

Assessment of different risks factors contribute to type 2 diabetes and evaluates the effect of natural treatment in prediabetic population in Taif city, Saudi Arabia

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Abstract

Aim: To evaluate the questionnaire on the assessment of risk factors for Diabetes Mellitus-2 and evaluate the effect of natural treatment in prediabetic population in Taif region, Saudi Arabia

Background: Diabetes mellitus-2 is one of the most common chronic illness characterized by hyperglycemia and impairment in carbohydrate, fat and protein metabolism. There are many factors like physical inactivity, family history, lack of knowledge on dietary restrictions, life style and stress level which contributed to rapid increase in the incidence of type 2 diabetes.

Methodology: The cross-sectional study will be carried out among diabetic patients and healthy subjects at the different hospitals in Taif region. Structured questionnaire was designed to obtain data regarding sociodemographic characteristics, physical activity, genetic factors, medical history, height, body weight, diet, life style and stress related factors contributes to Diabetes 2. To evaluate the effect of natural treatment on prediabetic population, a randomized controlled trial will be implemented in this study, using a 16-week study period. The endpoint indices include the reversion rate.

Result and discussion: The study included 339 diabetic patients and 206 controls. The age ranged between 30 and 84 years with a mean of 59.017 ± 12.34 . 82.5% in control groups was graduated or more when compared with diabetic group where 31.9% were graduates. 24.8% and 21.2% of control and diabetic group were found to be overweight or obese. 20.4% diabetic patient were diagnosed gestational diabetes which is highly significant ($p < 0.05$), when compared with control where 1.9% observed gestational diabetes. 70.9% and 88.5% of control and diabetic group were genetically arising diabetic. Similarly, more smoking and less physical activity was observed in patients. After three months of lifestyle management plan followed by prediabetic patients, 57.77 % of prediabetic population

returned to normal glucose level when compared with control groups in which only 12.8% ($p < 0.05$) of patients were reversed.

Conclusion: The finding suggests that family history of DM, low educational attainment, high BMI was associated with diabetes. High physical inactivity, smoking, Vitamin D deficiency and high triglycerides level also found as a contributing risk factor for development of type 2 diabetes. Results of life style management plan support an effectiveness of natural treatment in prevention or treatment of prediabetes.

Key words: *Diabetes mellitus; hyperglycemia; risk factors, physical activity, life style factors, prediabetes*

1. Introduction

Diabetes mellitus (DM) is one of the most common chronic illness characterized by hyperglycemia and impairment in carbohydrate, fat and protein metabolism [1-2]. The prevalence of type 2 diabetes has been increasing exponentially, and a high prevalence rate has been observed in developing countries and in populations undergoing “westernization” or modernization [3]. Globally in 2013, it is estimated that almost 382 million people suffer from diabetes with a prevalence of 8.3% in which Saudi Arabia is ranked 7th of the top ten countries of the world with rate of 23.9% [4].

Diabetes can be classified into insulin-dependent diabetes mellitus (type 1 diabetes mellitus, T1DM) and non-insulin-dependent diabetes mellitus (type 2 diabetes mellitus, T2DM). T2DM is the most common form of DM, which accounts for 90% to 95% of all diabetic patients and is expected to increase to 439 million by 2030 [3, 5]. It is characterized by hyperglycemia, insulin resistance and relative insulin deficiency [6, 7]. Type 2 DM resulted from interaction between genetic, environmental and behavioral risk factors [8, 9].

Epidemiological studies indicate a three to four times increased risk of type 2 diabetes in subjects with close relatives with diabetes [10]. In association with genetic factors, overweight and obesity have been found to have an impact in the development of diabetes and hypertension in various studies [11]. Lifestyle factors that have consistently associated with increased risk of T2DM are physical inactivity and diet composition, particularly with low fiber intake, a high trans fatty acid intake, a low unsaturated: saturated fat intake ratio and absence of or excess alcohol consumption [9]. People who have type 2 diabetes tend to have high levels of triglycerides and low levels of high-density lipoprotein (HDL) and similar low-density lipoprotein (LDL) levels than people who do not have diabetes [12]. Similarly, cigarette smoking and alcohol consumption may be an independent, modifiable risk factor for non-insulin dependent diabetes mellitus [13]. In T2DM, patients are often asymptomatic but may be present some symptoms such as lethargy, polyuria, nocturia and polydipsia [1].

The pathologic hallmark of DM involves the vasculature leading to both include macrovascular diseases (hypertension, hyperlipidemia, heart attacks, coronary artery disease, strokes, cerebral vascular disease, and peripheral vascular disease), microvascular diseases (retinopathy, nephropathy, and neuropathy) and cancers [14, 15]. Chronicity of hyperglycemia is associated with long-term damage and failure of various organ systems mainly affecting the eyes, nerves, kidneys, and the heart [16]. These complications can increase rates of morbidity and mortality at the forefront in diabetic populations that overwhelmingly arise from a delayed diagnosis, the intricate risk factors, failure of management and financial issue [5]. The disease effect on the quality of people's lives and generate enormous economic and social burdens and thus always in need of intervention [5, 15].

Prediabetes is an intermediate state of hyperglycemia with glycemic parameters above normal but below the diabetes threshold. While, the diagnostic criteria of prediabetes are not uniform across various international professional organizations, it remains a state of high risk for developing diabetes with yearly conversion rate of 5%-10% [18]. Observational evidence suggests as association between prediabetes and complications of diabetes such as early nephropathy, small fiber neuropathy, early retinopathy and risk of macrovascular disease. Several studies have shown efficacy of lifestyle interventions with regards to diabetes prevention with a relative risk reduction of 40%-70% in adults with prediabetes [19]. It is considered to be an at risk state, with high chances of developing diabetes. While, prediabetes is commonly an asymptomatic condition, there is always presence of prediabetes before the onset of diabetes. But world literatures lack sufficient data that prove effectiveness of natural treatment in prevention of prediabetes.

Multiple risk factors of diabetes, delayed diagnosis until micro- and macro-vascular complications arise, life-threatening complications, failure of the current therapies, and financial costs for the treatment of this disease, make it necessary to study risk factors in diabetic population in Saudi region. The proposed study was carried out to analyze some factors such social determinants, lifestyle habits, dietary and stress related factors to facilitate understanding their role in development of Type 2 diabetes and evaluate the effect of natural treatment as preventive measures in prediabetic patients.

