



## Effects of Diaphragmatic Breathing Exercises on Blood Sugar Levels in Working Class Females with Type-2 Diabetes Mellitus

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### ABSTRACT

**Background:** Type 2 Diabetes mellitus is a metabolic syndrome that leads to hyperglycemia and complications in many organ systems. There are many ways to control hyperglycemia including diet, exercise, drugs, and insulin. **Aim of the study:** The purpose of this study was to determine the effects of diaphragmatic breathing exercises on blood sugar levels and to identify the effects of regular diaphragmatic breathing exercise on HbA1c. **Subjects and Methods:** The study design used was a randomized controlled trial. Random sampling technique was used. Data was collected from working female nurses of Services Hospital Lahore and Jinnah Hospital Lahore who had type-2 diabetes mellitus. By using Ballot method 64 subjects were selected and equally divided into 2 groups randomly (32 subjects were in an interventional group and 32 in the control group). Data were analyzed using SPSS version 20. Mean difference was measured by using independent sample t-test and paired t-test to see the pre and post effects of the same group. Results were summarized as mean and standard deviation. **Results:** The study results indicated that there was a significant reduction in fasting blood sugar level ( $p=0.009$ ), post prandial blood sugar level ( $p=0.002$ ) and post interventional blood sugar level ( $p=0.000$ ) in the 9<sup>th</sup> week of the activity (breathing exercise). Pre and post the interventional mean difference in fasting blood sugar level was highly significant in the 12<sup>th</sup> week of intervention ( $p=0.000$ ). No significant difference was found in the results of HbA1c ( $p=0.963$ ). **Conclusion:** Diaphragmatic breathing exercise has favorable effects in controlling blood sugar levels among diabetes type-2 patients if it is combined with other exercises or therapies. Only breathing component cannot maintain the normal blood sugar level.

**Keywords:** Diaphragmatic breathing exercise, Fasting blood sugar, Post prandial blood sugar, Post interventional blood sugar level, HbA1c, Type 2 diabetes mellitus

### INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both [1]. There are 3 major types of diabetes:

- Type 1 in which the pancreas does not produce insulin
- Type 2 in which the body cells are resistant to the action of insulin that is being produced and over time the production of insulin progressively decreases
- Gestational diabetes which occurs in pregnancy and can cause some complications during pregnancy and at birth and increases the risk of type 2 diabetes in the mother and obesity in the off springs [2]

Persons with diabetes type 2 have insulin resistance that is; insulin is produced but it cannot metabolize glucose. These patients have relative rather than absolute insulin deficiency [3]. Insulin is a hormone that regulates blood sugar

levels. When there is a high level of sugar in the blood and it (sugar) cannot enter into cells, the resulting condition is called hyperglycemia or increased blood sugar level. Hyperglycemia leads to acute manifestations like excessive urination (polyuria), excessive thirst (polydipsia), excessive appetite (polyphagia), weight loss, lethargy, body aches, bone aches, and complications like infected wounds or delayed wound healing, long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels and the level of HbA1c > 7 [1]. Hemoglobin A1c is the type of hemoglobin that is formed due to prolonged exposure of hemoglobin to high blood sugar levels. Chronic hyperglycemia is associated with long term damage, dysfunction and failure of various organs specially the eyes, kidneys, heart, and blood vessels [1]. Nearly 90% of diabetic patients develop diabetes type 2 mostly relating to excess body weight. Furthermore, obesity is strongly inherited [4].

According to a report by WHO, it is estimated that 382 million people suffer from type-2 diabetes. The global prevalence (for all age groups) would increase from 2.8% in 2000 to 4.4% in 2030, more than doubling the number of people affected, from 171 million to 366 million [5]. A survey conducted in Pakistan revealed that the prevalence of newly diagnosed diabetic patients was 5.1% in men and 6.8% in women in urban areas and 5.0% in men and 4.8% in women in rural areas. Pakistan has become the 7<sup>th</sup> largest country in terms of diabetes population and it is predictable that it will be 4<sup>th</sup> largest by the year 2030 [6]. The International Diabetes Federation (IDF) has estimated similar predictions which hold that the number of diabetes sufferers would reach 471 million by 2035 [7].

