Original Article

From Iceberg of Pre-diabetes to Poor Glycemic Control in Diabetics: An Elderly Based Study in Shiraz, South of Iran

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Abstract

Background: Delay in diagnosis of diabetes mellitus (DM) in older adults is more catastrophic than other age groups. This study investigated the prevalence of pre-diabetes, DM, and glycemic control in the elderly. **Methods:** In this cross-sectional study, a sample of 412 older adults >60 years from Shiraz, Iran, were recruited through a multistage cluster random sampling. Demographic, clinical, and laboratory information were collected by interview, physical examination, and reviewing the medical records. Data were analyzed using SPSS 20. **Results:** Mean age was 68.1 ± 6.2 years and female-to-male ratio was 1.1. Out of all, 137 (33.2%) were diagnosed as diabetic including 128 (31%) as known cases and 9 (2.2%) as new cases of DM, whereas 275 (66.7%) were diagnosed as new cases of pre-diabetes. Multivariable analysis showed that low level of education (OR = 5.2, 95% CI: 1.5–16.6), hyperlipidemia (OR = 3.5, 95% CI: 2.1–5.8), liver disease (OR = 3.1, 95% CI: 1.4–6.9), and hypertension (HTN) (OR = 1.9, 95% CI: 1.1-3.2) were the most common predictors of DM in the elderly, respectively. Out of all diabetics, 33.6% had FBS >130 mg/dL and 25.5% had HbA1c >8%, whereas these figures were ≥100 mg/dL and ≥5.7% in 36.7% and 21.4% of pre-diabetics, respectively. **Conclusions:** The pre-diabetic elderly were mostly undiagnosed, while one-third to one-fourth of DMs had poor glycemic indices. These figures show the need for pre-diabetes and diabetes screening in the elderly, especially in those with low level of education, hyperlipidemia, liver disease, or HTN. Furthermore, regular monitoring of glycemic indices in the diabetic and pre-diabetic elderly is recommended.

Keywords: *Diabetes mellitus, diabetic, elderly, glycemic index, pre-diabetes*

Introduction

Diabetes mellitus (DM), as a chronic disease, is associated with micro- and macro-vascular complications and long-term damage or dysfunction of various organs such as eyes, kidneys, nerves, heart and blood vessels, and frailty.[1-3] The burden of DM is high and rising in many countries. It was reported that 382 million people lived with DM in 2014 and this figure is expected to rise to 592 million by 2035.[4] World Health Organization (WHO) estimates that DM will be the seventh leading cause of death in 2030, while this disease has been rising more rapidly in the middle and low-income countries.[5] According to the reports of Statistical Center of Iran, three million individuals with DM are currently living in Iran.[6] On the other hand, the population of older adults continues to increase and the elderly with DM are also expected to grow substantially.[7] The prevalence of DM is more than two times higher among elderly adults than middle age or young adults.[8] One-third to half of the elderly population have DM and three quarters of this group have pre-diabetes or DM, whereas nearly half of DM cases in older adults are undiagnosed.[3,9,10] A variety of factors contribute to the prevalence of DM in the elderly such as age-related changes in carbohydrate metabolism and insulin secretary capacity, reducing insulin activity, more glucose intolerance, and insulin resistance. Improper lifestyle factors leading to high weight, low physical activity, and increased adipose tissue contribute to the development of diabetes in the adults.[9-11] From the point of complications, as compared with the young population, older adults with DM are at greater risk of polypharmacy, cognitive impairment, urinary incontinence, falls and chronic pain, commonly called "geriatric syndrome."[12] Iran, as one the most populous countries in the Middle East, with an estimated population of 80 million,

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is facing population aging, and currently the elderly make about 6% of its population. Therefore, this study aimed to investigate the prevalence and determinants of DM and pre-diabetes as well as glycemic indices in the Elderly of Shiraz, Iran.