2. Materials and Method

2.1. Methodology for diabetes

2.1.1. Selection and description

The subjects for this study will be selected from Taif region, Saudi Arabia. The study included 339 diabetic patients and 206 controls. Subjects had to be age 18 years or older to participate. However gender will be not restricted. These subjects will be selected from Endocrinology Centre in King Abdul-Aziz and King Faisal Hospitals which is belong to Taif Region, Saudi Arabia.

2.1.2. Inclusion Criteria

Type-2 diabetic patients suffering from diabetes since 2 years.

2.1.3. Exclusion Criteria

- Type 2 Diabetic patients who will be critically ill and unable to communicate in the study period will be excluded from the study.
- Type 2 Diabetic patients who will not volunteering for the study were excluded from the study.
- Pregnant women will be excluded from the study.

2.1.4. Independent Variables

- Sociodemographic Characteristics: Age, gender, marital status, Level of education, occupational status, monthly Income
- Biomedical factors: GMI, gestational diabetes, Family history, hypertension, serum triglycerides
- Life style factors: Physical instability, smoking, alcohol consumption
- Dietary factors, Disease and medication related factors and stress

2.1.5. Sampling procedure

Cross-sectional study involving interview administered questionnaire will be utilized for data collection. Data collected by the researcher in each hospital. Cases will be selected from outpatient department of the hospitals and Controls who will non diabetic study subjects will be selected from the visitors and care givers at the data collection time in the study area. Screening will be carried for the non diabetic study subjects by determining either Fasting plasma glucose or Random plasma glucose. One record of fasting plasma glucose (FPG) <7.0 mmol/L (126 mg/dl) or, Random plasma glucose <11.1 mmol/l (200 mg/dl) was considered to select the controls. The number of study units to be sampled from cases and controls will select using population proportion to size allocation and, systematic random sampling will be employed to select each study subjects. Based on the sampling fraction a starting client will determine by using simple random sampling techniques. When an individual does not satisfy the inclusion criteria, the next participant will be included in the study [20].

2.1.6. Research Design

The questionnaire (**Appendix 1**) will adapted from WHO step wise approach for non communicable disease chronic disease risk factor surveillance in addition with considering previous researchers who also measured risk factors for diabetes [21, 22]. The survey included questions designed to obtain sociodemographic characteristics, physical activity, genetic factors, medical history, height, body weight, diet, life style and stress related factors contributes to Diabetes 2. Clients regarded as positive if either of parents, Sister or brother (s) have diabetes mellitus. BMI was calculated as weight (kilos)/height (meters) categorized as underweight (less than 18.5), normal weight (18.5 to 24.9), over weight (25 to 29.9) and obese (30 or more). Resting seated blood pressure was measured using sphygmomanometer. Education was classified into the following three categories: uneducated, <12th class and graduation or more. Current occupation status was categorized as Impossible/difficult to get employed all the time, Not too bad/easy to get employment or employed easily. Clients, who had practiced any regular physical activity per week, it is categorized as active those who practiced >300 minutes moderate physical activity, moderately active those who practiced 150 -300 minutes moderate physical activity like fast walking and swimming per week, physically inactive less than 150 minutes per week including for those in sedentary life style or its equivalent vigorous physical activity.

Daily consumption of fruits and vegetables will summarized in three categories: those consuming fewer than 2 fruits and vegetables (low), 3 to 5 fruits and vegetables (medium) and more than 5 fruits and vegetables (high). Smoking as grouped as 'daily smoker', 'occasional smoker' and 'non-smoker'. Occasional smoker is someone who is not daily smoker or has smoked less than 100 cigarettes life time while 'non-smokers are who never smoke.

2.2. Evaluation of natural treatment in prediabetes

2.2.1. Research Design

The study has received Institution Review Board (IRB) approval. After providing informed consent, participants are instructed on the details regarding schedule and diet plan. The researchers randomly assigned patients with prediabetes to receive a placebo or a natural treatment.

Groups

Treatment group: Natural treatment

Control group: Without any treatment

2.2.2. Selection and Screening of participants

The subjects of this study were selected from the Makkah province, Saudi Arabia and were prediabetic (for both groups). Subjects had to be age 18 years or older to participate. However, gender was not a restriction. The patients were divided into the treatment group (n= 45) and the control group (n=39). The sample size selected was 84. Participants were enrolled according to the diagnosis and inclusion criteria.

2.2.3. Inclusion and exclusion criteria

Inclusion criteria

- Fulfill the prediabetes diagnostic criteria
- Be aged 18–50 years old

Exclusion criteria

- History of diabetes (except gestational diabetes)
- Cardiovascular and liver diseases
- Endocrine disease, such as hyperthyroidism, auto-allergic disease, cancer or other serious or potentially fatal illness
- Pregnancy, preparation for pregnancy or active lactation in women
- Patients with mental illness or those who are uncooperative
- Participation in other clinical trial within the last 2 weeks
- Refusal to provide consent for the study

2.2.4. Intervention

The treated group was described to follow up guidelines for natural Treatment recommended by WHO²³ for treatment of prediabetes (eat a healthy, low complex-carbohydrate diet and exercise). The following instruction was given to the patients:

1. They are instructed to focus on Diet

- a. low-sugar
- b. low-carb diet that instead prioritizes eating high-nutrient veggies, leafy greens, lean proteins, and good fats.
- c. Eat more fibers
- d. Take more soya protein
- e. Apple cider vinegar: Two tablespoons right before or early in the meal.
- f. Adequate water (3- 4 liters)

2. They are instructed to focus on physical activity:

1. 30 minutes to 1 hour morning and 30 minutes walk after dinner

3. Improving life style

1. Reduce stress (30 minutes meditation)
2. Lifestyle changes: Follow healthy lifestyle (get up early in morning, exercise regularly and eat at fixed time while chewing properly), take adequate sleep (7-8 hr)

Follow up

- Screening period: 4 week before the intervention
- Intervention period: 12 weeks
- Follow-up period: 4 weeks after the intervention

Follow up data collection

The questionnaire (**Appendix-2**) was developed according to guidelines prescribed by World health organization [23], and was shown to be a reliable and valid measure to study the outcome of prediabetic patients [24]. The survey focuses on low-fat, fiber rich diet as an approach to diabetes treatment. Follow up Questionnaire composed of seven

questions which accompanied the physical activity, follow up of prescribed diet, measuring stress level, water intake and sleeping time in hours. The outcome measures blood glucose changes to normal (FPG <5.6 mmol/L).

2.3. Statistical analysis

Collected data was analyzed using SPSS 13 version (IBM, Illinois, Chicago). Frequency, percentage, means and standard deviation was calculated and associations between variables will be assessed using chi-square test. Also, t-test was used to find significant differences of two means and ANOVA was employed to find the significance of more than two means. In all cases, p value <0.05 was considered statistically significant.

