International Journal of Gerontology 11 (2017) 90–94

Contents lists available at ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Original Article

Prevalence of Prediabetes and Associated Factors in the Oldest Old. A Cross Sectional Study in the Octabaix Cohort☆

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ARTICLE INFO

Article history:
Received 1 September 2015
Received in revised form
22 March 2016
Accepted 27 May 2016
Available online 7 April 2017

Keywords:
aged 80 and over,
diabetes mellitus,
geriatric assessment,
prediabetic state,
risk factors

SUMMARY

Background: The leading high-risk state for diabetes mellitus (DM) – prediabetes – is increasing; however, a lack of information exists in oldest old subjects. The objective of this study is to describe the rate of prediabetes and the associated factors among community-dwelling 85-year-olds.

Methods: A cross-sectional survey including data from 321 subjects on cardiovascular risk factors, functional status, comorbidities and laboratory tests was conducted. Participants were divided in three groups: normoglycemic (fasting plasma glucose (FPG) < 5.6 mmol/L), prediabetes (FPG 5.6–6.9 mmol/L) and DM (FPG ≥ 7 mmol/L, or DM diagnostic, or antidiabetics use). Comparative analysis was performed between the 3 groups.

Results: One hundred seventy-nine (55.8%) participants were classified as normoglycemic, 86 (26.8%) as DM and 56 (17.4%) as prediabetic. Multinomial logistic regression model found no association of explanatory variables with normoglycemia in front of prediabetes, while there was significant association with DM (rather than prediabetes) and Angiotensin converting enzyme (ACE) treatment (OR: 7.04 95% CI 2.52–19.61), diuretics (OR: 2.46, 95% CI 1.04–5.78) and Charlson Index (OR: 2.67, 95% CI 1.77 –4.02), with higher odds of being in DM than in prediabetic group.

Conclusion: Prevalence of prediabetes is high among the 85-year-old population studied. The comparison between prediabetic and DM groups revealed that the major clinical differences were the higher Charlson comorbidity Index scores, diuretics and ACE drugs in the DM group.

1. Introduction

Diabetes mellitus (DM) represents one of the most serious challenges for health care systems worldwide. Approximately one-third of the elderly have DM, more than 60% of those patients with DM die due to vascular disease complications and an even greater percentage of the very old population develop other geriatric syndromes related to DM[1,2]. In the elderly, DM is clinically heterogeneous and its leading high-risk state, prediabetes—intermediate state of hyperglycemia—, is increasing. Currently, 50% of US adults older than 65 years have prediabetes and around 5–10% of them become diabetic every year[3,4]. Clinical improvements, lifestyle modifications, and pharmacotherapy interventions in prediabetic individuals have shown benefits for conversion back to normoglycemia and to diminish the incidence of diabetes. This is particularly significant in the older population[5]. In accordance, the European Diabetes Working Party for Older People

☆ Conflicts of interest: All contributing authors declare that they have no conflicts of interest.

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http://dx.doi.org/10.1016/j.ijge.2016.05.006

and the International Task Force of Experts in Diabetes[6,7] have led a major international movement toward large scale diabetes prevention efforts and for targeting those aged patients with diabetes.

The aim of this study was to evaluate the prediabetic status and its associated factors in a community-dwelling of 85-year-old subjects (Octabaix study).

2. Materials and methods

2.1. Study subjects

The Octabaix study is a prospective population-based investigation of 328 subjects, born in 1924 (aged 85 at the time of enrollment in 2009) described in detail elsewhere[8]. All participants were registered in one of the seven primary healthcare centers belonging to the Catalan Institute of Health. All primary care teams were placed in the South Metropolitan Area of Barcelona, Catalonia, Spain, and served a population of approximately 210,000 inhabitants, being the Hospital Universitari de Bellvitge the referral hospital. In brief, of a total of 696 potential participants, 487 were considered eligible to be included in the Octabaix study. Exclusion criteria were to live in a nursing home or the impossibility to contact at the time of enrollment. Compromised health status was not considered among the exclusion criteria. The study was approved by the institutional ethics committee of the Jordi Gol Institute for Primary Care Research. All patients or caregivers of those cognitively impaired subjects gave their written informed consent prior to the study enrollment.

All data were collected by personal interview and on the basis of a review of electronic medical data. A total of 321 participants (67.5%) were finally included in the present study. All participants were examined—in their place of residence or in the primary healthcare center—by a physician-nurse primary care team with long and trained experience attending elderly people.