Methods

This cross-sectional study was conducted in 2018 in Shiraz, Iran. Shiraz is a metropolitan city in south of Iran with about 2 million population including 1,72,000 >60 years adults. This population is covered by three medical university-affiliated health networks. The sample size according to z^2pq/d^2 formula was 400, considering the prevalence of DM 20% in the elderly,[6,13] error of 5%, confidence level of 95%, design effect of 1.3, and dropout of 25%. We applied a multistage cluster random sampling method. At first, we defined the proportion of elderly population in each of the three health networks of Shiraz. Then, sample size in each of these three networks was defined according to their proportion of the elderly population. In the next step, from the list of included health centers in each of the networks, while considering each health center as a cluster, several clusters were randomly selected. Then, we defined the proportion of the sample in each cluster based on their registered elderlies. After that, we selected elderlies (one person from each family) in each selected health center by systematic randomization. Then, phone numbers of selected persons were extracted from their records. In phone calls, at first, the trained staff introduced themselves and explained the aims of the study and invited them to come to the medical university-affiliated public clinic, if satisfied. They were also given the phone numbers of executive team for any questions about this study. The volunteer participants also were taught to be fast; no caloric intake for at least 8 h from the night before coming to the clinic.[14] In the clinic, the aims of the study were explained again. Then, a written consent form was signed, and thereafter, the participants were referred to the medical laboratory of the clinic. In the laboratory, three milliliter whole blood was taken from each subject for measuring fasting blood sugar (FBS) and glycosylated hemoglobin (HbA1c). In the next step, a glucose load containing an equivalent of 75 g anhydrous glucose dissolved in water was given to each participant for checking 2 h oral glucose tolerance test (OGTT). After collecting the laboratory samples, the data on demographic characteristics and medical history were collected, which included the following: DM and hypertension (HTN) and related treatments, symptoms of DM such as polyuria, polydipsia, and polyphagia and history of smoking, opioids, and alcohol. Then, a complete physical examination was done by a general practitioner. After 2 h from the first blood sampling and taking glucose syrup, participants were again referred to the laboratory for the second blood sampling in order to measure OGTT. It should be mentioned that, the American Diabetes Association guideline was used as the diagnostic criterion for diagnosis of DM, pre-diabetes, and goal of DM management.[15] Physical activity of the participants was assessed using rapid assessment of physical activity (RAPA) scale for older adults.[9] Validity and reliability of the Persian version of RAPA was approved by Khajavi *et al*.[16] The total score of the first seven items of RAPA is from 1 to 7 points, with the respondent's score categorized into one of five levels of physical activity: 1 = sedentary, 2 = underactive, 3 = regular underactive (light activities), 4 = regular underactive, and 5 = regular active. Responses to the strength training and flexibility items are also scored separately, with strength training = 1, flexibility = 2, or both = 3. Quality of life (QOL) of interviewees was detected by leiden-padua (LEIPAD) questionnaire.[17] Validity and reliability of the Persian version of LEIPAD was approved by Hesamzadeh *et al*.[18] LEIPAD is composed of 49 self-assessment items; 31 items as core components are grouped into 7 subscales: Physical function, self-care, depression and anxiety, cognitive functioning, sexual functioning, and life satisfaction. Score of each of these 31 items ranges from 0 to 3, based on 4 states Likert scale and the total score of core component is in the range of 0 to 93. The remaining 18 items serve as moderators for assessing the influence of social desirability factors and personality characteristics on the individual scores for the 7 core instrument subscales. The total score of this part is between 0 and 18, through 2 states Likert scale for each item. Those who refused to participate in the study and those with Alzheimer disease were excluded from the study. Data were entered into IBM SPSS statistics software package version 20 and the accuracy of data entry was checked by randomly selecting and matching completed questionnaires with the corresponding data in the software. Chi-square, *t*-test, Pearson correlation, and binary logistic regression model were used for data analysis. $P < 0.05$ was considered significant.

Ethics statement

The protocol of this study was approved by the ethics committee of Shiraz University of Medical Science (SUMS) by registration number IR.SUMS.REC.1395.S531 date of approval was 2016. Voluntary participation of selected persons, preserving the confidentiality of information, doing the interview in a private place, interviewee anonymity, no charging for referrals, keeping the right for participants to leave the study at any time they wanted, and referral to specialist in case of the need for more clinical assessment, were among the codes of ethics to which we were committed and were applied in this study.