3. Result

3.1. Assessment of risk factors contributes to diabetes

Table 1 presents their demographic characteristics. Their age ranged between 18 and 84 years with a mean of 59.017 ± 12.34 . More than half of them were females in diabetic group (53.1%) with a male to female ratio of 0.46:0.53. 31.9% was educated and have enough income (54.9%) while 11.5% and 33.6% revealed income management difficult and not too bad/easy in diabetic group. Whereas in control group 82.5% were graduated and 76.2% have good income.

Table 1. Socio-demographic variable contribute to type 2 diabetes.

Parameters		Diabetic control (n=206)	Diabetic (n=339)	p value
Age		55.21	59.01	0.009
Gender	Male	111 (53.8%)	53 (46.9%)	0.23
	Female	95 (46.11%)	60 (53.1%)	
Good Education Level		170 (82.5%)	36 (31.9%)	<0.0001
Income Management	Good	157 (76.2%)	62 (54.9%)	0.0008
	Not too bad/easy	39 (18.9%)	38 (33.6%)	0.00338
	Impossible/difficult all the time	10 (4.9%)	13 (11.5%)	0.0278

In diabetic patients, the fasting blood glucose level ranges from 82-500 mg/dL with a mean of 187.15 ± 64.87 mg/dL. For control group, the fasting blood glucose level was found to be normal, 73.5% diabetic patients have high triglyceride levels (n=249), when compared with non-diabetic patients where only 7.3% (n=15) was diagnosed with high value (**Figure 1**). In diabetic groups, 58.4% of them have a high physical inactivity. When contrast with control group, only 3.4% were having high physical inactivity in their daily routine life. Similarly, 35.9% and 87.6% in control and diabetic group were vitamin D deficiency. The results of assessment of biomedical factors contribute to type-2 diabetes is shown in **Figure 2.a**. In control group, 52.9% were healthy weight, whereas 24.8% and 2.9% were only overweight and obese. While in diabetic group, only 25.7% were healthy weight and 71.15% were found to be overweight or obese. A previous diagnosis of gestational diabetes (GDM) carries a lifetime risk of progression to type-2 diabetes of up to 60%. 20.4% diabetic patient was diagnosed gestational diabetes, which is highly significant (0.002) when compared with control where 1% observed gestational diabetes. Majority (86.7%) of cases with diabetes were positive family history of diabetes where either the parents or siblings were suffering from diabetes. Hypertension was diagnosed in 50.4% (n=171) of diabetic patients, whereas in non-diabetic patients, only 8.3% (n=17) were found to be hypertensive.

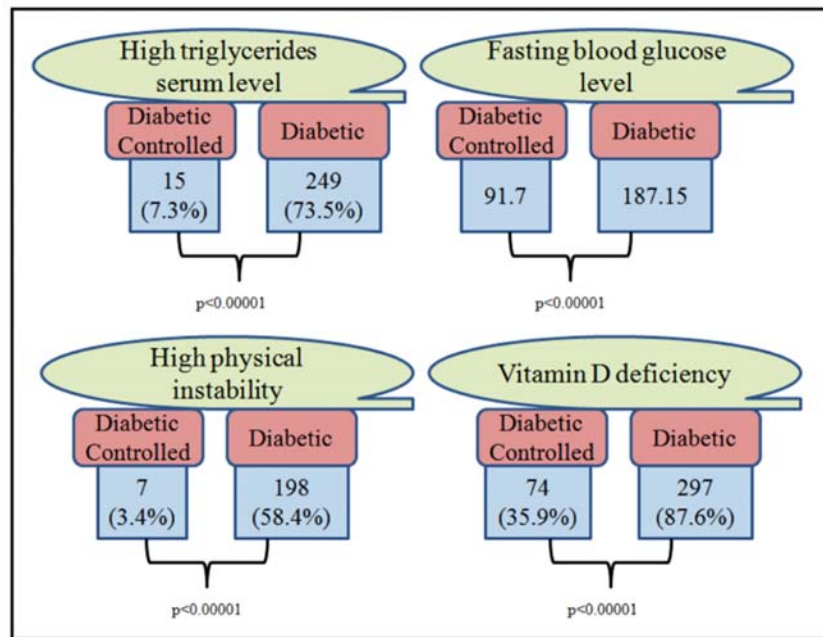
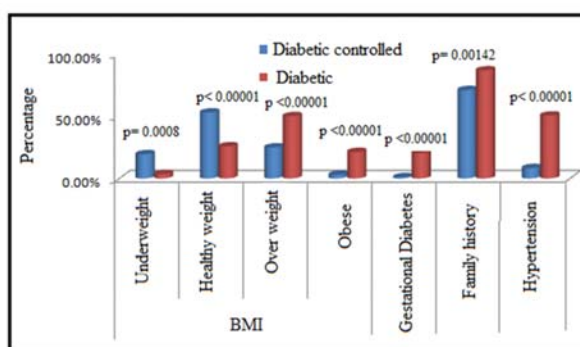
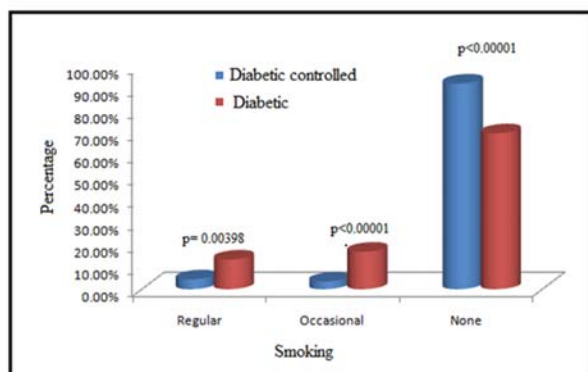


Figure 1

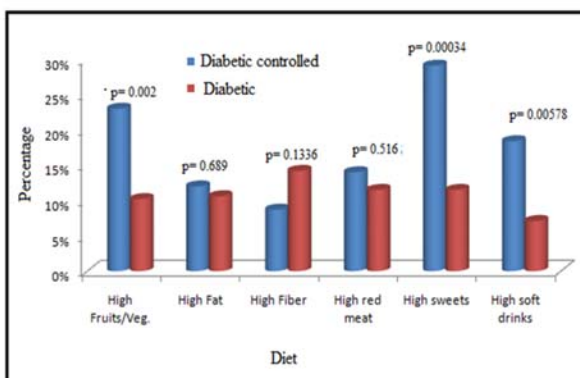
When considering smoking as a risk factor, 3.4% from a control group confirmed as an occasional smokers. While in diabetic group, 13.3% and 16.8% population was found to be regular (n=45) and occasional smoker (n= 57) ($p < 0.00001$). While, 92.2% (n=190) and 69.9% (n=237) in control and diabetic groups are non-smokers (**Figure 2.b**).



