cross-sectional study. Interviews and surveys were taken between January to April 2022 and data were calculated using SPSS version 23.

Sample size: 421

Main Outcome Measures: COVID-19 impact on the menstrual cycle.

Results: The majority of the respondents in this study were single, have normal BMI, and were recipients of the COVID-19 vaccines, where 59.7% of them were on their third dose. Before the beginning of the COVID-19 pandemic, most of them did not have heavy periods (75.8%), painful periods (54.6%), or even missed periods (78.1%). The majority reported that there were no changes observed in terms of premenstrual symptoms (61.5%) and libido/sex drive remained unchanged to most (88.1%). Preliminary findings show that there have been no significant differences in the menstrual cycle of the participants in terms of regularity, bleeding, pain, and heavy periods after receiving the COVID-19 vaccine.

Conclusion: The COVID-19 vaccine did not significantly change the menstruation period in women in terms of bleeding, heavy periods, pain, and regularity. Results can be used as evidence and supporting documents to convince and clear any kind of misinformation existing in the minds of those hesitant and unvaccinated individuals about receiving the COVID-19 vaccine and its implications on gynecological health.

Limitations: The majority of respondents were single and using contraceptives and these variables may also affect the results of less represented sample characteristics.

INTRODUCTION

March 2020 has radically changed the world, notably its effect on public health. It was the time when the novel coronavirus or the so-called COVID-19 began to emerge in Wuhan, China.^{1,2} Lockdowns and quarantines have been implemented by the governments in large parts of the world due to the alarming rates of infection and mortality rates caused by the virus. COVID-19 continues to have an effect on the world today, leading to conditions like kidney problems, acute respiratory distress syndrome (ARDS), gastrointestinal issues, pneumonia, and myocardial dysfunction.³ COVID-19 also detrimentally affects immunity, causing a rise in interleukin (IL)-6, IL-8, other cytokines, and tumor necrosis factor- α (TNF- α) levels as it may also lead to modification on hypothalamic-pituitary-gonadal axis.⁴ Based on the World Health Organization, as of July 2021 there are now a total of over 183 million infections and 3.9 million global mortality.⁵

While COVID-19 has produced several health risks in the population, the impacts of declaring it a pandemic have also affected other areas of concern—and one of these is gynecological and reproductive health.⁶ Perhaps no other more salient concern as of a date other than the menstrual period during this COVID-19 pandemic. The menstrual cycle is defined as the period during which secondary sex characteristics start to develop and the function to sexually reproduce is achieved.⁷ The changes during the menstruation period are both physical and psychological, including the growth of breasts and pubic hair as well as an increase in height.⁷ But the hallmark of the developmental changes of an adolescent female is the menarche, which is the onset of menstruation. There are several factors that can affect the mechanisms that trigger both menarche and puberty and these include nutrition, genetics, maturation of the hypothalamic-pituitary-ovarian axis, and the person's body weight.⁸ As the adolescent grows up, her menstrual cycles may also be influenced by different factors, which can include

* Department of Obstetrics and Gynecology
Faculty of Medicine, King Abdulaziz University
Jeddah, Saudi Arabia.
E-mail: Nmbahkali@kau.edu.sa

** Medical Intern, Faculty of Medicine
King Abdulaziz University, Jeddah, Saudi Arabia.

hormones, weight gain, as well as stress.⁹

According to Marquini, et al. (2022), the COVID-19 pandemic has globally affected the health of women, making it imperative the encouragement of the scientific community in developing recommendations for specialized care.¹⁰ Sharp and colleagues (2021), also underlines the importance of studies done in relation to the menstrual period.¹¹ This is especially crucial given the onset of vaccines to prevent the severe symptoms of COVID-19 and the hesitancy of some women receiving these, partly due to the anecdotal reports of how drugs can detrimentally impact reproductive health. To date, newer and newer studies are done to elucidate on this matter, such as the one by Laganà, et al. (2022) in Italy where menstrual cycles have been changed after receiving second and third doses of vaccine—but these are resolved eventually within few months.¹² Meanwhile, in the U.S. cohort study by Edelman and others (2022), a small change in menstrual cycle length was observed in unvaccinated participants but not observed in vaccinated females.¹³ Yet these are both contradicted in a Norwegian cohort study where no changes were observed or caused by vaccination.¹⁴