Traditionally type-2 diabetes is controlled and treated by increasing exercises and dietary changes, oral drugs, and insulin. If diaphragmatic breathing exercise is regularly practiced at home, it is beneficial to reduce HbA1c. A sedentary lifestyle is a risk for diabetes and can be controlled with the help of physical activity. Likewise breathing exercise can reduce stress and blood sugar and promote blood supply to all body parts. Such exercises stimulate insulin secretions in diabetes type-2 patients [8]. Fasting blood sugar and post prandial blood sugar can be decreased when diaphragmatic breathing exercises are performed regularly. Value of hemoglobin A1c is also decreased. Such exercises directly help to perk up lifestyle pattern and improve physical functions of patients with diabetes and thus reduce the complications of diabetes [9].

Diabetes is one of the most costly and troublesome endocrine disorders. The number of people with diabetes type-2 is increasing rapidly in each country, 80% of people who suffer from type-2 diabetes mellitus belong to poor and middle class [10]. Diabetes mellitus type-2 and its complications can cause severe problems for affected individuals and their families and thus impose a heavy burden on health service. According to International Diabetes Federation (IDF), total health expenditure to prevent and treat diabetes was 376 billion US dollar in 2010 and it is expected to increase by 490 billion USD in 2030 internationally [11].

In order to control hyperglycemia, diabetic patients are advised to perform different exercises according to their convenience like a morning walk, jogging, cycling, etc. All of these strategies are worth practicing to control blood sugar but once the patient is on insulin then such techniques are not of much use. Breathing exercises are very useful and if adopted on regular basis, it can prevent major complications of diabetes type-2. The purpose of this study was to determine the effects of diaphragmatic breathing exercise in diabetes type-2 patients. Limited studies have been conducted in Pakistan to determine the effects of diaphragmatic breathing exercises on blood sugar levels and HbA1c. Diaphragmatic breathing exercise is not very common in our context that's why the researcher was interested to conduct a study on this topic in Pakistan. The finding of this study may help to put forward recommendations regarding the implementation of diaphragmatic breathing exercises to diabetes clinics and health care settings in order to control hyperglycemia and minimize the development of complications associated with diabetes mellitus type-2. Breathing exercises are cost effective modality for diabetes type-2 management as the patients if trained can perform this activity at home without paying any expenses as they do for oral hypoglycemic drugs and insulin. Moreover, there are no harmful effects of this exercise. This may reduce the health expenditure on the management of diabetes among patients and in this way breathing exercises are very important for diabetic patients in a developing country like Pakistan.

### **Research Questions**

- Is there any effect of diaphragmatic breathing exercises on blood glucose levels among type-2 diabetic nurses?
- Do diaphragmatic breathing exercises have effects on HbA1c level?

**Research Hypothesis**

Breathing exercises effectively control blood sugar level in diabetes type 2 patients.

**PATIENTS AND METHODS****Study Design**

The study design used was the randomized controlled trial (RCT). RCT is considered as the most rigorous method of determining whether a cause-effect relationship exists between an intervention and outcome. The strength of the RCT lies in the process of randomization which is unique to this type of study design. In this study, the researcher has explored the effects of breathing exercises among interventional group and difference of results in control or non-interventional groups.

**Sampling Size**

Sample size in this study consisted of 64 subjects equally divided into 2 groups consisting of 32 subjects randomly in each group, one group for the control and other for the interventional purpose. These subjects were selected by following the inclusion and exclusion criteria. The sample size was calculated with the help of biostatistician. The formula of sample calculation is mentioned below.

**Sample Size Calculation**

The sample size was calculated by the following formula keeping the power of study equal to 80% and the level of significance equal to 5%.

Desired power of study=80%

Desired level of significance=5%

Mean reduction in blood glucose level in Group A=165.7 ± 8.1

Mean reduction in blood glucose level in Group B=158.7 ± 11.1

$$n_1 = \frac{(Z_{1-\beta} + Z_{1-\alpha/2})^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

The same sample size was used by Wilson, et al., in their study.

Standard deviation of Group A=8

Standard deviation of Group B=11

Calculated sample size in each group=32

**Study Duration**

The study was completed within 6 months after approval of the synopsis.

**Research Setting**

This study was conducted in 2 tertiary care hospitals of Lahore, Jinnah hospital and Services Hospital. Nurses suffering from diabetes type-2 were taken as the study participants.