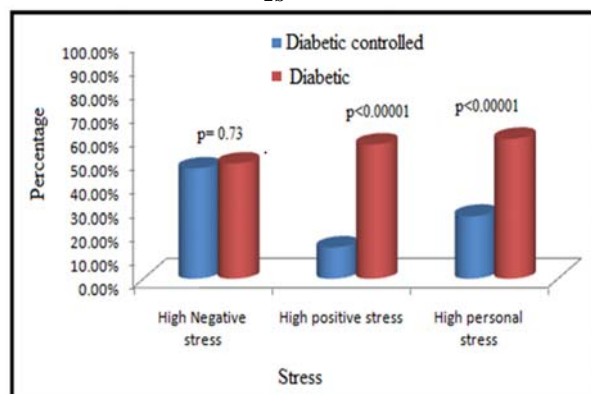
2a



2b



2c



2d

Figure 2

Effect of assessment of dietary factors contribute to type-2 diabetes is shown in **Figure 2.c**. In control group, 61.2% population was taking average fruits and vegetables, while 10.2% and 28.6% take high and low vegetables diet. In diabetic group, 61.1% and 15.9% were taken average and low fruits and vegetables. While 23% (n=78) were found to take high fruits and vegetables diet which is statistical significant when compared with control ($p=0.002$). Similarly in diabetic groups, 61.1% and 10.6% were taken average and high fat diet when compared with control where the value for average and high fat intake is 75.2% and 12.1, respectively. In case of fiber intake, 14.2% and 62.8% were take regular and occasional fibers. When considering the control group, 8.7% and 73.3% are regular and occasional taker of fibrous diet. While 23% and 18% of diabetic and control revealed that they don't include any fiber in their diet. In control group, 60.2% and 72.6% population have an average intake of red meat in control and diabetic group. 18% and 52.9% in control group and 41.6% and 46.9% in diabetic group take low and average sweets, respectively. Similarly 18.4% and 31.6% take high and average soft drinks, while in diabetic group, 7.1% take high and 47.8% take average soft drinks.

Effect of stress related factors in development of type-2 diabetes are shown in **Figure 2.d**. Negative stress in control group was found to be 46.6%, which was not statistically significant when compared with the diabetic groups (48.7%). While, 56.8% and 59.2% of diabetic population were significantly ($p<0.05$) under stressed with positive and personal stresses, when compared with control.

Results of assessment of disease and medication related factors contribute to type-2 diabetes is shown in **Figure 3**. In diabetic group, 7.1% of patient is taking antipsychotics which was significantly higher ($p=0.00028$) when compared with control where only 1% populations taken the same drug. 15% and 16.8% in control and diabetic group agreed with the sleep disorders, while 39.8% confirmed absence of any sleep problems in the both groups. In control and diabetic group, 0.5% and 4.4% was suffered from thyroid disorder. 36.1% patient was suffering from other disease such as hyperlipidemia, osteoporosis, prostatitis, chronic kidney disease, which was significantly higher (<0.05) when compared with control group where 6.8% population size suffered. 7.1% diabetic group was significantly ($p<0.05$) suffered from heart diseases in comparison with control where 1% was the sufferers. Regarding hormonal imbalances (cushing syndrome, acromegaly etc), no significant differences were measured between the two groups.

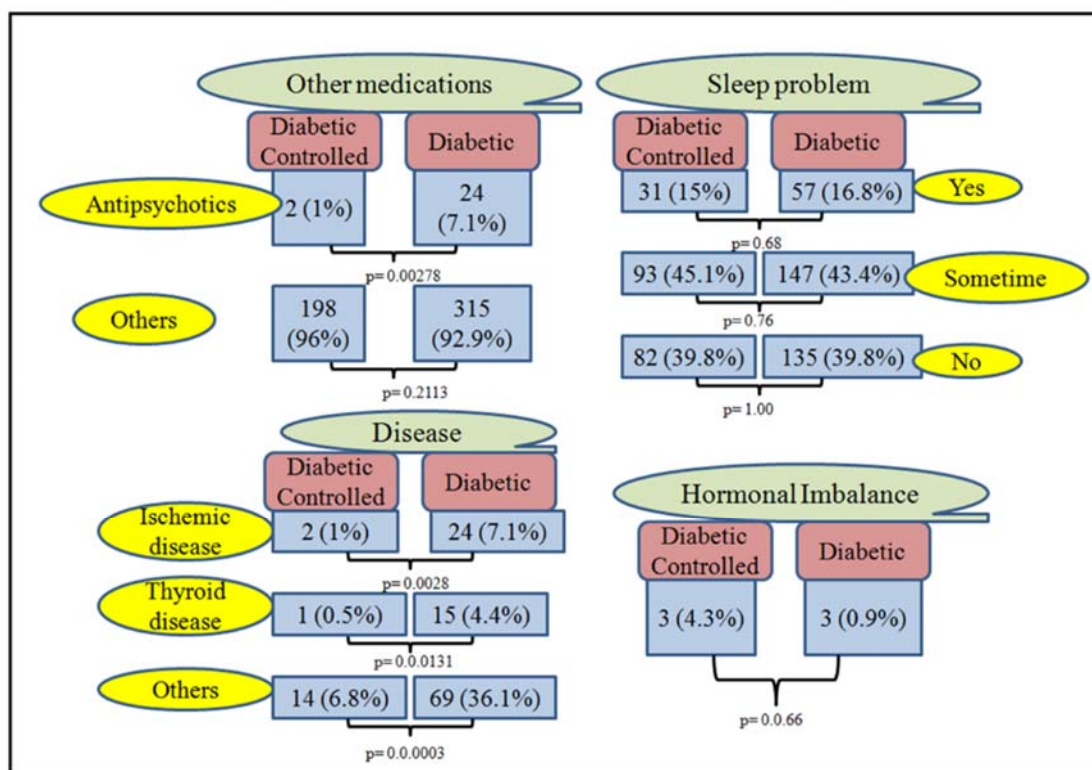


Figure 3

3.2. Assessment of risk factors contributes to prediabetes

The study included 45 prediabetes patients and 39 control. **Table 2** presents their demographic characteristics. Their age ranged between 22 and 59 years with a mean of 39.23 ± 12.36 years. More than half of them were females (66.66%). The level of education was good in both control and treatment with no significant difference.