Regardless, as COVID-19 pandemic still remains and there are still some women who are hesitant to take the vaccines, there are still many studies needed to determine on how vaccines can possibly affect the menstrual period in women. This is an emerging topic of concern and as there are many women in their reproductive age in the world, this becomes an important matter, too. While there are studies done in some parts of the world, our study aims to specifically focus on Saudi women in order to evaluate the effect of COVID-19 vaccine on the menstrual cycle among Saudi females in Jeddah City by estimating the incidences of these changes as well as by describing these changes that happened in menstrual period.

PATIENTS AND METHODS

Study Design: This work was done using a cross-sectional design between January and April of 2022. The goal was to determine how the COVID-19 vaccine affected the menstrual cycle in Saudi females in Jeddah. This study specifically estimated the incidence of menstrual cycle variation after receiving COVID-19 vaccine and described the changes that occurred during the menstrual period.

Study Population: This study included female Saudi participants living in Jeddah City who were between 19 to 43 years old. The said participants must have a regular menstrual period and must have no known uterine abnormalities at the time of the study or even before the pandemic started. Exclusion criteria also include those who are pregnant, those who live outside the city, those who are non-Saudi, those who have uterine pathological issues and on birth control pills.

Study Tool: The study tool was composed of 48 items of an online questionnaire created using Google Forms. The questionnaire was written in both English and Arabic languages. The first part of the questionnaire contained demographics such as age, marital status, number of children, weight, height, and contraceptives used. Succeeding questions also pertain to days of period of cycle as well as its quality (regular, amount of bleeding heavy, painful, and missed) to estimate the incidences of menstrual changes after receiving COVID-19 vaccine. In addition, the type of vaccine and the number of doses they received were included in the questionnaire.

Data Collection Procedure: Patients' information was pulled from the Directorate of Health Affairs in Jeddah City. Approval from the Research Ethics Committee (REC) of Faculty of Medicine, King

Abdulaziz University, Ministry of Higher Education, Saudi Arabia, with approval number 215/21. This research was done following the guidelines of the Code of Ethics of the World Medical Association (Declaration of Helsinki 2013) for experiments involving humans. Informed consent was done in two procedures—the first one was a written consent done via text message and the second one was a verbal confirmation, which was done via phone interview. The authors also ensured confidentiality of patients by concealing any identifiers such as names, phone or fax numbers, medical record number, initials, anywhere in the paper. Out of 485 participants, no one had withdrawn but there was also no follow up that occurred.

Statistical Analysis: This study was analyzed using IBM SPSS version 23 (IBM Corp., Armonk, N.Y., USA) and visually presented by using GraphPad Prism version 8 (GraphPad Software, Inc., San Diego, CA, USA). A simple descriptive statistics was used to define the characteristics of the study variables through a form of counts and percentages for the categorical and nominal variables while continuous variables are presented by mean and standard deviations. To compare the means of two variables for a single group and to compute the differences between values of the two variables for each case and tests whether the average differs from 0 a Paired-Samples T Test was used. To establish a relationship between categorical variables, this study used Chi-Square Test. These tests were done with the assumption of normal distribution. Lastly, a conventional p-value <0.05 was the criteria to reject the null hypothesis.

RESULTS

Demographics: A sample size of 421 with a 95% confidence level and 5% margin of error were computed using an online sample size calculator. In terms of demographics as describe in Table 1, the mean age was 24.26(4.7), with the majority of participants aged 21 to 25 and the fewest aged more than 30. The sample's BMI was 23.18(4.9), with the majority of participants (57.0%) being of normal weight, 19.6% being overweight, 13.8% being underweight, and 9.5% being obese.

Most of the participants were single (86.5%) and only 13.5% were married at least once. Majority also did not have children (91.0%) while only 38 out of 421 have children (9.0%). In terms of contraceptives used, majority of the participants were not using contraceptives (86.0%) while 10.9% were using combined oral contraceptive pill, 1.4% were using Intrauterine Device (copper coil), 0.5% were using Progesterone only pill, and 1.2% were using implant. Almost half of the respondents (48.0%) were recording their cycles using their Smartphone app, while 29.0% were using none, 16.9% were using other methods, and 6.2% were using a diary.

