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Comparison of "burden of disease" in elderly and non-elderly patients with pre-diabetes: A cross-sectional study

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ABSTRACT

OBJECTIVE: There are a lot of studies comparing elderly and adult patients with diabetes but not pre-diabetes systematically. We aimed to compare the discrepancies of clinical status and burden of disease in elderly (≥60 years old) versus non-elderly (18–59 years old) adult pre-diabetics.

METHODS: A total of 126 pre-diabetic patients were included in the study and were compared as two groups; the elderly (n=32) and non-elderly (n=94). Fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) levels, body mass index (BMI), the homeostasis model assessment of insulin resistance (HOMA-IR), health-related quality of life using the short form-36 (SF-36) questionnaire, and disability using the health assessment questionnaire (HAQ) were evaluated.

RESULTS: Gender, BMI, the presence of obesity, the ratio of HOMA-IR, FPG, and plasma glucose in the 2nd h oral glucose tolerance test were similar in non-elderly patients with pre-diabetes compared to the elderly ones. However, HbA1c levels were higher in elderly subjects in our study. According to the SF-36 questionnaire and HAQ score, there were no significant differences between groups. The median total HAQ scores were 0.125 (non-elderly) and 0.250 (elderly) for groups and there was no significant difference (p=0.099).

CONCLUSION: In the similar gender and BMI groups, pre-diabetes in the elderly gives different outcomes according to HbA1c. Since SF-36 questionnaire and HAQ scores were not statistically different in both pre-diabetic groups, the burden of disease is thought to be basically due to the presence of the disease rather than aging.

Keywords: Burden of disease; disability; elderly; pre-diabetes; quality of life.

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Pre-diabetes contains impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) which consists of serum glucose levels which are higher than normal but below the values of diabetes. According to the American Diabetes Association (ADA), IGT is described as a 2 h plasma glucose range of 140–199 mg/dL and IFG as a fasting plasma glucose (FPG) range of 100–125 mg/dL in the 75 g oral glucose tolerance test (OGTT). Pre-diabetes can also be characterized as glycated hemoglobin (HbA1c) value of 5.7–6.4% [1, 2].

Pre-diabetes is speedily becoming an important worldwide health theme. In adults, the prevalence of pre-diabetes is 38% in the USA [3], 35.7% in China [4], and 30.8% in Turkey [5]. Pre-diabetes is a risk factor for

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many systemic disorders such as neuropathic, renal diseases, and cognitive problems like type 2 diabetes mellitus (T2DM) [6]. As a result of pre-diabetes, complications arising are known to negatively impact a lot of conditions of the patient's life including the health-related quality of life (HRQoL) [7].

The geriatric population is increasing with the aging world. As the reflection of many diseases in the geriatric population is different, our approach to diseases should be different. In elderly population, T2DM is one of the major causes of disease burden [8]. This has been a noteworthy problem since the life expectancy has been increasing recently in diabetic patients [9]. Elderly diabetics have more difficulties in standing to their usual social relationships [10]. HRQoL is usually worse in elderly diabetic patients when compared to younger diabetics [11].

Hyperglycemia is such an important inconvenience that it affects not only the internal organs but also the skin. Diabetes is a disease that causes even skin lesions and affects the entire body [12]. Whereas one of the aims of the treatment of non-elderly diabetics is to prevent the development of microvasculary and macrovasculary complications, one of the significant aims in the treatment of elderly ones is to improve QoL. While there are a lot of studies comparing elderly and adult diabetics but not pre-diabetes systematically [8–11]. It is not known whether adding pre-diabetes to the effects of old age on quality of life and disability will create a synergy. We aimed in this study to present the discrepancies of clinical status and burden of disease in elderly versus non-elderly adult pre-diabetics.

MATERIALS AND METHODS

Participants

People, over the 18 years old, who were admitted to a tertiary hospital's internal medicine outpatient clinic between June 1, 2018, and August 31, 2018, for routine health control and who agreed to participate to the study were recruited. The patient's written informed consent to publish the clinical information and materials was obtained. This study was performed in accordance with the Declaration of Helsinki and Good Clinical Practice. The patient's written informed consent to publish the clinical information and materials was obtained. Erciyes University Clinical Research Ethics Committee approval was received (decision no: 2019/141).

Patients with newly diagnosed pre-diabetes according to ADA were recruited to the study, consecutively [2]. A total of 126 pre-diabetic patients were enrolled and compared between two groups; the elderly (18–59 years old) and non-elderly (≥60 years old).

Highlight key points

- HbA1c levels were statistically significantly higher in the elderly pre-diabetics.
- Health-related quality of life was similar between the elderly and non-elderly age groups.
- Disability index was slightly higher in elderly pre-diabetics than non-elderly ones.