**Sampling Technique**

Simple random sampling technique was used for this study to select suitable subjects according to inclusion criteria. The cases and control groups were chosen by using a random ballot method, 32 subjects were included in the interventional group and the other 32 in the control group.

**Inclusion Criteria**

Working class females (nurses) who had been diagnosed with diabetes type-2 for 3-5 years and who were on oral hypoglycemic drugs not on insulin therapy were included in the study.

### Exclusion Criteria

Subjects with co-morbidities like COPD, HTN, glaucoma, type-1 diabetic, and those having any other complication of diabetes mellitus type-2 were excluded from the study.

### Ethical Considerations

Ethical considerations were followed according to the ethical principles of the Helsinki declaration.

- Written permission was obtained from the respective heads of the concerned organization
- Proper explanation was given to participants regarding the nature of the study and the discomfort involved and informed consent was obtained
- Privacy and confidentiality of the participant were maintained
- The collected information was only used for research purpose

### Data Collection

Fasting blood sugar levels of the interventional group were monitored before participants attended diaphragmatic breathing exercises for 20 minutes at 1<sup>st</sup>, 3<sup>rd</sup>, 6<sup>th</sup>, 9<sup>th</sup>, and 12<sup>th</sup> week of the study under the supervision and guidance of respiratory therapist by using the special guidelines. Pre and post intervention blood sugar was monitored. HbA1c was monitored after 12 weeks to compare the effects of this intervention among subjects of both the groups. Participants were trained to perform this activity at home for 20 minutes per day as well. Fasting blood sugar and post prandial blood sugar was monitored by using a glucometer. Hemoglobin A1c was checked by laboratory method.

### Data Analysis

Data analysis is the most important part of research to depict the real picture of information. Data analysis was done by using SPSS software version IBM-20. Data were presented in the form of percentages and frequencies for qualitative variables. Mean and the standard deviation was calculated for quantitative variables. Independent sample t-test was used to compare the mean of both groups and paired t-test was used to see the pre and post effects of breathing exercise on the same group.

### Dependent Variables

- Blood sugar level
- HbA1c

### Independent Variables

- Age
- Diaphragmatic breathing exercise

## RESULTS

In the interventional group, the mean age calculated was  $43.28 \pm 2.95$  (S.D) and in the control group, it was  $44.34 \pm 3.76$  (S.D) (Table 1).

**Table 1 Mean Difference of age in both groups**

Group	N	Mean $\pm$ Std. Deviation
Cases	32	$43.28 \pm 2.95$
Controls	32	$44.34 \pm 3.76$

Distribution of subjection of the study subjects in the two hospitals showed that 53.1% of the subjects were from Jinnah Hospital Lahore and 46.9% were from Services Hospital, Lahore (Table 2).

**Table 2 Distribution of subjects in the hospitals**

Variables	Frequency	Percent
Jinnah Hospital Lahore	34	53.10%

Services Hospital Lahore	30	46.90%
Total	64	100.00%

The mean fasting blood sugar (FBS) levels calculated in cases and control groups after 1<sup>st</sup> week of the intervention were  $143.34 \pm 52.807$  and  $141.31 \pm 45.515$  respectively with a p-value of 0.870 that is not significant and t-test value as 0.165. After having breakfast by following their diet chart, the mean post prandial blood sugar level (PPBSL) in cases was  $199.06 \pm 60.653$  and in control group, it was  $203.66 \pm 46.136$  with a p-value of 0.734 and t-test value as 0.341. The mean blood sugar levels were checked again among cases and control group after carrying out diaphragmatic breathing exercise for 20 minutes. The mean post intervention blood sugar levels (PIBSL) values were as  $209.25 \pm 51.887$  in cases and  $203.59 \pm 46.034$  in control group with a p-value of 0.646 and t-test value as 0.461 (Table 3). After the 1<sup>st</sup> week of interventions, the results showed no significant effects. HBA1c was  $7.74 \pm 1.3$  and  $7.89 \pm 1.4$  with p-value as 0.670 and t-test value 0.428.