Results

All the 412 invited, participated in this study. The mean age was 68.1 ± 6.2 years ranging from 60 to 90 and a median of 67 years. Female (216) to male (196) ratio was 1.1, whereas only 130 (31.5%) were educated over 5 years, and 288 (69.9%) were married and lived

with their spouse. Overall, 47 (11.4%) were employed at the time of the interview, 299 (72.6%) were under coverage of supplementary insurance and in 80 (19.4%) the monthly income-to-cost ratio was below one. No anyone had history of Alzheimer disease. Of all the elderly, 128 (31%, CI95%: 27%–35%) were known cases of DM, 231 (56%, CI 95%: 51%–61%) were known cases of hypertension, 198 (48%, CI95%: 43%–53%) had hyperlipidemia, and 277 (67%, CI95%: 63%–71%) had a type of chronic pain. More details of the studied variables are shown in Table 1. Among known cases of DM, 111 (86.7%) were on antidiabetic medications, 17 (13.2%) did not receive any treatment and 16 (12.5%) were also under nutritionist supervision. Twenty-five (19.5%) of DMs did not have any symptom, whereas others had at least a type of symptom such as polyuria (43;33.5%), polydipsia (23;17.9%), polyphagia (16;12.5%), or symptoms, such as weight loss, fatigue, numbness of limbs, or a combination of these symptoms (21;16.4%). Moreover, in 6 (4.6%), 62 (48.4%), 33 (25.7%), and 27 (21.0%) of DM cases 1, 1–5, 6–10, and >10 years was passed from their DM detection, whereas mean of FBS, GTT, and HbA1c was 130.7 ± 53.8 mg/dL, 270.9 ± 122.2 mg/dL, and 7.0% ± 1.8%, respectively. Our results showed that 25.5% of 128 known cases of DM patients had HbA1c >8%, whereas 33.6% had FBS >130 mg/dL and 70% had GTT >180 mg/dL at the time of this study [Figure 1]. Out of 412 interviewees, 9 (2.2%, CI95%: 0%–4.6%) were diagnosed as new cases of DM. This group included five men and four women, whereas eight cases had a level of education <12 years and mean of FBS, GTT, and HbA1c was 157.3 ± 85.7 mg/dL, 295.3 ± 108.6 mg/dL, and 7.2% ± 2.3%, respectively. We also found that 275 (66.7%, CI95%: 51.6%–81.8%) of participants were pre-diabetics and mean of FBS, GTT, and HbA1c was 91.7 ± 16.8 mg/dL, 122.6 ± 43.6 mg/dL, and 5.3% ± 0.5%, respectively. It was also shown that 36.7% of pre-diabetics had FBS ≥100 mg/dL, 27.6% had GTT ≥140 mg/dL, and 21.4% had HbA1c ≥5.7% at the time of the study [Figure 2]. Of all 275 pre-diabetics, 95 (34.5%) had no hallmark symptoms related to DM such as polyuria, polydipsia, or polyphagia, whereas 67 (24.3%) had at least polyuria, 29 (10.5%) had at least polydipsia, 20 (7.2%) had at least polyphagia, 3 (1%) had polyuria and polydipsia, and 1 (0.3%) had three symptoms. Others had symptoms such as weight loss, fatigue, numbness of limbs, or a combination of these symptoms.

Results of univariate analysis in Table 2 showed that level of education, proportion of those under coverage of supplementary insurance and QOL were lower, whereas prevalence of HTN, hyperlipidemia, liver disease, and sexual dysfunction were higher in DM cases compared with pre-diabetics ($P < 0.05$). Other studied variables such as age, gender, marital status, job status, income-to-cost ratio, physical activity, daily intake of carbohydrate (CHO), protein or fat, daily calories intake, body mass index (BMI), taking vitamin supplements, using cigarette, alcohol or opioid substances, drinking tea or coffee, history of myocardial or cerebrovascular infarction, thyroid dysfunction, kidney disease, visual impairment, sleep disorder, and chronic