Interventions

Participants' age and gender were recorded. The number of comorbid conditions (hypertension, muscle-joint-bone disease, gastrointestinal diseases, heart disease, hyperlipidemia, respiratory system diseases, depression/anxiety disorders, and other rare chronic diseases), drugs taken daily (suitable for comorbidity) and operations were also recorded. Their height and weight were measured. Body mass index (BMI) was calculated and then categorized as normal (BMI <30 kg/m^2) and obese (BMI: 30 kg/m^2 and above) [13].

Plasma glucose values at the 0th and 2nd h were conducted by OGTT, and HbA1c levels were measured for all participants. Pre-diabetes was defined as 0 h plasma glucose value (OGTT – 0th) of 100–125 mg/dL (IFG) and/or 2 h plasma glucose value (OGTT – 2nd) of 140–199 mg/dL (IGT). HbA1c value of 5.7–6.4% was also considered to be pre-diabetes [2]. A fasting venous blood sample (FBS) was collected after an overnight fast of at least 12 h for biochemical investigations and samples were processed at the hospital laboratory on the same day. Glucose levels were estimated using a Roche Cobas 8000 immunoassay analyzer (Roche Diagnostics, USA). The level of HbA1c was estimated using a Adams A1c HA-8180V automatic analyzer (Arkray Diagnostics, USA). All assays were performed with kits and calibrators supplied by the manufacturers.

Insulin Resistance (IR)

Twelve hours FBSs were obtained for fasting plasma insulin (FPI) and FPG determinations to calculate the homeostasis model assessment of IR (HOMA-IR). It was calculated by the formula [14]:

HOMA-IR=FPI (mU/L)×FPG (mmol/L)/22.5. If the result is ≥2.5, it means that there is an IR. The higher the score, the greater the IR is measured.

HRQoL using the Short Form-36 (SF-36) Questionnaire

We used SF-36 that is a valid and reliable questionnaire to assess both physical and mental components of HRQoL [15, 16]. SF-36 contains 36 items associated to eight dimensions: Physical functioning for the limitation in performing all physical activities, role physical for problems with work or other daily activities, bodily pain, general health, vitality, social functioning, role emotional, and mental health [15]. SF-36 is also a valid and reliable questionnaire in Turkish people [17].

Disability using the Health Assessment Questionnaire (HAQ)

The another dependent variable in this study was disability. To assess the disability, the Stanford HAQ-20 was used [18]. Qualification of HAQ was also proven [19, 20]. HAQ is a reliable, valid, sensitive questionnaire in both general and patient populations [21]. The HAQ assesses disability in eight fields (dressing and grooming, rising, reach, hygiene, eating, walking, grip, and activity). In each section, there are two or three questions. Scoring within each question is from 0 (without any difficulty) to 3 (unable to do). For each section, the score given to that section is the worst score within the section, that is, if one question is scored 1 and another 2, then the score for the section is [3]. Furthermore, if an aid or device is used or if help is required from another individual, then the minimum score for that section is 2. The mean score of the eight sections is disability index (DI), ranges from 0.00 to 3.00, that the higher the score, the greater the disability is determined. In this study, patients with a DI lower than 0.50 were considered not disabled, a DI from 0.50 to 1.00 was considered as mild disability while a DI of 1.00 or higher was regarded as severe disability [22]. HAQ-DI is also a valid and reliable questionnaire in Turkish people [23].

SF-36 and HAQ questionnaire were fulfilled by assistance of a rheumatologist (KE) who was blinded the patients' clinical data, as required.

Statistical Analysis

A power analysis program was used to calculate the post hoc power analysis. It was done considering HAQ as a primary outcome measure. It was determined that the study was designed to have 78% power to detect in HAQ scoring between both groups. Statistical analyses were performed using the SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). Parametric variables were presented as means and standard deviations, non-parametric variables were presented as medians and interquartile ranges (25^{th}–75^{th} percentiles). Shapiro–Wilk test and histograms analyses were used to determine whether continuous variables were normally distributed. Two independent groups of parametric variables were compared using Student's t-test. For non-parametric variables, Mann–Whitney U-test was administered. Number of cases and percentages were used for categorical variables. Categorical data were analyzed by Chi-square or Fisher's exact test, where appropriate. $P<0.05$ was considered to indicate statistically significant differences.

RESULTS

Newly diagnosed 126 pre-diabetics, admitted our internal medicine outpatient clinic, were recruited consecutively. Thirty-two of them (25%) were the elderly and the others (75%) were non-elderly. Gender, height, weight, BMI, the presence of obesity, the ratio of HOMA-IR, fasting glucose level (0-h OGTT), and glucose level in 2 h OGTT were similar in elderly patients with pre-diabetes compared to non-elderly ones. However, HbA1c levels were higher in elderly subjects. Whereas the number of comorbid conditions and drugs taken daily of patients were higher in the elderly group, the number of operations was similar in both groups. Comparison of clinical data of elderly and non-elderly patients is mentioned in Table 1.