Table 2. Socio-demographic variable and biomedical factors contributes to prediabetes.

Parameters		Prediabetic control (n=39)	Prediabetic treatment (n=45)	p value
Age		39.2	41.4	0.4
Gender	Male	9(23.07%)	15(33.3%)	0.29
	Female	30(76.92%)	30(66.6%)	
Good Education Level		31 (82.05%)	32 (71.11 %)	0.242
BMI	Healthy weight	9 (23.1%)	8 (17.7%)	0.55
	Over weight	23 (59%)	26 (57.7%)	0.91
	Obese	5 (2%)	10 (22.2%)	0.26
	Clinical obese	2 (5.1%)	1 (2.2%)	0.47
Family history		38 (97.4%)	43 (95.6%)	0.64
Fasting blood glucose level before management		115.4	114.37	0.9

In control group, 23.1% was having healthy weight, whereas 59.0%, 2% and 5.1% were only overweight, obese and clinical obese (**Table 2**). While in prediabetic group, only 17.77% were having healthy weight and 57.77%, 22.22% and 2.22% were found to be overweight, obese and clinical obese. Similarly 97.8% in prediabetic group have genetic diabetes which was not difference when compared with control group. In prediabetic patients, the level of fasting blood glucose ranges from 100-126 mg/dL with a mean of 115.4 ± 8.59 mg/dl for control group, the mean was 114.37 ± 8.45 for prediabetic

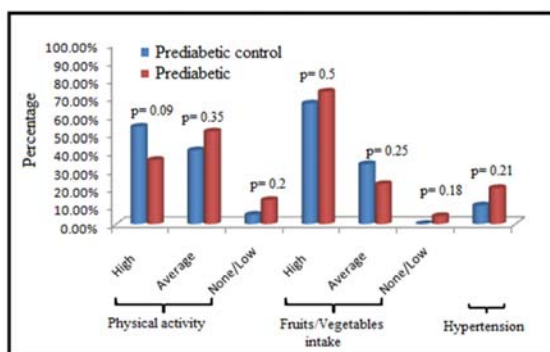
The results of assessment of Life style factors in prediabetic population are shown in **Figure 4.a**. In control groups, 41% of population has an average physical activity. Whereas 53.8% and 5.1% have either high or no physical activity. When contrast with prediabetic group, only 51.1% of them were having average physical activity while 13.3% patients revealed no physical activity in their daily routine life. In control group, 33.3% population was taken average fruits and vegetables, while 66.7 % and 0% take high and low vegetables diet. In prediabetic group, 22.2% and 4.4 % were taken average and low fruits and vegetables. While 73.3% (n=33) were found to take high fruits and vegetables diet. 10.3% (control group) and 20% (prediabetic group) of them was suffering from hypertension.

3.3. Evaluation of effectiveness of natural treatment for prediabetes

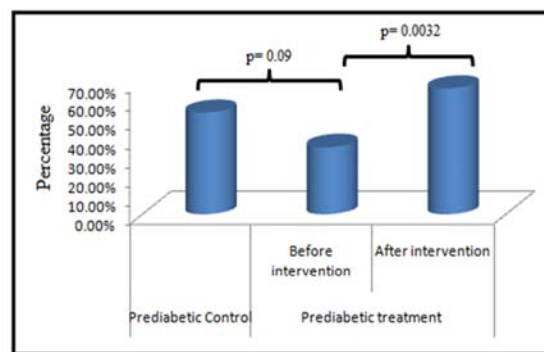
As shown in **Table 3**, 71.1% prediabetic patients strictly follow the proposed management plan in which 80% take proper fruits and vegetables, whereas 62.2% adhered with the fibrous diet. Water treatment was followed by 73.3% of prediabetic patients. Similarly high proportion (66.7%) follows routine 30 minutes of physical activity or exercises (**Figure 4.b**). 68.9% of patients has taken adequate sleep and minimizes their stress level. Fasting blood glucose level ≥ 120 mg/dl and ≥ 100 mg/dl was found in 31-38.4% and 28.2-33.3% prediabetic population. After management plan, 57.77% of prediabetic population returned to normal glucose level when compared with control groups ($p < 0.05$) in which only 12.8% of patients were reversed (**Figure 4.c**). Similarly in control group 46.1% patients have fasting blood glucose level ≥ 120 mg/dl. Whereas in treatment group only 11.1% of patients have ≥ 120 mg/dl fasting blood glucose levels.

Table 3. Management plan for prediabetic patients.

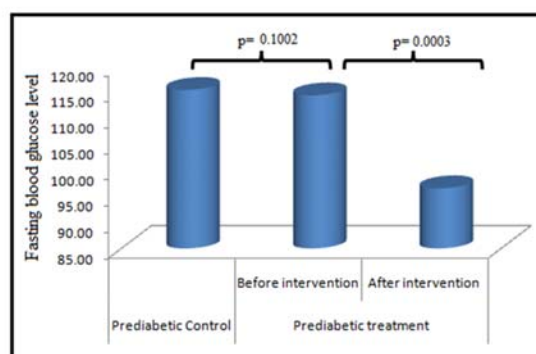
Management plan		Prediabetic treatment (n=45)
Follow prescribed management	yes	32 (71.1%)
	Sometime	13 (28.9%)
Fruits/Vegetables after management	yes	36 (80%)
	Sometime	9 (20%)
Fiber after management	yes	28 (62.2%)
	Sometime	15 (33.3%)
Water after management	yes	33 (73.3%)
	Sometime	12 (26.7%)
Physical activity or exercise	yes	30 (66.7%)
	Sometime	15 (33.3%)
Change stress	yes	31 (68.9%)
	Sometime	14 (31.1%)



a



b



c

Figure 4

Discussion

Type-2 diabetes is caused by a combination of genetic factors related to impaired insulin secretion and insulin resistance and environmental factors such as obesity, overeating, lack of exercise, stress and aging [25]. It is typically a multifactorial disease involving multiple genes and environmental factors to varying extents [26]. Total numbers enrolled in the study were 319 in which 206 was control and 113 were diabetic with mean average age of 59.01 years. 53.1% of them were females. 82.5% in control groups was graduated when compared with diabetic group where 31.9% were graduates, which correlate low level of education with a higher risk of diabetes [27, 28]. A study conducted in Thailand by **Papier and coworkers**, showed that for both sexes, factors most strongly associated with developing T2DM were increasing with age and higher BMI [22, 29]. According to the World Health Organization, nearly 90% of diabetic patients develop T2DM mostly relating to excess body weight [21]. In our study similarly,

55.7% diabetic patient were overweight or obese which further confirm the role of weight management in progression of diabetes.