Table 1: Demographic, social, economic, and medical characteristics of studied elderlies (*n*=412)

Variable		Variable		Variable	
Age, *n* (%) (year)		Number of children		Yes	128 (31)
60-69	236 (63.8)	Median (min-max)	5 (0-13)	No	279 (67.7)
70-79	122 (29.6)	Co-living people in one house, *n* (%)		Hypertension, *n* (%)	
≥80	27 (6.6)	Median (Min-Max)	3 (1-12)	Yes	231 (56)
Gender, *n* (%)		Occupation, *n* (%)		No	181 (43.9)
Male	196 (47.6)	Employed	47 (11.4)	Hyperlipidemia, *n* (%)	
Female	216 (52.4)	Jobless	364 (88.3)	Yes	198 (48)
Level of education, *n* (%) (years)		Supplementary insurance, *n* (%)		No	214 (51.9)
Illiterate	108 (26.2)	Yes	299 (72.6)	Chronic pain, *n* (%)	
<5	174 (42.2)	No	113 (27.4)	Yes	277 (67.2)
6-12	93 (22.5)	Being the main decision maker about family finances, *n* (%)		No	135 (32.7)
>12	37 (8.9)	Yes	270 (65.5)	Psychological Disease, *n* (%)	
Marital status, *n* (%)		No	142 (34.5)	Yes	92 (22.3)
Married	288 (69.9)	Income to cost ratio, *n* (%)		No	320 (77.7)
Single	124 (30.1)	≥1	244 (59.2)	Sexual dysfunction, *n* (%)	
Birth place, *n* (%)		<1	80 (19.4)	Yes	61 (14.8)
City	372 (90.3)	BMI (kg/m^2) (mean±SD)	26.1±4.5	No	350 (85)
Village	40 (9.7)	Physical activity (mild to severe), *n* (%)			
Relativity with spouse, *n* (%)		Yes	289 (70.1)		
Yes	169 (41)	No	123 (29.8)		
No	241 (58.5)	History of diabetes mellitus, *n* (%)			

pain did not show any significant difference between DM patients and pre-diabetics [Table 2]. Multivariable analysis showed that low level of education (OR = 5.2, CI95%: 1.5%–16.6), hyperlipidemia (OR = 3.5, CI95%: 2.1–5.8), liver disease (OR = 3.1, CI95%: 1.4–6.9), and HTN (OR = 1.9, CI95%: 1.1–3.2) were more prevalent in DM cases compared with pre-diabetic elderlies. Other studied variables showed no significant association in this regard [Table 3]. Bivariate Pearson correlation showed that in known cases of diabetes, the highest correlation between glycemic indices was between GTT and HbA1c (r = 0.70, P < 0.001) followed by FBS and HbA1c (r = 0.68, P < 0.001) and FBS and GTT (r = 0.64, P < 0.001). However, in pre-diabetics, GTT and HbA1c (r = 0.26, P < 0.001) and FBS and GTT (r = 0.19, P = 0.001) were weakly correlated and FBS and HbA1c (r = 0.08, P = 0.1) were not correlated to each other. Binary logistic regression also showed that among FBS (OR = 1.01, CI 95% = 1–1.03), GTT (OR = 1.01, CI 95% = 1.01–1.02), and HbA1c (OR = 2.3, CI 95% = 1.4–3.7) markers, HbA1c had the strongest association with known cases of DM compared with pre-diabetics.

Discussion

This study revealed that one-third of elderlies had DM, whereas at least one-fourth of known cases of DM had poor glycemic control in spite of their coverage by public health centers. Moreover, more than two-third of this group had HTN and/or hyperlipidemia and about one-fifth had liver disease and/or sexual dysfunction. Level of education was low in DM patients. We also found that pre-diabetes