All dimensions and total scores of SF-36 were similar between elderly and non-elderly patients. HAQ-DI scores were a little higher in elderly patients than non-elderly ones but this difference was not statistically significant. All of the SF-36 and HAQ-DI scores are mentioned in Table 2.

DISCUSSION

In this study, pre-diabetics under age 60 and elderly ones were compared. To the best of our knowledge, HRQoL and DI in elderly and non-elderly pre-diabetics were conducted and compared first in the literature. Pre-diabetes associated laboratory findings were similar between groups. The number of comorbid conditions and drugs were statistically significantly higher in the elderly. Comparable QoL levels were found. DI scores were worse in the elderly group than non-elderly group, but not statistically significant.

TABLE 1. Comparison of elderly and non-elderly pre-diabetic patients' clinical data*

	Non-elderly (n=94)	Elderly (n=32)	p
Gender, female/male (%)	71/23 (75.6/24.4)	22/10 (68.8/31.2)	0.489
Age, years, median (per 25–75)	48 (42–52)	65 (62–69)	**<0.001**
Weight (kg), mean±SD	88.28±18.93	87.39±13.75	0.808
Height (m), mean±SD	1.62±0.80	1.60±0.07	0.206
BMI (kg/m^2), mean ± SD	34.02±7.94	34.54±6.19	0.738
Glucose in 0 h OGTT (mg/dL), mean±SD	104.19±8.41	104.09±9.16	0.956
Glucose in 2 h OGTT (mg/dL), mean±SD	130.50±32.48	133.36±33.70	0.669
HbA1c, mean±SD	5.87±0.34	6.05±0.27	**0.006**
Obesity (obese/non-obese), (%)	64/30 (68.1/31.9)	26/6 (81.3/18.7)	0.180
HOMA-IR, median (per 25–75)	2.59 (1.65–3.94)	2.39 (1.51–4.52)	0.340
The number of comorbid conditions (per 25–75)	0 (0–1)	2 (1–3)	**<0.001**
The number of drugs taken daily (per 25–75)	0 (0–1)	2.5 (1.25–4.75)	**<0.001**
The number of operations (per 25–75)	1 (0–2)	1 (1–3)	0.051

BMI: Body mass index; OGTT: Oral glucose tolerance test; HbA1c: Glycated hemoglobin; HOMA-IR: The homeostasis model assessment of insulin resistance; SD: Standard deviation; *: Data are presented as a mean±SD of the mean, a median with (per 25–75), or number (percentage), where appropriate (p<0.05 considered statistically significant).

TABLE 2. Medians of the scales in the SF-36 and HAQ in pre-diabetics*

SF-36 dimensions	Non-elderly (n=94)	Elderly (n=32)	p
Physical functioning	80 (51.25–100)	72.5 (45–90)	0.136
Role physical	12.5 (0–100)	0 (0–100)	0.472
Bodily pain	57.5 (45–77.5)	55 (27.25–77.5)	0.363
Social functioning	62.5 (50–87.5)	62.5 (40.63–85)	0.678
Mental health	60 (44–72)	64 (52–71)	0.645
Role emotional	33.3 (0–100)	33.33 (0–100)	0.775
Vitality	60 (45–75)	60 (46.25–80)	0.999
General health	55 (30–80)	55 (40–75)	0.952
SF-36/PCS	57.19 (35–84.84)	52.19 (30.16–79.84)	0.350
SF-36/MCS	55.02 (36.81–79.81)	63.96 (35.66–76.49)	0.864
SF-36/TS	52.81 (37.51–81.11)	59 (32.50–79.19)	0.594
HAQ	0.125 (0–0.375)	0.250 (0–0.813)	0.099

SF-36: Short form-36; SF-36/PCS: Short form-36 physical component score; SF-36/MCS: Short form-36 mental component score; SF-36/TS: Short form-36 total score; HAQ: Health assessment questionnaire; *: Data are presented as a median (per 25–75); SF-36 dimension scores range from 0 to 100, where a higher score reflects better functioning. P<0.05 considered statistically significant.

There is no consensus on the change of BMI with age in pre-diabetic patients. While the studies by Rabijewski et al. [24]. (with 196 participants) and Wu et al. [25] (with 1347 participants) showed that BMI values increased with the age, there were no significant differences between elderly and non-elderly patients in studies of Yan et al. [26] (with 2735 participants) and Chen et al. [27] (with 1374 participants). Elderly and non-elderly pre-diabetic patients had similar BMI in our study, too.