Table 1. Socio-demographic characteristics of the 421 Saudi Arabian women.

Demographics	N	Min	Max	Mean	SD
What is your age?	421	19	43	24.26	4.7
BMI	419	15	45.3	23.18	4.9
Missing	2				
				Count %	
Total				421	100.0
				<=20 years	61 14.5
				21-25 years	260 61.8
				26-30 years	51 12.1
				>30 years	49 11.6

BMI	Underweight	58	13.8
	Normal weight	239	57.0
	Overweight	82	19.6
	Obese	40	9.5
What is your marital status?	Single	364	86.5
	Married at least once	57	13.5
Do you have children?	Yes	38	9.0
	No	383	91.0
Are you currently using any of the following contraceptives?	Yes	59	14.0
	None	362	86.0
Are you currently using any of the following contraceptives?	Combined oral contraceptive pill	46	10.9
	Progesterone only pill	2	0.5
	Intrauterine System/Device (copper coil)	6	1.4
	Implant	5	1.2
	None	362	86.0
Do you record your cycles using:	Diary	26	6.2
	Smartphone app	202	48.0
	Other method	71	16.9
Are you currently breastfeeding?	None	122	29.0
	No	421	100.0
BMI missing n=2			
What is your marital status? Married at least once (Married n=34, Separated/divorced n=20, Widowed n=3).			

In Table 2, the type of vaccine and the number of doses received by female participants were shown. Based on the results, most of the participants received Pfizer-BioNTech vaccine (64.1%), followed by Oxford Astrazeneca (33.45%), then by Moderna (1.7%), and lastly, by Janssen (0.7%). In terms of the number of doses administered, there are 241 women who received three doses of COVID-19 vaccine and 168 women who received two doses. However, only seven women received only one dose of the COVID-19 vaccine.

Table 2. The type of COVID-19 vaccines and the number of doses received by 421 Saudi Arabian women.

Variables	Count	%	
Total	421	100.0	
Did you get COVID-19 vaccine?	No	5	1.2
	Yes 1 does	7	1.7
	Yes 2 doses	168	39.9
	Yes 3 doses	241	57.2
If yes, What type of vaccine?		Count	%
	Pfizer-BioNTech	263	64.1
	Oxford AstraZeneca	137	33.4
	Moderna	7	1.7
	Janssen	3	0.7
	Missing	6	

Menstrual experiences before receiving COVID-19 vaccine: Before the COVID-19 pandemic, participants' menstrual bleeding in average is 5.63(1.4) days.

The majority of the study participants had regular (62.5%) and did not have heavy periods (68.9%) and did not miss any (73.6%). More than half of the participants (54.2%) did not suffer from any psychological

issues. To those who experienced these issues, Table 3 show that anxiety (28.0%), low mood (27.1%), and depression (26.1%) were the three leading psychological problems. It is crucial to remember that participants in this study might experience multiple psychological problems.

Table 3. Menstrual conditions experienced before COVID-19 vaccine.

Before the COVID19 Vaccine	N	Min	Max	Mean	SD
How many days of bleeding on average would you have during your period?	414	1	9	5.63	1.4
		Count		%	
Total		421	100.0		
Do you usually get regular periods?	Yes	263	62.5		
	No	158	37.5		
Would you say that you had heavy periods?	Yes	131	31.1		
	No	290	68.9		
Would you say that you had painful periods?	Yes	171	40.6		
	No	250	59.4		
Would you say that you missed periods?	Yes often	25	5.9		
	Yes occasionally	56	13.3		
	No	310	73.6		
	N/A	30	7.1		
	Anxiety	118	28.0		
	Depression	110	26.1		
	Eating disorder	48	11.4		
	Low mood	114	27.1		
	Poor appetite	46	10.9		
	Poor sleep	83	19.7		
Have suffered from any of the following? ^a	Poor concentration	71	16.9		
	Loneliness	57	13.5		
	Illicit drug use	9	2.1		
	Significant stress	86	20.4		
	Nor of the above	228	54.2		

^a- Multiple response question please don't add up the counts and percentages.