**Table 3 Mean blood sugar levels of both groups at 1<sup>st</sup> week of breathing exercises**

Variables	Group	N	Mean	Std. Deviation	p-value	t-test
FBS 1	Cases	32	143.34	52.807	0.870	0.165
	Controls	32	141.31	45.515		
PPBS 1	Cases	32	199.06	60.653	0.734	-0.341
	Controls	32	203.66	46.136		
PIBSL 1	Cases	32	209.25	51.887	0.646	0.461
	Controls	32	203.59	46.034		
HBA1c 1	Cases	32	7.74	1.334	0.670	-0.428
	Controls	32	7.89	1.463		

The 2<sup>nd</sup> session of this activity was arranged on the 3<sup>rd</sup> week. Subjects were trained to perform the activity at home 3-4 times in a day for 20 minutes. A similar sequence of activity was followed as in a 1<sup>st</sup> week and the blood sugar levels were monitored. In the 3<sup>rd</sup> week, the mean FBS levels among cases and control group were as  $152.69 \pm 26.868$  and  $137.31 \pm 25.778$ , respectively with a p-value of 0.023 and t-test value as 2.336. The mean PPBS levels among cases and control group were as  $226.97 \pm 226.97$  and  $218.28 \pm 31.560$ , respectively with a p-value of 0.275 and t-test value as 1.100. The mean blood sugar levels were checked again among cases and control group after the intervention. The PIBSL values were as  $223.09 \pm 31.626$  in cases and  $221.25 \pm 31.548$  in control group with a p-value of 0.816 and t-test value as 0.233 (Table 4).

**Table 4 Mean blood sugar levels of both groups at the 3<sup>rd</sup> week of breathing exercises**

Variables	Group	N	Mean	Std. Deviation	p-value	t-test
FBS 3	Cases	32	152.69	26.868	0.023	2.336
	Controls	32	137.31	25.778		
PPBS 3	Cases	32	226.97	31.599	0.275	1.100
	Controls	32	218.28	31.560		
PIBSL 3	Cases	32	223.09	31.626	0.816	0.233
	Controls	32	221.25	31.548		

The same activity was carried out on a 6<sup>th</sup> week by following the sequence as mentioned in the 3<sup>rd</sup> week. The mean FBS levels were  $139.75 \pm 16.961$  among cases and  $133.94 \pm 15.895$  control group with a p-value of 0.162 and value of t-test as 1.415. The mean PPBS levels were  $232.34 \pm 31.197$  among cases and  $242.62 \pm 24.083$  among control group with the level of significance as 0.145 and value of t-test as -1.476. After performing diaphragmatic breathing exercise the mean PIBSL were  $227.69 \pm 31.070$  among cases and  $247.47 \pm 23.623$  among control group with a p-value of 0.006 and t-test value as -2.867 (Table 5).

**Table 5 Mean blood sugar levels of both groups at 6<sup>th</sup> week of breathing exercises**

Variables	Group	N	Mean	Std. Deviation	p-value	t-test
FBS 6	Cases	32	139.75	16.961	0.162	1.415
	Controls	32	133.94	15.895		

PPBS 6	Cases	32	232.34	31.197	0.145	-1.476
	Controls	32	242.62	24.083		
PIBSL 6	Cases	32	227.69	31.070	0.006	-2.867
	Controls	32	247.47	23.623		

A similar pattern of activity was followed in the 9<sup>th</sup> week, based on the guidelines and instruction of a respiratory therapist. Blood sugar levels were monitored by using a glucometer. Results showed the mean FBS levels as  $136.78 \pm 24.866$  among cases and  $156.66 \pm 33.555$  among control group with a p-value of 0.009 and value of t-test as -2.692. The mean PPBS levels were  $223.31 \pm 28.489$  among case and  $250.28 \pm 37.305$  among control group with a p-value of 0.002, that was significant and value of t-test as -3.250. The mean PIBSL were  $217.09 \pm 27.909$  among the interventional group and  $249.81 \pm 37.456$  among control group with a p-value of 0.000, that was highly significant and value of t-test as -3.962 (Table 6).