2.2. Measures

Collected variables included: social and demographic information, geriatric assessment, hypertension, diabetes, dyslipidemia, other chronic conditions, laboratory and drug prescription data.

2.3. Geriatric assessment

Functional status measured using Barthel Index (BI)[9] for basic activities of daily living (ADL) and Lawton Index (LI)[10] for instrumental activities of daily living (IADL). Cognitive status was evaluated with the adapted and validated Spanish version of Minimental State Examination (MEC)[11]. Nutritional status was assessed using Mini Nutritional Assessment (MNA)[12]. Quality of life (QoL) was assessed using EuroQol 5-Dimension 3L[13] with the visual analog scale of perceived health (EQ-EVA).

2.4. Clinical data

Comorbidity was measured with Charlson comorbidity Index[14] and information regarding written diagnosis of the most common chronic conditions as stroke, heart failure, vasculopathy, ischemic cardiopathy and renal failure[15] was also recorded.

2.5. Laboratory data

It included total leukocytes (WBC), hemoglobin, platelets, fasting plasma glucose (FPG), creatinine, estimated glomerular filtration rate (eGFR) using the Modification Diet in Renal Disease formula MDRD-4, total cholesterol, high (HDL-C) and low (LDL-C) density lipoprotein cholesterol.

2.6. Procedure

For the present study, we analyzed participants who at baseline had undergone a blood test to assess FPG. Participants were defined as having DM according to self-report, clinical reports, use of antidiabetic agents and FPG ($\geq$7 mmol/L). Hemoglobin A1c (HbA1c) was not included as a criteria because the Octabaix study was planned and the data compiled in 2009, and it was not until 2010 when the American Diabetes Association clearly recommended the HbA1c in DM definition[16]. Non DM participants were divided into normoglycemic or prediabetic group as follows: FPG < 5.6 mmol/L, (normoglycemic) or FPG 5.6–6.9 mmol/L (prediabetes).

2.7. Statistical analyses

Descriptive categorical variables were given as absolute and relative frequencies [n (%)]. Continuous variables were presented in terms of means and Standard Deviations (SD) or median and interquartile range (IQR) depending on normality of variables (tested with the Kolmogorov–Smirnov test). In the bivariate analysis, Fisher's exact test was used for the comparison of categorical variables while parametric Student's T test, or the non-parametric Kruskal–Wallis or Mann–Whitney U test were applied to compare continuous variables. In order to evaluate the adjusted association of aforementioned factors on being normoglycemic or diabetic in relation to the prediabetes group, a multinomial logistic regression model was fit, in which the categorical dependent variable was “normoglycemia”, “prediabetes” or “DM” (with “prediabetes” as the reference category), and significant variables in bivariate analyses were included as explanatory variables. Despite of the ordinal nature of the dependent variable, ordered logistic regression was not adjusted because the aim of the study was not the association of factors with a latent degree of diabetes but the differential profile of prediabetes in front of normoglicemia and diabetes. As all the participants were the same age, adjusting for age was not applied.

The adjusted odds ratio (OR) with a 95% confidence interval (CI) was calculated and results were considered significant when $p < 0.05$. All statistical analyses were performed by using R 2.14.2 software.

3. Results

Of the 321 inhabitants analyzed, 197 were women (61.4%). Comorbidity measured by Charlson Index revealed a mean of 1.5 (±1.6 SD). Hypertension had been previously diagnosed in 245 (76.3%) participants, dyslipidemia in 163 (50.8%), stroke in 49 (15.3%), heart failure in 42 (13.1%), chronic kidney disease in 23 (7.2%) and ischemic cardiopathy in 20 (6.2%). Regarding geriatric assessment, the mean for BI was 87.6 (±19.3 SD) and 5.4 (±2.6 SD) for LI. When evaluating cognitive status, the mean MEC score was 26.7 (±6.9 SD) and when assessing nutritional status, the median MNA score was 25.0 [IQR 22.5–27.5]. The mean EQ-5D EVA was 62.4 (±21.3 SD). In detail, 113 (35.2%) subjects were on hypolipemic therapy, 184 (57.3%) were using angiotensin converting enzyme (ACE) drugs (which included 122 (38.0%) ACE inhibitors and 62 (19.3%) angiotensin receptor blockers), 41 (12.8%) b-blockers and 142 (44.2%) were on diuretic treatment, with a median of 6 [IQR 4–8] chronically prescribed drugs. Blood measurements revealed the following values: WBC 6.6 $\times$ 10^3 cells/μL [IQR 5.4–7.8], hemoglobin 13.3 g/dL [IQR 12.2–14.3], creatinine 89.8 μmol/L (±30.2 SD), total cholesterol

levels 5.04 mmol/L [IQR 4.38–5.54], HDL-C 1.46 mmol/L (±0.40 SD) and LDL-C 2.93 mmol/L [IQR 2.40–3.50].