A wide variety of lifestyle factors are also of great importance to the development of T2DM, such as sedentary lifestyle, physical inactivity and smoking [30]. Similar to our study, 37.1% diabetic population showed no physical activity which support meta-analysis conducted by **Chen and coworkers** where lifestyle intervention which included change in diet, exercise and education showed significant benefit in a number of risk factors [31]. A high proportion (58.4%) of diabetic population was found to be physically inactive when compared with control, where the value is 3.4%.

It has long been known that T2D is, in part, inherited [32]. The genetic component can be analyzed by comparing the risk of developing disease between relatives of patients with T2D and the background population [33]. Family studies have revealed that first degree relatives of individuals with T2D are about 3 times more likely to develop the disease than individuals without a positive family history of the disease. The lifetime risk of developing T2D is 40% for individuals who have 1 parent with T2DM and almost 70% if both parents are affected. Our study revealed that 86.7% of population size from diabetic group was genetically arises which strongly confirmed the hypothesis. Smoking may lead to insulin resistance or inadequate compensatory insulin secretion, impaired glucose tolerance, with a direct effect on beta cells and chronic pancreatitis [34]. Our study was consistent with the results where 13.3% and 16.8% diabetic population was found to be heavy and occasional smoker.

The role of diet in the etiology of T2DM was proposed by Indians as mentioned earlier, who observed that the disease was almost confined to rich people who consumed oil, flour, and sugar in excessive amounts [35]. A case-control study conducted in Lebanon measured the association between diet and T2DM which showed that refined grains and desserts and fast food patterns significantly increased the risk of T2DM. High intake of red meat, sweets and fried foods, contribute to the increased risk of insulin resistance and T2DM [36]. In our study, control group was associated with significant higher intake of fruits and vegetables when compared with diabetic population. Consumption of fruits and vegetables may protect the development of T2DM, as they are rich in nutrients, fiber and antioxidants which are considered as protective barrier against the diseases [37, 38]. In contrast, an inverse correlation was found with sweets and soft drinks where controls are higher in taker. The obvious reason is recommended diet control followed as a preventive measure by diabetic population.

Vitamin D plays a vital role in calcium metabolism. A low level of vitamin D has been associated with onset and progression of DM [39, 40]. Previously studies suggested that low vitamin D (<50 nmol/L) doubled the risk of newly diagnosed type 2 diabetes [39]. Likewise our finding support an inverse correlation between DM and vitamin D level as 87.6% of diabetic population were diagnosed of low vitamin D levels which is statistically significant when compared with control.

Increasingly, psychological stress is being explored as a risk factor for chronic conditions, such as cardiovascular disease, diabetes and arthritis. Pathophysiological mechanisms linking stress to diabetes have included direct neuroendocrine effects (e.g. the fact that stress hormones such as cortisol and adrenaline are counter-regulatory to insulin), and indirect effects mediated by traditional risk factors (e.g. stress may reduce the likelihood of exercising) [41]. A high positive and personal stress level was predicted in diabetic group as compared to control. While no significant differences were observed when considering negative stress level between the two groups.

Certain diseases have been found to correlate with diabetes. In our study we find the significantly higher % of patients was taking antipsychotics drugs. We compared associations of diabetes mellitus (DM) with other diseases also such as cardiovascular disease, brain disorder, hormonal imbalance, thyroid disorder etc and our finding support a correlation between progression of type-2 diabetes and various such disorders. It has been reported that high Tg and low HDL-C levels associated with higher risk for DM [42]. As significant high proportion of diabetic population diagnosed high triglycerides level which highly correlated with increased diabetes risk. Similarly high prevalence of thyroid dysfunctions has been found in diabetic patients [43]. In our study we find a significant correlation between thyroid dysfunction and diabetes. A significant correlation between ischemic disease and diabetes is due to impaired ability of ischaemic tissue to abrogation of new vessel formation and remodeling of the pre-existing vasculature [44]. We didn't find any significant correlation between hormonal imbalances and diabetes.

Our study also assessed the risk factors for prediabetes. The association between hypertension and prediabetes has been reported previously [45]. In our study, hypertension displayed an important association as 10-20% prediabetic population was hypertensive when compared with other diseases such as osteoporosis or thyroid disorder where prevalence was lower. In contrast no relationship was found between consumption of healthy diet and the presence of prediabetes as more than 50% were already taking fruits and vegetable on daily basis. The Diabetes Prevention Program Research Group has published several studies showing that Type 2 diabetes may be preventable by life style modification such as diet and exercise. Several researchers hypothesized that lifestyle intervention would prevent or delay the development of diabetes. The lifestyle intervention reduced the incidence by 58% compared with placebo

[46]. A three months lifestyle management plan was followed by prediabetic patients who include modification of diet, stress and exercise. It was observed that 57.77% of prediabetic population returned to normal glucose level when compared with control groups in which only 12.8% of patients were reversed which support an effectiveness of natural treatment in prevention or treatment of prediabetes.

Conclusion

The finding suggest that female gender, age > 50 years, family history of DM, low educational attainment (illiterate or having completed primary school), high BMI was significantly associated with diabetes. It was found that current smoking status is an independent modifiable risk factor for T2DM since it is associated with glucose intolerance, impaired fasting glucose and consequently, leads to T2DM. Similarly a direct correlation was found between diabetes and other diseases which suggest the indirect links between the different parts of the body. On the other side expectedly, some role of stress level and dietary factors was observed in progression of type-2 diabetes. Life style management plan was found an effective measure in treatment of prediabetes and thus may decrease the risk of developing diabetes-2 in prediabetic population. Results reveal that intensive, structured lifestyle interventions, particularly those that include both exercise and dietary modification, yield significant improvements in fasting blood glucose levels.