In many studies, glucose in FP (0 h OGTT) and 2nd h OGTT were statistically significantly higher in elderly pre-diabetic patients than young and middle-aged groups [24–26, 28]. In our study, FPG was similar between two age groups. However, glucose in 2 h OGTT was higher in elderly pre-diabetics, but not statistically significant. In the process leading to diabetes, while the 1st time postprandial blood glucose (or 2 h OGTT) increases, we think that this will be more obvious with advancing age. Rabijewski et al. [28] argued that older patients with pre-diabetics had a worst quality of life than middle-aged ones, with a small degree of imbalance in glucose. Considering this direction for our study, it may be said that the similarity between the groups in terms of quality of life may relate to similar plasma glucose levels.

Whereas glucose levels of groups were similar, HbA1c levels were statistically significantly higher in the elderly. In many studies, it was shown that HbA1c values associated with a limited sensitivity in elderly population. Moreover, HbA1c is not suitable for diagnosing diabetes in this population [29–31]. The National Health and Nutrition Examination Survey data showed that if only HbA1c is used to diagnose DM in the elderly, the frequency of DM may be higher than it is [32]. Pani et al. [33] showed that HbA1c levels are positively associated with age in non-diabetic populations, even after the exclusion of participants with IGT, and suggested that an age-specific diagnostic criterion of HbA1c is needed [26]. High HbA1c values in elderly pre-diabetics that we found in our study suggest that there is a need for age-adjusted HbA1c values in prediabetes diagnosis.

A large observational prospective study using the data of 4566 patients (normal, pre-diabetes, and T2DM) showed that aging is associated with increased HOMA-IR score in elderly Chinese population [34]. In another study with 1374 patients by Chen et al. [27], elderly (≥60 years) pre-diabetic patients had higher HOMA-IR scores than young (<40) pre-diabetic patients. Contrary to the literature, in our study, there were no statistically differences in IR (the ratio of HOMA-IR) between elderly and non-elderly participants. The fact that FPG, glucose in 2 h OGTT and BMI values were not statistically different between groups may have caused this situation.

The gender, BMI, and laboratory results of the two groups were also comparable. The outcome of this clinical result provided us with the opportunity to compare the HRQoL and DI on similar terms between the groups. In many studies, it is reported that poorer QoL in diabetic patients; however, data regarding QoL in pre-diabetics are scarce. In a study of 176 pre-diabetic patients by Rabijewski et al., mental health, vitality, and general health were significantly lower in pre-diabetics than the control group. Rabijewski et al. made up their study exclusively from men and studied them in two groups, middle-aged men (40–60 years) and the elderly (60–80 years). The mean scores for mental health, vitality, general health, and physical functioning were significantly higher in case of middle-aged pre-diabetic men. Whereas the middle-aged group presented with higher SF-36 physical component scores, the SF-36 mental component scores were not different [28]. Our study was a more comprehensive study involving both genders and all ages (18–80 years). No significant difference was found between elderly and non-elderly patients according to the SF-36 questionnaire results. We would like to reemphasize that these outcomes were obtained in similar groups, especially in terms of gender, height, weight, BMI, the presence of obesity, the ratio of HOMA-IR, FPG, and glucose level in 2 h OGTT. These findings show that the decrease in quality of life is mainly related to pre-diabetes rather than old age in pre-diabetic patients. It is known that the quality of life decreases with increasing age [35–37]. Although the number of comorbid conditions, drugs, and operations were higher in the elderly, SF-36 components were found similar in our study. Therefore, pre-diabetics seem to affect the quality of life more than factors such as age and comorbidity.

There are a few studies on health assessment in elderly diabetics. In a controlled survey, study of 116 diabetic participants who are African-Americans aged 70 years and over, the elderly had worse DI scores (using the HAQ) than the control group. They reported that disability is related with lesser additive from the number of drugs, medical problems, and hyperglycemia due to multivariable analyses [38]. There are several studies evaluating elderly patients with diabetic foot ulcers and a lower HAQ score than those without diabetic foot ulcers [35–39]. In our study, HAQ scores were higher in elderly pre-diabetics, but not statistically significant. The number of comorbid conditions and drugs taken daily, which were higher in the elderly, can have an effect on the HAQ scores. Differences could have become significant if our study had been conducted with more participants.

There are some limitations of our study: First, conditions related to the occupational and social life of the patients may affect the scales. Second, since it is the first study in the literature, the number of participants is limited. This may have affected the results. However, this may become a reference article for larger future studies.

Conclusion

Except HbA1c, diabetes-related laboratory parameters were similar between elderly and non-elderly pre-diabetics. HRQoL was similar between two age groups, and DI was slightly higher in elderly pre-diabetics than non-elderly ones but not statistically significant. In pre-diabetic patients, the burden of disease is thought to be basically due to the presence of the pre-diabetes rather than aging. This study, which we first gained to raise awareness in the literature of pre-diabetics, should be elaborated with further studies.

Ethics Committee Approval: The Erciyes University Clinical Research Ethics Committee granted approval for this study (date: 20.02.2019, number: 2019/141).

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