Of the overall 321 participants, prediabetes was present in 56(17.4%), 86(26.8%) were classified as DM and 179 (55.8%) as normoglycemic. Table 1 shows the general geriatrics and clinical characteristics of the three groups according to the predefined glycemic status. Table 2 shows laboratory data according to the same groups. When comparing prediabetic with normoglycemic and DM population, prediabetic subjects were more likely to have hypertension than normoglycemic but less than DM subjects, as well as a higher total WBC, lower HDL-C and to be on treatment with ACE drugs. In addition, prediabetic patients compared with DM ones had higher levels of total cholesterol and LDL-C.

In Table 3, logistic regression analysis showed no significant association of any of the covariables with normoglycemic subjects in front of the prediabetic reference group, whereas the odds of being in the diabetic group gets multiplied by 2.67 for each unitary increase in Charlson comorbidity Index ($p < .001$, OR: 2.67, 95% CI 1.77–4.02). Also, individuals on treatment with ACE ($p < .001$, OR: 7.04, 95% CI 2.52–19.61) and diuretic drugs ($p = 0.039$, OR: 2.46, 95% CI 1.04–5.78) had higher odds of being in the DM group than in the prediabetic. Contrary, subjects with renal failure ($p < .001$, OR: 0.03, 95% CI 0.00–0.24) had lower odds of being in the DM group than in the prediabetic.

4. Discussion

Results of our study documented a relative high prevalence of prediabetes (17%) among octogenarian population, similarly to that found in other previous studies made in aging population such as the 15–30% found by the DECODE Study Group in subjects over 60 years[17]. However, our prevalence was lower than that reported for the general population in Denmark (37.6%)[18], United States (28.2%)[3], China (27.2%)[19] and also in the over-65-year-old group of the NHNES (50%)[5]. In addition to the influence of aging, there are other possible reasons for explaining these differences such as the diverse diagnostic criteria applied, which varies depending on the clinical practice at physician, institution or country level[20]. The higher prevalence of prediabetes in some studies may be because FPG and HbA1c tests were routinely applied since 2010 according to the ADA recommendations, in opposition to the 1999 WHO criteria used by the DECODE Study Group[17]. Therefore, these results highlight the importance of the diagnostic tool used to identify individuals at risk[20].

The analyses of geriatric characteristics of the prediabetic group included in the Octabaix study were similar to other described populations[21]. Although there was a tendency (not statistically significant) to detect more difficulties in ADL, worse impaired cognition and higher presence of health related complications in the DM group when compared with the prediabetic group, the geriatric assessment didn't seem to have any clinical role favoring the prediabetic state.

Clinical characteristics were also similar to those recently reported in other studies[1,21,22]. Accordingly, in our study an increase in one point in Charlson comorbidity Index multiplies by 2.67 the risk of being in the diabetic group in front of the prediabetic group. The rate of hypertension of our participants was globally higher (prediabetic group 75%, DM group 89%) when compared with other studies which found 58% in 85-years-old individuals[21] and 48% in prediabetic adults >53-years-old[22], suggesting that greater preventing measures should be implemented after detection of a prediabetic state in order to avoid concomitant damages. As shown in the STOP-NIDDM trial[23], there were 5% more occurrence of hypertension and cardiovascular events among the prediabetic patients who developed DM than in the prediabetic that did not progress to DM. Dyslipidemia, which was the most important cardiovascular risk factor in the UKPDS[24], had a higher rate in our prediabetic group than in the DM one. Those findings, although not statistically significant, may be related with the different dyslipidemia diagnostic and treatment criteria recommended for individuals with or without diabetes in the Catalan health system, aiming an LDL-C concentration of ≤2.5 mmol/L for DM patients or ≤3.4 mmol/L for those with prediabetes[25]. The proportion of lipid lowering therapy in the DM group (43%) was higher than in the prediabetic group (35.7%), but lower than the 74% reported in other groups[26]. Therefore, it could be suggested that higher target assessment needs to be implemented at 85-years-old population in order to reach primary prevention and therapeutic goals. Furthermore, other analytical findings in our study were the low HDL-C and elevated WBC among participants with DM. If these

Table 1
Geriatric assessment and clinical characteristics according to glycemic status in 85-year-olds patients. (n = 321).