Changes after receiving COVID-19 vaccine: Since the beginning of COVID-19, participants had an average of 5.70(1.6) days of menstrual bleeding and average of 0.52(1.3) missed periods as shown in Table 4. Most of the participants in the current study during COVID-19 pandemic did not have heavy (72.4%) and painful periods (58.2%), did not miss periods (72.4%) and PMS were unchanged (58.0%). In terms of change in libido/sex drive, there were no observed change according to the participants (89.3%). Overall, 71.5% of the participants did not notice any change in their menstrual cycle (Table 4).

Table 4. Menstrual conditions experienced after receiving COVID-19 vaccine.

After the COVID19 Vaccine	N	Min	Max	Mean	SD
How many days of bleeding on average have you had during your period?	411	1	12	5.70	1.6
How many periods would you say that you have missed?	421	0	7	0.52	1.3

		Count	%
Total		421	100.0
Would you say that you have had heavy periods?	Yes	116	27.6
	No	305	72.4
Would you say that you have had painful periods?	Yes	176	41.8
	No	245	58.2
Would you say that you missed periods?	Yes often	30	7.1
	Yes occasionally	47	11.2
	No	305	72.4
Have you noticed any change in your premenstrual symptoms (PMS)?	N/A	39	9.3
	PMS better	12	2.9
	PMS worse	93	22.1
	PMS unchanged	244	58.0
Have you noticed any change in your libido/sex drive?	N/A	72	17.1
	Increased libido	16	3.8
	Decreased libido	29	6.9
Overall have you noticed any change in your menstrual cycle?	Libido unchanged	376	89.3
	Yes	120	28.5
	No	301	71.5

Table 5 notes if there are any changes in the menstrual period after taking the second and third dose of the COVID-19 vaccine. Results showed that after administering the second dose, most of the participants did not feel any change in their menstrual period (55.9%). And for those who received their second dose, most of the participants have Pfizer-BioNTech vaccine (81.1%). On the other hand, for those who received their third dose of the vaccine, about 59.7% of the participants did not feel any change in their menstrual period, and most of them have received Pfizer-BioNTech as their COVID-19 vaccine.

Table 5. Changes after COVID-19 vaccine

Variables	Count	%
Total	421	100.0
Overall have you noticed any change in your menstrual cycle after your second dose of COVID19 vaccine?	No	174 55.9
	Yes	74 23.8
	N/A	63 20.3
	Missing	110
Total	74	100.0
Type of Vaccine	Pfizer-BioNTech	43 81.1
	Oxford AstraZeneca	10 18.9
	Missing	21
Total	421	100.0
Overall have you noticed any change in your menstrual cycle after your third dose of COVID19 vaccine?	No	148 59.7
	Yes	40 16.1
	N/A	60 24.2
	Missing	173
Total	40	100.0
Type of Vaccine	Pfizer-BioNTech	26 96.3
	Moderna	1 3.7
	Missing	13

DISCUSSION

There was limited scientific research available specifically on the impact of COVID-19 vaccines on the menstrual cycle of females. However, anecdotal reports suggested that some individuals experienced changes in their menstrual cycles after receiving the vaccine. These changes included alterations in menstrual flow, cycle length, and timing of periods. It is important to note that anecdotal reports alone cannot establish a definitive link between the vaccine and menstrual changes.

It's worth mentioning that menstrual cycle variations can occur due to various factors, including stress, illness, changes in routine, or other external influences. It is possible that the stress or physiological responses to receiving the vaccine could temporarily affect the menstrual cycle in some individuals.

Based on the results of the survey, most of the participants did not find any significant changes in their menstrual cycle. Similar results were also obtained in the study conducted by Edelman *et al.* 2022.¹³ Their study involved a large group of samples where the dataset came from 19 622 individuals with different nationalities. Survey showed that a large percentage of the participants were administered with Pfizer-BioNTech COVID-19 vaccine, and were followed by Moderna, Oxford-AstraZeneca, then Johnson&Johnson. According to their study, they found that there is a small possibility that the COVID-19 vaccine had temporarily affected the length of the menstrual cycle. Moreover, they observed that there is a correlation between the number of dose administered and the cycle length.

