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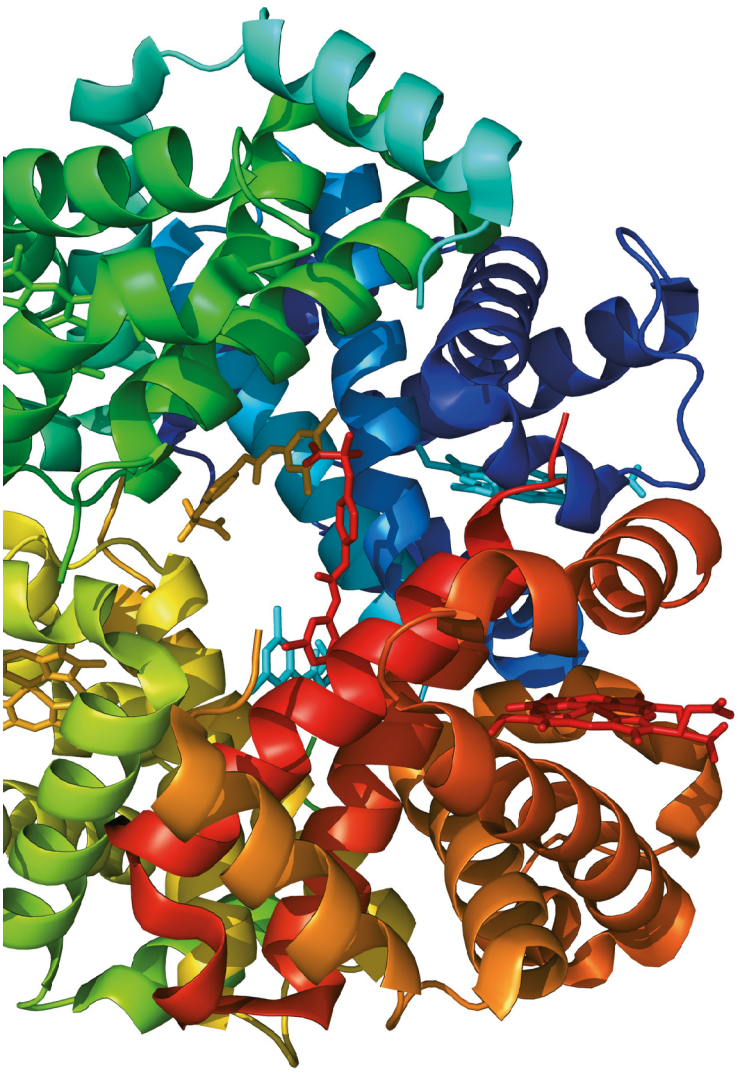

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Editorial Address:
Via Medica
ul. Świętokrzyska 73, 80–180 Gdańsk, Poland
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Contents

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EDITORIAL
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Vinod K. Abichandani
MSc Endocrinology, University of South Wales, United Kingdom

Is Vitamin D a Panacea for the Octogenarian with Type 2 Diabetes?

Advances in medicine have led to an increase in the life expectancy of elderly patients with diabetes, especially of the growing population called the "oldest old," those octogenarians in their mid-80s upwards. Considering the significant increase in the overall elderly population of more than 761 million worldwide, we can surmise the impact of diabetes and its complications.

Depression, mild cognitive impairment (MCI), and dementia are frequently encountered co-morbidities in clinical practice. These impose significant social, medical, and economic burdens, especially in the geriatric population with type 2 diabetes (T2D). A plethora of evidence suggests that T2D not only leads to vascular dementia but also to Alzheimer's disease-type dementia. Oldest adults with diabetes have a high risk of undiagnosed cognitive dysfunction, depression, and functional incapacities. Cognitive impairment in this population is associated with poor diabetes control [1].

Excellent tools like the Montreal Cognitive Assessment (MoCA) for MCI, the Geriatric Depression Scale (GDS-30), and the Hospital Anxiety and Depression Scale (HADS) are available to assess the psychiatric profile of senior citizens with T2D.

The predictors of MCI in octogenarians with T2D include a bias towards the female gender, low HDL cholesterol, increased HADS anxiety score, fasting blood glucose (FBG,) and longer duration of diabetes [2]. According to these researchers, 76% of the 400 patients included in their study had depression of varying degrees, while 56.8% of studied patients had MCI. Decreased levels of HDL-cholesterol and increased HADS anxiety scores were significant predictors of depression.