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References

- [1] Wells BG, DiPiro J, Schwinghammer TL, DiPiro CV. Pharmacotherapy Handbook (Seventh Edit). Ingris: McGraw-Hill Education Companies 2009.
- [2] American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes-2018. Diabetes care. 2008;41(1): S13-S27 .<https://doi.org/10.2337/dc18-S002>
- [3] Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci. 2014; 11(11): 1185-200. Doi: 10.7150/ijms.10001.
- [4] Naeem Z. Burden of Diabetes Mellitus in Saudi Arabia. Int J Health Sci. 2015; 9(3): V-VI.
- [5] Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus- present and future perspectives. Nat rev endocrinol. 2012; 8(4): 228-236. doi: 10.1038/nrendo
- [6] Maitra A, Abbas AK. Endocrine system. In: Kumar V, Fausto N, Abbas AK (eds). Robbins and Cotran Pathologic basis of disease (7th ed). Philadelphia, Saunders 2005; 1156-1226.
- [7] Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman medical J 2012; 27(4): 269-73 .doi: 10.5001/omj.2012.68.
- [8] Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus- present and future perspectives. Nat Rev Endocrinol. 2011; 8(4): 228-36. doi: 10.1038/nrendo.2011.183.
- [9] Tuomi T, Santoro N, Caprio S, Cai M, Weng J, Groop L. The many faces of diabetes: a disease with increasing heterogeneity. The Lancet. 2014; 383(9922): 1084-1094. doi: 10.1016/S0140-6736(13)62219-9
- [10] Carlsson S, Midtjell K, Grill V. Influence of family history of diabetes on incidence and prevalence of latent autoimmune diabetes of the adult (LADA): Results from the Nord-Trøndelag health study. Diabetes Care. 2007; 30(12): 3040-5.
- [11] Mandal A. Study of prevalence of type 2 diabetes mellitus and hypertension in overweight and obese people. J Family Med Prim Care. 2014; 3(1): 25-8. doi: 10.4103/2249-4863
- [12] Pathak R, Pathak A. Study of life style habits on risk of type 2 diabetes. Int J Appl Basic Med Res. 2012; 2(2): 92-96. doi: 10.4103/2229-516X.106349
- [13] Bazzano LA, Serdula M, Liu S. Prevention of type 2 diabetes by diet and lifestyle modification. J Am Coll Nutr. 2005; 24(5): 310-9.
- [14] Chawla A, Chawla R, Jaggi S. Microvascular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocr Metab. 2016; 20(4): 546-551. DOI: 10.4103/2230-8210.183480
- [15] Orasanu G, Plutzky J. The pathologic continuum of diabetic vascular disease. J Am Coll Cardiol. 2009; 53(5): S35-42. doi: 10.1016/j.jacc.2008.09.055.
- [16] Review Standards of Medical Care in Diabetes: Summary of Revisions. Diabetes Care. 2016; 39(1): S4-5. <https://doi.org/10.2337/dc16-S003>
- [17] Tabesh M, Shaw JE, Zimmet PZ, Söderberg S, Koye DN, Kowlessur S, Timol M, Joonas N, Sorefan A, Gayan P, Alberti KGMM, Tuomilehto J, Magliano DJ. Association between type 2 diabetes mellitus and disability: What is the contribution of diabetes risk factors and diabetes complications? J Diabetes. 2018; 10(9): 744-752. doi: 10.1111/1753-0407.12659
- [18] Bansal N. Prediabetes diagnosis and treatment: A review. World J Diabetes. 2015; 6(2): 296-303. doi: 10.4239/wjd.v6.i2.296.
- [19] Kanat M1, DeFronzo RA, Abdul-Ghani MA. Treatment of prediabetes. World J Diabetes. 2015; 6(12): 1207-22. doi: 10.4239/wjd.v6.i12.1207.
- [20] Giday TK, Aseffa H, Kidanemariam A. Assessment of Risk Factors associated with Type-2 Diabetes Mellitus in central zone of Tigray, North Ethiopia. Int J Pharm Biol Sci Fundamentals. 2014; 7(1).
- [21] WHO stepwise approach Surveillance of risk factors for non communicable diseases. Geneva: WHO Press 2011.
- [22] Papier K, Jordan S, D'Este C, Bain C, Peungson J, Banwell C, Yiengprugsawan V, Seubsman SA, Sleigh A. Incidence and risk factors for type 2 diabetes mellitus in transitional Thailand: results from the Thai cohort study. BMJ Open. 2016; 6(12): e014102. doi: 10.1136/bmjopen-2016-014102.
- [23] World Health Organization (2006). Guidelines for the prevention, management and care of diabetes mellitus. 2006; 38-41.
- [24] Li X, Liu H, Feng H, Xian, Z, Chen Y, Chen J, Tang C, Lai X, Lan X, Huang H. Acupuncture paired with herbal medicine for prediabetes: study protocol for a randomized controlled trial. Trials. 2017; 18: 297. doi: 10.1186/s13063-017-2014-4.