In addition, no significant change in the behavior of menstrual cycle (i.e., regularity, bleeding, painful, or heavy periods) were found in our study, as well as in other studies using different samples. Medina-Perucha *et al.* (2022)¹⁵ discovered the same in their Spanish sample of 17, 455 women, as did Ozimek *et al.* (2022)⁶ in their American sample of 210 female respondents.

However, some studies show that there is a significance change in the menstrual cycle after receiving COVID-19 vaccine. Based on the study conducted by Lagana and colleagues in 2022,¹² Italian participants reported that they experienced menstrual irregularities after administering the COVID-19 vaccine, but such incidence have been resolved within two months after receiving the vaccine. Similar case was also reported in the study of Muhaidat and colleagues in 2022.¹⁶ Their participants live in North Africa and Middle East, and upon conducting their survey, 2269 women exhibited menstrual irregularities after COVID-19 vaccine administration.

Regulatory agencies, such as the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), have not identified menstrual changes as a known side effect of COVID-19 vaccines. Experts generally agree that the benefits of vaccination outweigh any potential transient menstrual changes.

CONCLUSION

The current study found that there is no overall significant change in the menstrual period in Saudi Arabian women after receiving COVID-19 vaccine. However, further studies are needed to determine the potential and long-term health effects of receiving COVID-19 vaccine. Furthermore, more data sets are needed to confirm the validity of this study.

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Competing Interest: None

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APPENDIX

Table 6. Average days of bleeding of the patients before and after COVID19 vaccination

How many days of bleeding on average would you have during your period?	Before COVID19 Vaccine	After COVID19 Vaccine	Mean Differences	95% C.I. Difference		p-value	
				Lower	Upper		
Total	5.63 ± 1.4	5.70 ± 1.6	-0.07 ± 0.5	-0.115	-0.026	0.002a	
What is your age?	<=20 years	3.44 ± 0.7	3.13 ± 0.8	0.31 ± 0.5	0.192	0.431	<0.001 ^a
	21-25 years	5.54 ± 0.7	5.57 ± 0.8	-0.03 ± 0.3	-0.063	0.001	0.059
	26-30 years	7.00 ± 0.0	7.10 ± 0.3	-0.10 ± 0.3	-0.183	-0.014	0.024 ^a
	>30 years	7.79 ± 0.7	8.69 ± 1.0	-0.90 ± 0.6	-1.091	-0.704	<0.001 ^a
What is your marital status?	Single	5.36 ± 1.2	5.33 ± 1.3	0.03 ± 0.3	-0.003	0.063	0.070
	Married at least once	7.66 ± 0.7	8.51 ± 1.0	-0.85 ± 0.6	-1.024	-0.678	<0.001 ^a
Do you have children?	Yes	3.11 ± 0.7	2.68 ± 0.6	0.42 ± 0.5	0.257	0.586	<0.001 ^a
	No	5.88 ± 1.1	6.00 ± 1.4	-0.12 ± 0.4	-0.163	-0.078	<0.001 ^a
BMI	Underweight	5.36 ± 1.6	5.50 ± 1.9	-0.14 ± 0.5	-0.281	0.005	0.059
	Normal weight	5.77 ± 1.3	5.83 ± 1.6	-0.06 ± 0.4	-0.117	-0.002	0.043 ^a
	Overweight	5.39 ± 1.3	5.45 ± 1.6	-0.06 ± 0.4	-0.158	0.033	0.199
	Obese	5.66 ± 1.4	5.71 ± 1.7	-0.05 ± 0.4	-0.184	0.079	0.422
Are you currently using any of the following contraceptives?	Yes	3.42 ± 0.7	3.10 ± 0.8	0.32 ± 0.5	0.199	0.445	<0.001 ^a
	None	5.99 ± 1.1	6.13 ± 1.3	-0.14 ± 0.4	-0.180	-0.093	<0.001 ^a

^a-significant using Paired Samples Test at <0.05 level.