Chakraborty et al. [3], while assessing cognitive function in different age groups of persons with T2D, reported a prevalence of MCI in T2D patients in the age group 81–90 years of 75% using the MoCA, and a Digit Symbol Substitution Test (DSTT) score of 18.8% for cognitive functions.

Vitamin D is an essential micronutrient called "the sunshine vitamin." Although generally referred to as a vitamin, it is a hormone due to its steroid structure and mechanism of action. Vitamin D deficiency is yet another rampant health problem posing multiple wellness hazards to this vulnerable age group. Vitamin D deficiency can lead to skeletal consequences like reduced bone mineral density, osteomalacia, frailty, and fractures. Specific extra-skeletal effects include added risks for falls, reduced muscle strength, diabetes, cancer, and cardiovascular disease. Vitamin D deficiency contributes to both the initial insulin resistance and the subsequent onset of diabetes, facilitated by a dwindling functional β-cell mass. Vitamin D supplementation mitigates inflammation — a contributing factor for insulin resistance.

Vitamin D supplementation may avert the onset of dementia by several neuroprotective mechanisms that include increased phagocytosis of amyloid-beta peptide, regulation of neurotrophins (a family of proteins that help neurons survive, develop, and function) and calcium homeostasis, anti-inflammatory, and antioxidant [4]. The insufficiency or deficiency of vitamin D may lead to decreased memory and MCI.

Address for correspondence:
Vinod K. Abichandani, MD
e-mail: vkabichandani57@gmail.com
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Vitamin D receptors exist in the human cortex and hippocampus, which are crucial areas for cognitive functioning, and an absence or malfunction of these receptors has been implicated in the occurrence of neurodegenerative dementia such as Alzheimer's disease. Vitamin D deficiency is widespread in super elderly patients with Alzheimer's disease, with an incidence of 70% to 90% [5].

There is a clear association between vitamin D deficiency and severe retinopathy, diabetic peripheral neuropathy, and poor cognitive performance in the oldest persons with T2D. At the same time, there is agreement about the beneficial effect of vitamin D supplementation on peripheral artery disease, foot ulceration prevention, and wound healing. However, the beneficial effects of vitamin D supplementation on major cardiovascular adverse events, endothelial dysfunction, and diabetic kidney disease remain controversial. Despite the inconsistent results of many randomized control trials of vitamin D in the aged, most support the idea that vitamin D supplementation improves metabolic parameters (lipids, insulin resistance, glucose) and reduces the complications of T2D in elderly patients [6].

It is very important that we determine the appropriate vitamin D dose to be administered to the elderly person with diabetes. While low dosages may be ineffective, large doses of vitamin D may have harmful consequences by disrupting intracellular calcium signaling.

Conflict of interest

The author declares no conflict of interest.

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Awadhesh Kumar Singh[1–3], Ritu Singh[2], Kalyan Kumar Gangopadhyay[4]
[1]G. D Hospital and Diabetes Institute, Kolkata, West Bengal, India
[2]Horizon Multispecialty Hospital, Kolkata, West Bengal, India
[3]Sun Valley Hospital & Diabetes Research Centre, Guwahati, Assam, India
[4]Calcutta Medical Research Institute and CK Birla Hospital, Kolkata, West Bengal, India

Cardiovascular Risk in Women with Type 2 Diabetes: Still an Enigma?

The Lancet Women and Cardiovascular Disease Commission: reducing the global burden by 2030 — has aptly summarized — "cardiovascular disease in women remains understudied, under-recognized, underdiagnosed, and undertreated" [1]. Historically, the Framingham study was one of the first large-scale studies conducted in 1974 that suggested an excess risk of heart failure (HF) and cardiovascular (CV) death in women with type 2 diabetes (T2D) compared to men [2, 3]. Two large meta-analyses conducted subsequently also suggested an increased rate of stroke, coronary artery disease (CAD), and all-cause mortality (ACM) in women with T2D compared to men including people from Asia-Pacific [4, 5]. Notwithstanding, several other studies did not find any gender-related difference in HF, CAD, stroke, CV death, and ACM in people with T2D [6–10]. Therefore, the relative impact of T2D on CV disease and mortality remains intriguing, gender-wise.