Characteristics	Normoglycemia n = 179	Prediabetes n = 56	DM n = 86	Normoglycemia vs Prediabetes	Normoglycemia vs DM	Prediabetes vs DM
Female, n (%)	109 (60.9)	34 (60.7)	54 (62.8)	1.000	0.789	0.860
Living alone, n (%)	53 (29.6)	22 (39.3)	22 (25.6)	0.191	0.561	0.097
Hypertension, n (%)	126 (70.4)	42 (75.0)	77 (89.5)	0.611	*<.001*	*0.034*
Dyslipidemia, n (%)	89 (49.7)	30 (53.6)	44 (51.2)	0.648	0.896	0.864
Coronary artery disease (%)	10 (5.59)	0 (0.0)	10 (11.63)	0.123	0.088	*0.006*
Previous stroke, n (%)	27 (15.1)	7 (12.5)	15 (17.4)	0.828	0.720	0.484
Heart failure, n (%)	23 (12.8)	6 (10.7)	13 (15.1)	0.818	0.702	0.615
Vasculopathy, n (%)	8 (4.5)	2 (3.6)	6 (7.0)	1.000	0.392	0.480
Renal failure, n (%)	16 (8.9)	5 (8.9)	2 (2.3)	1.000	0.065	0.112
Charlson Index, mean (SD)	1.2 (1.5)	0.9 (1.2)	2.3 (1.7)	0.371	*<.001*	*<.001*
Lawton Index, mean (SD)	5.3 (2.6)	6.0 (2.2)	5.1 (2.5)	0.246	0.731	0.113
Barthel Index, mean (SD)	86.7 (21.2)	90.8 (15.7)	87.3 (17.1)	0.343	0.970	0.535
Spanish version of the Mini-Mental State Examination, mean (SD)	26.7 (7.0)	27.8 (6.5)	25.8 (7.0)	0.560	0.563	0.208
Mini Nutritional Assessment, median [IQR]	25.0 [22.5–27.5]	26.2 [24.0–28.1]	25.0 [22.5–27.0]	0.110	0.997	0.154
Euro QoL-5D visual analog scale, mean (SD)	62.3 (20.6)	64.7 (22.2)	60.9 (22.3)	0.741	0.867	0.548
Drugs taken, median [IQR]	6.0 [3.0–8.0]	5.0 [3.0–7.0]	7.5 [6.0–9.0]	0.611	*<.001*	*<.001*
Statins, n (%)	56 (31.3)	20 (35.7)	37 (43.0)	0.624	0.074	0.484
Angiotensine-converting enzyme drugs, n (%)	82 (45.8)	28 (50.0)	74 (86.0)	0.644	*<.001*	*<.001*
Beta-blockers, n (%)	20 (11.2)	5 (8.9)	16 (18.6)	0.805	0.125	0.148
Diuretics, n (%)	71 (39.7)	31 (55.4)	40 (46.5)	*0.045*	0.352	0.391

SD = Standard deviation; IQR = interquartile range.

Table 2
Laboratory data according to glycemic status in 85-year-olds patients. (n = 321).

Characteristics	Normoglycemia n = 179 (55.8%)	Prediabetes n = 56 (17.4%)	DM n = 86 (26.8%)	Normoglycemia vs Prediabetes	Normoglycemia vs DM	Prediabetes vs DM
Total cholesterol (mmol/L), median [IQR]	5.05 [4.42–5.61]	5.28 [4.74–5.97]	4.76 [4.16–5.38]	0.176	0.114	*0.006*
HDL-C (mmol/L), mean (SD)	1.52 (0.43)	1.41 (0.32)	1.38 (0.35)	0.150	*0.015*	0.897
LDL-C (mmol/L), median [IQR]	2.86 [2.43–3.52]	3.27 [2.78–3.76]	2.78 [2.15–3.31]	0.064	0.073	*<.001*
Serum creatinin (μmol/L), mean (SD)	91.6 (33.9)	84.7 (26.2)	89.5 (23.6)	0.304	0.862	0.628
eGFR < 60, (mL/min per 1.73 m^2), n (%)	76 (42.5)	17 (30.4)	38 (44.2)	0.119	0.793	0.114
White-cell count (1000/μL), median [IQR]	6.4 [5.3–7.3]	6.7 [5.2–8.4]	7.3 [56.0–8.5]	0.105	*<.001*	0.407
Hemoglobine (g/dL), median [IQR]	13.3 [12.1–14.3]	13.8 [12.4–14.4]	13.1 [12.3–14.2]	0.271	0.705	0.117

SD = Standard deviation; IQR = interquartile range.