Table 7. Average number of periods of the patients before and after COVID19 vaccination

How many periods would you say that you have missed?	Since/During COVID-19	After COVID19 Vaccine	Mean Differences	95% C.I. Difference Lower	Upper	p-value	
Total	0.50 ± 1.3	0.49 ± 1.2	0.01 ± 0.2	-0.013	0.028	0.492	
What is your age?	<=20 years	0.00 ± 0.0	0.00 ± 0.0	-	-	-	
	21-25 years	0.00 ± 0.0	0.00 ± 0.0	-	-	-	
	26-30 years	0.78 ± 0.6	0.86 ± 0.6	-0.08 ± 0.3	-0.173	0.016	0.103
	>30 years	3.57 ± 1.7	3.43 ± 1.4	0.15 ± 0.5	-0.001	0.299	0.051
What is your marital status?	Single	0.07 ± 0.3	0.09 ± 0.3	-0.01 ± 0.1	-0.026	-0.002	0.025 ^a
	Married at least once	3.31 ± 1.7	3.16 ± 1.5	0.15 ± 0.5	0.014	0.277	0.031 ^a
Do you have children?	Yes	0.00 ± 0.0	0.00 ± 0.0	-	-	-	
	No	0.55 ± 1.3	0.54 ± 1.2	0.01 ± 0.2	-0.015	0.030	0.492
BMI	Underweight	0.52 ± 1.0	0.50 ± 1.0	0.02 ± 0.1	-0.017	0.052	0.322
	Normal weight	0.48 ± 1.2	0.49 ± 1.2	-0.01 ± 0.2	-0.042	0.017	0.407
	Overweight	0.46 ± 1.4	0.43 ± 1.3	0.04 ± 0.2	-0.005	0.078	0.083
	Obese	0.63 ± 1.7	0.58 ± 1.5	0.05 ± 0.2	-0.021	0.121	0.160
Are you currently using any of the following contraceptives?	Yes	0.00 ± 0.0	0.00 ± 0.0	-	-	-	
	None	0.58 ± 1.4	0.57 ± 1.3	0.01 ± 0.2	-0.015	0.032	0.492

^a-significant using Paired Samples Test at <0.05 level.

Table 8. The occurrence of heavy periods among patients before and after COVID19 vaccination

Would you say that you have had heavy periods?	Total	Before COVID19 vaccine		p-value
		Yes	No	
<i>After COVID19 vaccine</i>	<i>Yes</i>	<i>116</i>	<i>116(100%)</i>	<i><0.001^a</i>
	<i>No</i>	<i>305</i>	<i>15(4.9%)</i>	

^a-significant using Chi-Square Test at <0.05 level.

Table 9. The occurrence of painful periods among patients before and after COVID19 vaccination

Would you say that you have had painful periods?	Total	Before COVID19 vaccine		p-value
		Yes	No	
<i>After COVID19 vaccine</i>	<i>Yes</i>	<i>176</i>	<i>171(97.2%)</i>	<i><0.001^a</i>
	<i>No</i>	<i>245</i>	<i>0(0.0%)</i>	

^a-significant using Chi-Square Test at <0.05 level.

Table 10. The occurrence of missed periods among patients before and after COVID 19 vaccination.

Would you say that you missed periods?	Total	Before COVID19 vaccine		p-value
		Yes	No	
<i>After COVID19 vaccine</i>	<i>Yes</i>	<i>77</i>	<i>77(100.0%)</i>	<i><0.001^a</i>
	<i>No</i>	<i>305</i>	<i>4(1.3%)</i>	

^a-significant using Chi-Square Test at <0.05 level.

Table 11. The number of patients who noticed changes in their premenstrual symptoms before and after COVID19 vaccination

Have you noticed any change in your premenstrual symptoms (PMS)	Total	Since/During COVID-19		p-value
		Yes	No	
<i>After COVID19 vaccine</i>	<i>Yes</i>	<i>105</i>	<i>105(100%)</i>	<i><0.001^a</i>
	<i>No</i>	<i>244</i>	<i>10(4.1%)</i>	

^a-significant using Chi-Square Test at <0.05 level.