In this issue of *Clinical Diabetology*, Weerawickrama et al. [11] have attempted to assess the prevalence of CV risk factors and compare the capability of the World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction score and Framingham Risk Score (FRS) to predict CV disease risk in Sri Lankan women with T2D but without overt CV disease. This assumes relevance given the dearth of such risk prediction tools in South Asian women with T2D in general and Sri Lankans in particular. The authors further divided the patients into premenopausal, early post-menopausal (< 5 years), and late post-menopausal (> 5 years). Of note, more than 97% of patients in all three groups had central obesity although close to 40% had body mass index (BMI) < 25 kg/m^2. Perhaps, choosing a cutoff BMI of < 23 kg/m^2 (as advocated for Asians) would have identified more patients with overweight or obesity. The study also demonstrated a higher incidence of dyslipidemia among premenopausal women than postmenopausal women; however, statistical analysis was not documented to see if it reached statistical significance. There was a significant discrepancy in risk prediction by the WHO/ISH and FRS. The WHO/ISH score chart had high specificity but poor sensitivity. In contrast, FRS had low specificity but high sensitivity meaning therefore that the WHO/ISH score chart would fail to appropriately predict risk for women with high CV risk. In contrast, FRS would classify the same group as moderate or high risk. This was explained by the fact that FRS included high-density lipoprotein cholesterol (HDL-C) in the risk calculation and in the present study close to 20% of patients had low HDL-C. Perhaps including a third commonly used scoring system the QRISK3 would have been more helpful as it covers more extensive parameters and can be region-specific as it has options to choose from the ethnicity section including Indian, Pakistani, Bangladeshi, etc. [12]. Nevertheless, this study opens

Address for correspondence:
A. K. Singh
G.D Hospital & Diabetes Institute
Kolkata 700013, India
e-mail: drawadheshkumarsingh@gmail.com
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up the discussion on why women would be different from men regarding CV risk in T2D.

There could be several factors underpinning the uncertain CV risk in women with T2D compared to men. Altered CV risk in women could be akin to — i. psycho-socio-cultural differences; ii. Geno-phenotype differences; iii. women-related factors: polycystic ovarian syndrome, primary ovarian insufficiency, and menopause; iv. pregnancy-related factors: gestational hypertension, preeclampsia, gestational diabetes, and preterm birth (< 37 weeks); v. pharmacokinetic-dynamic (PK-PD) factors; vi. differential response to anti-diabetes and CV drugs, and vii. exaggerated adverse events, compared with men. Several studies have reported poorly controlled diabetes, blood pressure (BP), and lipid levels, and delays in diagnosis and treatment of T2D and CV diseases in women due to psycho-socio-cultural differences, compared to men [13–15]. Higher BMI, a higher frequency of atypical angina, a higher rate of coronary microvascular dysfunction (CMD) such as MINOCA/INOCA (Myocardial Infarction/Ischemia and No Obstructive Coronary Artery Disease), and longer corrected QT interval (QTc) in women owing to the biological effects of female sex hormones akin to geno-phenotype difference [16, 17]. Both women-related and pregnancy-related factors are associated with a varying increased risk of T2D, hypertension, CV disease, and CAD [18]. Concerning PK-PD differences, women have a higher percentage of body fat, lower plasma volume, and lesser organ blood flow that can alter the PK-PD of lipophilic vs. hydrophilic drugs, plasma/tissue drug concentrations, hepatic enzyme activity (cytochrome 450 and P-glycoprotein family) as well as drug clearance [19]. For example – in women, levels of metoprolol and propranolol in plasma are higher due to a lower volume of distribution and a slower clearance causing a greater reduction in exercise-induced heart rate and BP compared to men. However, metoprolol has been found to exert a greater effect on stress-induced angina in men compared with women despite higher plasma levels in the latter. Likewise, levels of plasma statin concentrations are generally 15–20% higher in women than in men. However, women metabolize lipophilic statins faster due to higher concentrations of cytochrome 4503A4. Similarly, women have faster clearance of verapamil and amlodipine due to the lower activity of P-glycoprotein and higher activity of CYP3A4 [19].