- [25] Chamberlain JJ, Rhinehart AS, Shaefer CFJ, Neuman A. Diagnosis and management of diabetes: synopsis of the 2016 American Diabetes Association standards of medical care in diabetes. *Ann Intern Med*. 2016; 64(8): 542-52. doi: 10.7326/M15-3016
- [26] Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J Physiol Pathophysiol*. 2013; 4(4): 46-57. <https://doi.org/10.5897/JPAP2013.0001>
- [27] Kohei K. Pathophysiology of type 2 diabetes and its treatment policy. *JMAJ*. 2010; 53: 41-46.
- [28] Muller G, Hartwig S, Greiser KH, Moebus S, Pundt N, Schipf S. Gender differences in the association of individual social class and neighbourhood unemployment rate with prevalent type 2 diabetes mellitus: a cross-sectional study from the DIAB-CORE consortium. *BMJ Open*. 2013; 3(6): 1-11. doi: 10.1136/bmjopen-2013-002601.
- [29] Roche MM, Wang PP. Factors associated with a diabetes diagnosis and late diabetes diagnosis for males and female. *J Clinical Translational Endocrinol*. 2014; 1(3): 77-84. doi: [10.1016/j.jcte.2014.07.002](https://doi.org/10.1016/j.jcte.2014.07.002).
- [30] Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med*. 2001; 345(11): 790-7.
- [31] Chen L, Pei JH, Kuang J, Chen HM, Chen Z, Li ZW, Yang HZ. Effect of lifestyle intervention in patients with type 2 diabetes: a meta-analysis. *Metabolism*. 2015; 64(2): 338-347. doi: 10.1016/j.metabol.2014.10.018.
- [32] Ali O. Genetics of type 2 diabetes. *World J Diabetes*. 2013; 4(4): 114-23. doi: 10.4239/wjd.v4.i4.114.
- [33] Ahlqvist E, Ahluwalia TS, Groop L. Genetics of Type 2 Diabetes. *Clin Chem*. 2011; 57(2): 241-254. doi: 10.1373/clinchem.2010.157016.
- [34] Saeed AA. Association of tobacco products use and diabetes mellitus-results of a national survey among adults in Saudi Arabia. *Balkan medical J*. 2012; 29: 247-51. doi: 10.5152/balkanmedj.2012.035.
- [35] Sami W, Ansari T, Butt NS, Hamid MRA. Effect of diet on type 2 diabetes mellitus: A review. *Int J Health Sci (Qassim)*. 2017; 11(2): 65-71.
- [36] Panagiotakos DB, Tzima N, Pitsavos C, Chrysohooou C, Papakonstantinou E, Zampelas A, Stefanadis C. The relationship between dietary habits, blood glucose and insulin levels among people without cardiovascular disease and type 2 diabetes; the ATTICA study. *Rev Diabet Stud*. 2005; 2(4): 208-15.
- [37] Villegas R, Shu XO, Gao YT, Yang G, Elasy T, Li H, Zheng W. Vegetable but not fruit consumption reduces the risk of type 2 diabetes in Chinese women. *J Nutr*. 2008; 138(3): 574-80.
- [38] Kelly SJ, Ismail M. Stress and type 2 diabetes: a review of how stress contributes to the development of type 2 diabetes. *Annual review of public health*. 2015; 36: 441-462. doi: 10.1146/annurev-publhealth-031914-122921.
- [39] Nakashima A, Yokoyama K, Yokoo T, Urashima M. Role of vitamin D in diabetes mellitus and chronic kidney disease. *World J Diabetes*. 2016; 7(5): 89-100. doi: 10.4239/wjd.v7.i5.89.
- [40] Dalgard C, Petersen MS, Weihe P, Grandjean P. Vitamin D Status in Relation to Glucose Metabolism and Type 2 Diabetes in Septuagenarians. *Diabetes Care*. 2011; 34(6): 1284-1288. doi: 10.2337/dc10-2084.
- [41] Tusso P. Prediabetes and Lifestyle Modification: Time to Prevent a Preventable Disease. *Perm J*. 2014; 18(3): 88-93. doi: 10.7812/TPP/14-002.
- [42] Bhowmik B, Siddiquee T, Mujumder A, Afsana F, Ahmed T, Mdala IA, Moreira NCV, Khan AKA, Hussain A, Holmboe-Ottesen G, Omsland TK. Serum Lipid Profile and Its Association with Diabetes and Prediabetes in a Rural Bangladeshi Population. *Int J Environ Res Public Health*. 2018; 15(9): 1944. doi: 10.3390/ijerph15091944
- [43] Uppal V, Vij C, Bedi GK, Vij A, Banerjee BD. Thyroid Disorders in Patients of Type 2 Diabetes Mellitus. *Indian J Clin Biochem*. 2013; 28(4): 336-341. doi: 10.1007/s12291-012-0293-9.
- [44] Howangyin KY, Silvestre JS. Molecular Mechanisms of Vascular Repair Dysfunction Diabetes Mellitus and Ischemic Diseases. *Arteriosclerosis, Thrombosis, and Vascular Biol*. 2014; 34: 1126-1135. doi: 10.1161/ATVBAHA.114.303090.
- [45] Diaz-Redondo A, Giráldez-García C, Carrillo L, Serrano R, García-Soidán FJ, Artola S, Franch J, Díez J, Ezkurra P, Millaruelo JM, Seguí M, Sangrós J, Martínez-Candela J, Muñoz P, Goday A, Regidor E. Modifiable risk factors associated with prediabetes in men and women: a cross-sectional analysis of the cohort study in primary health care on the evolution of patients with prediabetes (PREDAPS-Study). *BMC Fam Pract*. 2015; 16: 5. doi: 10.1186/s12875-014-0216-3.
- [46] McGavock J, Dart A, Wicklow B. Lifestyle Therapy for the Treatment of Youth with Type 2 Diabetes. *Curr Diab Rep*. 2015; 15: 568. doi: 10.1007/s11892-014-0568-z.

Appendix 1. Diabetes-2 Risk Factors Questionnaire

Sociodemographic Characteristics			
Name			
Age			
Gender	Male	Female	
Marital Status	Single	Married	
Educational attainment	Uneducated	12th or less	Graduation or more
Income management	Impossible/difficult all the time Not too bad/easy Good		
When you were first diagnosed with diabetes?	Year:	Age:	
Blood Glucose level	Fed	Fasted	
Medication taken for Diabetes			
Biomedical Factors			
BMI	Underweight Obese	Healthy weight	Overweight
Gestational Diabetes	Yes	No	
Family History	Yes	No	
Hypertension Diagnosis	Yes	No	
High blood triglyceride (fat) levels	Normal	High	
Life Style Factor			
Physical inactivity	High Average None/Low		
Smoking	Regular	Occasional	None
Alcohol consumption	Regular	Occasional	None
Dietary Factor			
Fruits/Vegetables	High	Average	Low
Fat	High	Average	Low
fiber	High	Average	Low
Red Meat	High	Average	Low
Sweets	High	Average	Low
Soft Drinks	High	Average	Low
Disease and medication related factors			
Other medications	Antipsychotics HIV	Glucorticoids Others:	
Hormonal Disbalance	Cushing's syndrome	acromegaly	Other:
sleep problems	Yes	Sometime	No
a history of heart disease or stroke	Yes	No	
Polycystic ovarian syndrome	Yes	No	
Brain Disorder	Yes If yes Specify:	No	
Liver Diseases	Yes If yes Specify:	No	
Thyroid Disease	Yes If yes specify type:	No	
Vitamin D Deficiency	Yes	No	
Other Disease	Yes If yes specify type:	No	
Stress Related Factor			

Positive stress	No stress Minimal Stress High/Moderate Stress
Negative Stress	No stress Minimal Stress High/Moderate Stress
Other Personal stress	No stress Minimal Stress High/Moderate Stress

Appendix-2. Prediabetic Follow up Questionnaire

Personal Details			
Name		
Age		
Gender	Male	Female	
weight		
Height		
Marital Status	Single	Married	
Educational attainment	Uneducated 12th or less Graduation or more		
Do you usually do some physical activity for at least 30 minutes each day?	Yes	No	
Income management	Impossible/difficult all the time Not too bad/easy Good		
How often do you eat vegetables or fruits?	Every day Not every day		
Blood Glucose level before follow up	Fed	Fasted	
Do you have any chronic diseases?	Yes	No	
Does anyone in your family have diabetes	Yes	No	
if you answer yes , who is he?		
Blood Glucose level after follow up	Fed	Fasted	
Change in life style			
Exercise	Yes	Sometime	No
Adequate Sleep	Yes	Sometime	No
Stress	Yes	Sometime	No
Dietary Factor			
Follow the diet prescribed	Yes	Sometime	No
Fruits/Vegetables	High	Average	Low
fiber	High	Average	Low
Water	High	Average	Low