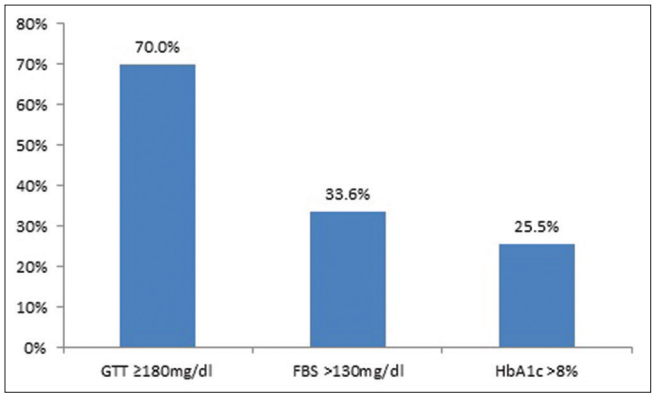

Figure 1: Proportion of elderlies with diabetes mellitus and glycemic indices above the therapeutic thresholds

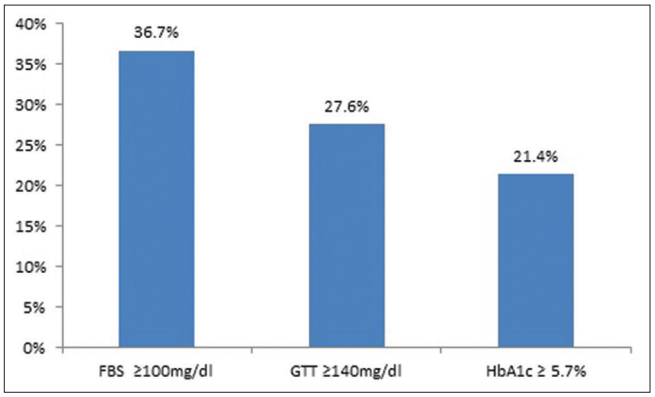

Figure 2: Proportion of elderlies with pre-diabetes and glycemic indices above the therapeutic thresholds

Table 2: Significant associated factors with diabetes mellitus and pre-diabetes in the elderlies based on univariable analysis

Variables	Diabetics *n*=137	Pre-Diabetics *n*=275	Statistic	*P*	OR	95% CI
Hyperlipidemia, *n* (%)						
Yes	96 (70)	102 (37)				
No	41 (30)	173 (63)	χ^2=39.8	<0.001	3.9	2.5-6.1
Education *n* (%) (year)						
≤12	132 (96.4)	243 (88.4)				
>12	5 (3.6)	32 (11.6)	χ^2=7.1	0.008	3.4	1.3-9.1
Liver disease, *n* (%)						
Yes	23 (16.8)	20 (7.2)				
No	114 (83.2)	255 (92.8)	χ^2=8.8	0.003	2.5	1.3-4.8
Hypertension, *n* (%)						
Yes	97 (71)	134 (48.7)				
No	40 (29)	141 (51.3)	χ^2=18	<0.001	2.5	1.6-3.9
Sexual dysfunction, *n* (%)						
Yes	27 (19.7)	34 (12.4)				
No	110 (80.3)	240 (87.6)	χ^2=3.8	0.05	1.7	1.0-3.0
Supplementary insurance, *n* (%)						
Yes	91 (66.4)	208 (75.6)				
No	46 (33.6)	67 (24.4)	χ^2=3.8	0.04	1.5	1.0-2.4
Quality of life (score of 93)	68.1±11.6	71.2±9.8	*t*=2.6	0.01		

OR=Odds ratio; CI=Confidence interval

Table 3: Significant associated factors with diabetes mellitus in the elderlies based on multivariable analysis

Variables	ß	SE	Wald	*P*	EXP (ß)	95% CI
Education	1.3	0.5	5.8	0.007	5.2	1.5-16.6
Hyperlipidemia	1.2	0.2	24	<0.001	3.5	2.1-5.8
Liver disease	1.1	0.3	8.3	0.004	3.1	1.4-6.9
Hypertension	0.6	0.2	6.9	0.008	1.9	1.1-3.2

SE=Standard error, CI=Confidence interval

was common among elderlies and they consisted two-third of older adults in this study, whereas more than one-third of them had high FBS and more than one-fifth had high HbA1c.