Concerning the differential effect of anti-diabetes drugs, the MASTERMIND consortium (n = 22,379), a UK Clinical Practice and Research Datalink, showed a significantly greater response with thiazolidinediones (TZDs) and lesser response to SUs in obese women compared with men. Moreover, a significantly higher weight gain and edema risk with TZDs was observed in obese women compared with men [20]. Similar findings were observed in the TODAY (made Treatment Options for Type 2 Diabetes in Adolescents and Youth) trial showing a better glycemic response with TZDs in obese women compared to non-obese women and obese men [21]. Women also showed differential responses to glucagon-like peptide-1 receptor agonists (GLP-1RAs). While weight loss with short-acting exenatide at 1 year was significantly higher in women, a significantly lower glycemic efficacy was observed in women compared with men [22]. Moreover, a recent meta-analysis of cardiovascular outcome trials (CVOTs) found a pronounced effect of GLP-1RAs and a lesser beneficial effect of sodium-glucose cotransporter-2 inhibitors (SGLT2i) on the composite of major cardiovascular events in women compared to men [23].

With regards to CV drugs, in primary prevention studies, while aspirin lowered the risk of stroke it did not reduce myocardial infarction or CV death in women compared with men [24]. Similarly, the effects of statins in primary prevention are less evident in women [25]. Angiotensin-converting enzyme inhibitors (ACEi) have shown a significant reduction in heart failure hospitalization (HHF) and mortality in men than in women in earlier heart failure trials [26]. Likewise, few studies showed beta-blockers did not improve survival in women with hypertension and/ or heart failure [27]. Digoxin therapy was less effective in women in reducing HHF than in men in the DIG (Digitalis Intervention Group) trial [28]. A meta-analysis of glycoprotein (GP) IIb/IIIa antagonist trials found no treatment benefit in women than in men with non-ST elevated acute coronary syndromes [29].

Finally, a higher frequency of adverse events of drugs could cause poor compliance in women. An increased incidence of cough (ACEi), myopathy (statins), edema (amlodipine), hemorrhagic complications (anticoagulants/ anti-platelets/ thrombolytics), electrolyte abnormalities (diuretics) in women compared with men could be associated factor [19]. Drug-induced torsades-de-pointes are more frequent in women than in men due to longer corrected QT interval (QTc) [19]. Table 1 summarizes the possible mechanism underpinning the altered CV risk in women.

However, any interpretation of these data should be made in light of certain limitations. Most of the data have been collected through observational and cohort studies and these findings could merely be an association. There are clear inconsistencies between observational studies, randomized trials, and meta-analyses. Unfortunately, women with T2D have been

Table 1. Possible Mechanism Underpinning Altered Cardiovascular Risks in Women [13–29]

Areas of differences	Overall effect	Other effects observed
1. Psycho-socio--cultural difference	i. Poorly controlled diabetes, BP, and lipid levels, ii. Delays in diagnosis and treatment of T2D and CV diseases	—
2. Geno-phenotype difference	i. Higher percentage of body fat, ii. Higher BMI, iii. Higher frequency of atypical angina, iv. Higher rates of CMD such as MINOCA/INOCA, v. Longer QTc	—
3. Women-related factors	i. Polycystic ovarian syndrome (PCOS) ii. Premature ovarian insufficiency (POI) iii. Menopause	i. PCOS is associated with an increased risk of T2D, HTN, and CVD ii. POI is associated with an increased risk of CVD and CHD
4. Pregnancy--related factors	i. Pregnancy-induced hypertension (PIH) ii. Preeclampsia iii. Gestational diabetes mellitus (GDM) iv. Premature/ pre-term delivery (<37 weeks)	i. PIH, preeclampsia, and GDM are associated with an increased risk of future HTN, T2D, CVD, and CHD ii. Mothers having preterm delivery have shown an increased risk of HTN, T2D, and CVD
5. PK-PD difference	i. Lower plasma volume, ii. Lesser organ blood flow iii. Altered PK-PD of lipophilic vs. hydrophilic drugs iv. Altered plasma/tissue drug concentrations v. Altered hepatic enzyme activity (cytochrome 450 and P-glycoprotein family) vi. Altered drug clearance	i. Levels of metoprolol and propranolol in plasma are higher ii. Plasma statin concentrations are 15–20% higher iii. Metabolize lipophilic statins faster iv. Faster clearance of verapamil and amlodipine
6. Differential effects of anti-diabetes drugs	i. Greater response with TZDs ii. Lesser response to SUs iii. Lesser HbA1c but higher weight reduction with GLP-1RAs iv. More pronounced effect of GLP-1RAs on MACE outcome v. Less pronounced effect of SGLT2i on MACE outcome	i. Higher weight gain and edema risk with TZDs
7. Differential effects of CV drugs	i. The effect of statins in primary prevention is less evident ii. Lesser effect of ACEi on HHF iii. Lesser effect of BB on survival in HTN and HF iv. Lesser effect of digoxin on HHF in HF v. Lesser effect of GP-IIb/IIIa antagonists in ACS	i. Lower risk of stroke but not MI or CV death with statin in primary prevention ii. Increased ACM with digoxin in HF
8. Differential adverse events	i. Two-fold increase in cough with ACEi ii. Higher incidence of myopathy with statins iii. Higher incidence of amlodipine-induced edema iv. Higher incidence of hemorrhagic complications with anticoagulants, anti-platelets, and thrombolytics v. Increased electrolyte abnormalities with diuretics	i. Higher drug-induced torsades-de-pointes