Table 3
Multinomial logistic regression results according to glycemic status. Association with clinical characteristics among prediabetic 85-year-olds patients.

	Normoglycemia		DM	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value
(Intercept)	6.89 (0.45–106.45)	0.167	0.02 (0.00–0.59)	0.024
Hypertension	1.25 (0.52–2.99)	0.618	2.03 (0.61–6.78)	0.252
Dyslipidemia	0.86 (0.46–1.61)	0.641	0.86 (0.39–1.86)	0.694
Previous stroke	0.95 (0.34–2.69)	0.929	0.36 (0.11–1.22)	0.102
Vasculopathy	0.94 (0.17–5.13)	0.947	0.64 (0.10–4.13)	0.636
Renal failure	0.53 (0.13–2.22)	0.386	0.03 (0.00–0.24)	*<.001*
Charlson Index	1.28 (0.89–1.85)	0.188	2.67 (1.77–4.02)	*<.001*
Lawton Index	0.96 (0.80–1.16)	0.698	1.01 (0.80–1.27)	0.957
Barthel Index	0.99 (0.97–1.02)	0.578	1.01 (0.98–1.04)	0.612
Spanish version of the Mini-mental State Examination	1.00 (0.94–1.06)	0.962	0.95 (0.89–1.02)	0.181
White-cell count	0.85 (0.72–1.00)	0.052	1.10 (0.90–1.35)	0.334
Angiotensine-converting enzyme drugs	0.92 (0.45–1.88)	0.818	7.04 (2.52–19.61)	*<.001*
Diuretics	1.93 (0.94–3.96)	0.074	2.46 (1.04–5.78)	*0.039*

OR = odds ratio; CI = confidence interval.

results might be associated with the pathogenic mechanism of inflammation suggested to explain DM related cardiovascular complications or insulin resistance still remains to be elucidated, since other acute phase reactants showed no differences between DM, prediabetic and normoglycemic groups[27,28]. Regarding to chronic kidney disease, when assessed by clinical records, it had lower odds of being in the DM group than in the prediabetic group, but when assessed by eGFR revealed no differences between the three groups. This could reflect a lack of registration of multimorbidities in routine clinical practice.

ACE drugs were the most frequently prescribed cardiovascular antihypertensive treatment in our study, especially among participants with DM who had 7 odds higher ACE prescriptions than those with prediabetes. In our opinion, these results probably reflect a good compliance of the international consensus which encourages the use of these drugs in order to profit its well-known cardiovascular protective effect in patients with high comorbidity and reducing DM complications[29]. It was difficult to state any conclusion concerning diuretic treatment. Although diuretics have been associated with insulin-resistance[30] and new onset diabetes[31] in individuals with prediabetes, our study showed that the use of diuretics was 3 odds higher in DM patients than in prediabetic ones. So, it seems crucial to adequate the rate of these drugs for addressing the incidence of prediabetes and DM in these population.

Results of our investigation must be interpreted in light of some limitations such as the cross-sectional design, which does not let to establish any causal relation with respect to prediabetic state and only provides mere associations. Moreover, the classification of glycemic state was based on FPG, as in other population studies[20,22], instead of its combination with a glucose tolerance test (TTOG). Then, it is expected that the lack of TTOG data leads to a suboptimal estimation of glycemic state because, especially in elderly, normoglycemic group may include some individuals with impaired glucose tolerance that should have been included in prediabetic group, but it reflects the real limitation to perform TTOG in clinical practice at the community. Finally, since the Octabaix study is a multicenter community based sample of the oldest old—with similar characteristics and with no exclusion criteria applied due to comorbidity or functional and cognitive status—, results obtained may be those of the octogenarian population living in our area. Considering the goal population, a larger cohort would have probably provided a greater power of the statistical analyses.

5. Conclusions

This study found a high prevalence of prediabetes among the 85-year-old population studied, but lower than that has been reported in people aged 65 or over. The major clinical differences between prediabetic and DM groups were the higher Charlson comorbidity Index scores, diuretics, and ACE drugs in the DM group.

Acknowledgments

This work was supported by a public funding from the Fondo de Investigación Sanitaria, Instituto de Salud Carlos III, Spain (Number PS09/00552).

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