**Table 6 Mean blood sugar levels of both groups at 9<sup>th</sup> week of breathing exercises**

Variables	Group	N	Mean	Std. Deviation	p-value	t-test
FBS 9	Cases	32	136.78	24.866	0.009	-2.692
	Controls	32	156.66	33.555		
PPBS 9	Cases	32	223.31	28.489	0.002	-3.250
	Controls	32	250.28	37.305		
PIBSL 9	Cases	32	217.09	27.909	0.000	-3.962
	Controls	32	249.81	37.456		

The same activity was performed at 12<sup>th</sup> week and data were collected in the same order. Results showed the mean FBS levels as  $119.06 \pm 23.065$  among the interventional group and  $130.66 \pm 37.197$  among control group with a p-value of 0.139 and value of t-test as -1.498. The mean PPBS levels were  $200.25 \pm 36.687$  among cases and  $214.25 \pm 39.869$  among control group with a p-value of 0.149 and the value of t-test as -1.462. The mean PIBSL were  $192.69 \pm 34.834$  among cases and  $215.88 \pm 39.293$  among control group with a p-value of 0.015 and the value of t-test as -2.498 (Table 7). The results of HbA1c were collected after 12 weeks that showed the mean levels in the interventional group as  $7.51 \pm 1.098$  and in the control group as  $8.12 \pm 1.362$  with a p-value of 0.053 and t-test value as -1.971 (Table 7).

**Table 7 Mean blood sugar levels of both groups at the 12<sup>th</sup> week of breathing exercises**

Variables	Group	N	Mean	Std. Deviation	p-value	t-test
FBS 12	Cases	32	119.06	23.065	0.139	-1.498
	Controls	32	130.66	37.197		
PPBS 12	Cases	32	200.25	36.687	0.149	-1.462
	Controls	32	214.25	39.869		
PIBSL 12	Cases	32	192.69	34.834	0.015	-2.498
	Controls	32	215.88	39.293		
HbA1c 12	Cases	32	7.51	1.098	0.053	-1.971
	Controls	32	8.12	1.362		

At the 12<sup>th</sup> week of interventions, the results showed significant differences in Fasting blood sugar levels (FBSL) in both groups with a p-value of 0.000 and t-test value as 2.408. However, Post prandial blood sugar levels (PPBSL), Post interventional blood sugar level (PIBSL) and Hemoglobin A1-c showed no significant pre and post intervention difference (Table 8).

**Table 8 Pre and post intervention differences in blood sugar levels and HbA1c at the 12<sup>th</sup> week of interventions**

Variables	Mean	N	Std. Deviation	p-value	t-test value
FBSL 1	142.330	64	48.914	0.000	2.408
FBSL 12	124.860	64	31.253		
PPBSL 1	201.360	64	53.507	0.146	-0.714
PPBSL 12	207.250	64	38.655		
PIBSL 1	206.420	64	48.740	0.568	-0.275
PIBSL 12	204.280	64	38.643		

<b>HbA1c 1</b>	7.8181	64	1.39292	0.963	0.013
<b>HbA1c 12</b>	7.815	64	1.26492		

### DISCUSSION

The findings of the current study showed that at 1<sup>st</sup> week, there were no significant differences observed in Fasting blood sugar levels (FBSL) in the intervention group and the control group. After carrying out the diaphragmatic breathing exercise for 20 minutes, the sample of case and control group were taken on the spot. The mean PIBSL was  $209.25 \pm 51.887$  mg/dl in cases whereas in the control group it was as  $203.59 \pm 46.03$  mg/dl. These values indicate that PIBSL was slightly high in cases than in the control group which is against the proposed hypothesis. This might be due to high anxiety levels of the subjects when they were exposed to diaphragmatic breathing exercise. That's why their blood sugar levels increased instead of getting decreased. Physical and mental stress raises blood sugar level [12].

The 2<sup>nd</sup> session of the activity was arranged on the 3<sup>rd</sup> week during which the subjects were trained to perform the activity on their own. The results at 3<sup>rd</sup> week showed no significant differences in the mean blood sugar levels of cases and control groups. A similar study already conducted revealed that at the baseline the results were not significant ( $p > 0.05$ ). All the variables showed significant results ( $p < 0.05$ ) at the completion of 25 weeks of interventions [13].