ACM — all-cause mortality; ACS — acute coronary syndrome; BB — beta-blockers; BMI — body-mass-index; BP — blood pressure; CHD — coronary heart disease; CMD — coronary microvascular dysfunction; CV — cardiovascular; CVD — cardiovascular disease; GLP1-RAs — glucagon-like peptide-1 receptor agonists; GP-IIb/IIIa — glycoprotein-IIb/IIIa; HF — heart failure; HHF — hospitalization due to heart failure; HTN — hypertension; MI — myocardial infarction; MACE — major adverse cardiovascular events; MINOCA/INOCA — myocardial infarction/ischemia due to non-obstructive coronary disease; PCOS — polycystic ovarian syndrome; PK-PD — phenotype-genotype; SGLT2i — sodium-glucose transporter-2 inhibitors; SUs — sulfonylureas; T2D — type 2 diabetes; TZD — thiazolidinedione

underrepresented in randomized controlled trials. This was evident in older statins and aspirin trials. Notwithstanding, even most of the recent CVOTs trials exclude women of childbearing age where renin-angiotensin system blockers (RASB) are contraindicated owing to potential teratogenicity which could potentially impact the inclusion of women of reproductive age in clinical trials. Needless to say, more research is required to exactly know the biological mechanism underpinning the risk of CV disease in women.

Authorship

All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship and take responsibility for the integrity of the work. They confirm that this paper will not be published elsewhere in the same form, in English or in any other language, including electronically.

Conflict of interest

The authors declare no conflict of interest.

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Dinesh Kumar Upadhyay, Gurusha Bahl, Tekchand Narang
School of Pharmaceutical Sciences, Jaipur National University, Jaipur, Rajasthan, India

Assessment of Health-Related Quality of Life of Patients with Type 1 and Type 2 Diabetes Using ADDQoL Questionnaire in a Tertiary Care Hospital: A Cross-Sectional Study

ABSTRACT

Objective: This study aimed to determine the health-related quality of life (HRQoL) of patients with diabetes (PwD) using the Audit of Diabetes-Dependent Quality of Life (ADDQoL) questionnaire.

Material and methods: A cross-sectional, observational study was conducted among 300 PwD to evaluate their HRQoL by using ADDQoL questionnaire. The association between impact, importance, and weighted impact scores were assessed by applying various tests. Chi-square test was used to find the association between condition-specific domains and weighted impact scores. Kruskal-Wallis test was used to determine the association between patient-related demographic variables and average weighted impact scores (AWIS). All analysis was done at significance level $p \leq 0.05$.

Results: The mean age of the participants was 55.49 years. Out of 300 patients, the majority were male (n = 153), married (96.7%) and urban residents (57.7%). The most affected domain was family life (–5.18) followed by financial situation (–4.52) and physical health (–4), and the least affected domain was people's reactions (–1.27) followed by local or long-distance journeys (–1.38) and holidays (–1.39). The mean AWI score (–3.31) indicated most of the patient's QoL was impacted by diabetes. Kruskal-Wallis test identified that gender, residence, marital status, education, and family income were confounding factors associated with HRQoL of patients.