Using standard checklists, considering design effect and drop out in calculation of sample size, applying multistage proportional and cluster random sampling, diversity of studied variables and statistical modeling provide the evidence for reliability, external, and internal validity of the findings of this study.

DM as lifestyle-dependent disease is growing and becoming an alarming worldwide public health problem in developed and in developing countries.[19] The results of some studies show that one from two old persons are diabetic or pre-diabetic, whereas other studies concluded that 8 from 10 old persons have some dysglycemia.[10] Wang *et al*. revealed that the prevalence of DM among people aged ≥50 years in China was 16.6% (19.3% for men and 15.3% for women) and the proportion of patients with undiagnosed DM was 32.7%;[20] These results are more or less similar to our results, respectively. A study in Iran concluded that DM type II was found in 22% of elderlies,[6] less than what we found in this study. The results of our study showed that level of education was lower in elderlies with DM; consistent with the findings of other studies.[19,21-23] Another study found that level of education was a significant correlate of DM.[24] We did not find any significant association between DM and age, gender, BMI, diet habit, tobacco or opioid or alcohol consumption, in contrast to other studies.[19,20] This study also concluded that one out of four elderlies with DM and one out of five whom with pre-diabetes had poor glycemic control and only a small group of DM patients were under the supervision of a nutritionist. These findings are in line with other reports that showed the average of HbA1c in DM patients in some Asian countries including China, India, and Vietnam, was about 8.2%.[21,22,25] In Iran, the average of HbA1c in 18- to 75-year-old diabetics was 8.89%.[26] In line with our study, Huisa *et al*. showed that hyperlipidemia was common in diabetic patients.[25] According to one study, nonalcoholic fatty liver disease (NAFLD) is a predictor of diabetes but not for pre-diabetes disease;[26] however, association between DM or pre-diabetes with NAFLD and its severity was proven by Yilmaz and coworkers.[27] Similarly, our results showed an increased prevalence of liver disease in diabetics compared with pre-diabetic patients. Among other findings of this study was higher prevalence of HTN in diabetics compared with pre-diabetics, in line with other studies that indicated HTN is related to a higher prevalence of abnormal glucose regulation (AGR).[28] WHO proposed that people who suffer from HTN need to have a regular evaluation for AGR.[28] Derakhshan *et al*. revealed that HTN is associated with an increased risk of type 2 diabetes;[29] however, another study found no relationship between HTN and diabetes.[23] Several studies concluded that HbA1c is an effective and easy indicator for the diagnosis of diabetes and pre-diabetes.[30-32] In our study, a higher association was found between HbA1c and DM compared with pre-diabetes, so HbA1c also can be relied as a good indicator for differentiation of diabetes from pre-diabetes. This study had some limitations as we could not include elderlies who were admitted in nursing homes. Therefore, we recommend that next studies include these groups as well. Furthermore, by aging the population and growing prevalence of DM[33] or pre-diabetes among elderlies, especially that many years may last to DM appears clinically and its diagnosis become possible[34], active screening for these diseases and proper care for controlling glycemic index are lifesaving.[3] It is also recommended to integrate active screening into routine duties of all primary healthcare centers. However, advocacy by health policy makers and establishment of infrastructures are needed to achieve these goals, as emphasized by another study.[35] In addition, new techniques for diagnosis of DM and monitoring its therapeutic goals, such as salivary factors may enhance options in better management of this disease.[36] In conclusion, pre-diabetic elderlies were mostly undiagnosed, while one-third to one-fourth of DMs had poor glycemic indices. These figures show the need for pre-diabetes and diabetes screening in the elderly, especially in those with low level of education, hyperlipidemia, liver disease, or HTN. Furthermore, regular monitoring of glycemic indices in diabetic and pre-diabetic elderlies is recommended.

Conclusions

Pre-diabetic elderlies were mostly undiagnosed, while one-third to one-fourth of DMs had poor glycemic indices. These figures show the need for pre-diabetes and diabetes screening in the elderly, especially in those with low level of education, hyperlipidemia, liver disease, or HTN. Furthermore, regular monitoring of glycemic indices in diabetic and pre-diabetic elderlies is recommended.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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