The 3<sup>rd</sup> session of activity was carried out in the 6<sup>th</sup> week of the study. The results showed that PIBS levels were slightly better in the interventional group. The mean PIBSL among cases were  $227.99 \pm 31.07$  mg/dl and were as  $247.47 \pm 23.52$  mg/dl in control group ( $p = 0.006$ ). This provided the evidence that diaphragmatic breathing exercises have favorable effects on patients' glycemic levels. The 4<sup>th</sup> session of the activity, carried out on 9<sup>th</sup> week revealed high significance ( $p = 0.000$ ) of the interventions and this justified our proposed hypotheses (Table 6).

The 5<sup>th</sup> session, carried out in 12<sup>th</sup> week demonstrated no statistically significant differences in pre and post interventions blood sugar levels although mean values were better (reduced) in an interventional group compared to non-interventional group (Table 6). HbA1c values at 12<sup>th</sup> week also did not show significant differences ( $p = 0.053$ ) although it was better in cases ( $7.51 \pm 1.098$ ) than in the control group ( $8.12 \pm 1.362$ ).

In the current study, reduction in FBS, PPBS and PIBSL levels respectively was observed in the 9<sup>th</sup> week (FBS,  $p = 0.009$ , PPBS,  $p = 0.002$ , PIBSL,  $p = 0.000$ ) of the activity. Similar evidence was provided by a study conducted in India where FBS, PPBS, and HBA1C level were measured on 0 months, after 6<sup>th</sup> month and 9<sup>th</sup> month of intervention. There was a reduction in mean FBS by  $3.5 \pm 33.27$  mg/dl in the interventional group while it increased by  $3.6 \pm 35.07$  mg/dl in the non-interventional group ( $p = 0.85$ ). The mean PPBS reduced in interventional group ( $9.65 \pm 42.72$  mg/dl) while increased in non-interventional group ( $5.35 \pm 59.27$  mg/dl) [9].

The pre and post intervention insignificant differences in BSL and HbA1c at week 1, 3 and 6 may be due to a number of reasons that need to be highlighted. One of them is poor compliance of the subjects with the interventions. Breathing exercise is an important element of yoga that's why people do not follow the guidelines and do not perform this exercise at home routinely. In countries like China, Japan, Russia, and India, studies have found a significant improvement in blood sugar level because yoga is a very common practice there. However, it is not a common practice in Pakistan and that is why it was the main aim of this study to highlight its importance in this country. The second reason might have been the non-adherence of the study participants to breathing exercise activity because of their busy work schedule in the hospital and then at home. Another factor might be not taking the drugs regularly to meet the desire blood sugar levels among diabetes type-2 patients. A large portion of the diabetics' population is reported to have poor adherence to oral diabetes medications, which is strongly associated with poor glycemic control [14]. Moreover, the subjects might not have been relaxed when they were performing these exercises. The relaxation of mind and body is compulsory while performing this exercise [15]. The effects of breathing exercises on HbA1c were also not significant in the current study. The same reasons for non-compliance with pharmacological treatment regimen could be applied for this as well. In a previous study, it was concluded that diaphragmatic breathing can be incorporated as add-on therapy to standard care in improving the blood sugar levels and like HbA1c in type-2 diabetes. Breathing exercises alone may not produce significant results [16].

### CONCLUSION

Diaphragmatic breathing exercises can produce better effects on patients' blood sugar levels if it is combined with other exercises. The goal of decreasing the blood sugar levels among diabetes type 2 patients requires performing



breathing exercises regularly. When it is incorporated with other exercises like posturing, walking, meditation, guiding imagery and others, it will produce favorable effects in controlling blood sugar level. To achieve the desired goal, compliance of the subjects with standard treatment and breathing exercises is necessary.

#### IMPLICATION

The findings of this study may draw the attention of the researchers to investigate the additional effects of breathing exercises. Large sample size can be used to conduct this study in order to achieve more significant and generalizable results.

#### RECOMMENDATIONS

Keeping in mind the favorable effects of breathing exercises, doctors, nurses and respiratory therapists who are working in diabetes centers should motivate patients to adopt these exercises as a routine practice at home. Quality of life of type-2 diabetic patients can be improved significantly if patients' compliance with these exercises is assured. There is a dire need to introduce such complimentary therapies other than medications, among diabetic patients in Pakistan.

#### LIMITATIONS

Data collection took more time than expected because the subjects were working class females and it was difficult to spare time out of their tough job schedule and another busy routine. Compliance and cooperation of subjects were poor in this study.

#### DECLARATIONS

##### Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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