Conclusions: Diabetes was found to have a greater negative impact on HRQoL. Most of the patients rated their present QoL to be bad and thought that QoL would be slightly better if they did not have diabetes.
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Keywords: audit of diabetes-dependent quality of life, average weighted impact score, health-related quality of life, type 1 diabetes, type 2 diabetes, weighted impact score

Address for correspondence:
Gurusha Bahl
School of Pharmaceutical Sciences, Jaipur National University
Jaipur, Rajasthan, 302017, India
e-mail: gurushabahl@gmail.com
phone: 9772186313
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Introduction

Diabetes mellitus (DM) is a combination of various metabolic conditions with symptoms such as hyperglycemia (high blood glucose levels), polyphagia, polydipsia, and polyuria [1, 2]. It contributes to approximately 6% of the total worldwide mortality, leading to an

international healthcare catastrophe requiring novel approaches for its prevention and treatment [3]. The level of mortality and morbidity because of diabetes and related complications are alarming, resulting in increased health challenges and medical expenditures on individuals as well as the community [4]. Quality of life (QoL) refers to an individual's opinion of how good or bad their daily life is [5–7]. In comparison to QoL, the term health-related quality of life (HRQoL) entails a more comprehensive viewpoint that incorporates several facets of an individual's well-being, such as psychological, physical and social aspects of life [6]. Numerous tools have been created, authenticated, and employed to estimate the HRQoL in individuals with DM. One such instrument is the Audit of Diabetes-Dependent Quality of Life (ADDQoL) [7]. It is a tool for evaluating HRQoL in people with DM because of its individualized and reliable nature that allows respondents to examine life domains that are specific to them and describe how important these aspects are in terms of their HRQoL as well as how diabetes impacts those domains [8]. Considering the enormous growth in the diabetic population, there are only a few research studies that could assess and evaluate the accurate status of the condition, and so there is urgent demand for studies that can estimate the potential catastrophic increase in the diabetes population. Moreover, we want to conduct this study to provide insight into how the HRQoL is affected because of diabetes. Furthermore, we intend to investigate how certain demographic aspects influence patient's QoL in connection to diabetes, so the rationale of the study is to examine diabetes patients HRQoL by utilizing the ADDQoL questionnaire [9, 10].

Materials and methods

Study design

A cross-sectional, single-centered study was done among patients with diabetes (PwD) as participants for a duration of 6 months (based on time capsule frame). Demographic parameters including gender, age, place of residence, education, marital status, smoking and alcoholic status, monthly income, diabetes duration along with laboratory investigations including random blood glucose levels, fasting blood glucose, glycated hemoglobin (HbA1c) levels, and complications (if present) were obtained from the diabetic patients. The questionnaire and methodology for this study was approved by the Human Research Ethics Committee of Jaipur National University Institute of Medical Science and Research Centre (No. JNUIMSRC/IEC/2022/97).

Study population

Patients with type 1 diabetes (T1D) and type 2 diabetes (T2D) who have been diagnosed with the disease at least 3 months before enrollment in the study and visited the outpatient and inpatient Department of Internal Medicine of Jaipur National University Hospital, Jaipur were recruited for the study purpose. In addition, prior to inclusion in the study, all subjects supplied written informed consent. The following were the inclusion criteria: (1) patients with diabetes aged ≥ 18 years; (2) both genders; (3) patients with comorbid conditions (DM-related complications); (4) patients wanting to engage in the study and providing written consent. Patients less than 18 years with gestational diabetes and patients with learning disabilities were excluded from the study.

Study tools

For the better comprehension of the diabetes patients in the area, all the study tools including the consent form, demographic form, and ADDQoL questionnaire were prepared in both Hindi and English language (wherever needed).

ADDQoL questionnaire

The ADDQoL is an individualized questionnaire designed to examine the HRQoL of patients with diabetes. The questionnaire is composed of two sections, the first of which has two overview items (Statement I and Statement II), while the second one contains 19 condition-specific life domains (Statements 1 to 19), each of which reveals the general and overall HRQoL. The impact and importance of a specific condition are assessed for each domain in statements (a) and (b) [11]. The maximum score for the negative and positive impact of diabetes is –9 and +3, respectively. Higher negative score values indicate poorer HRQoL, whereas lower negative values (in the positive direction) indicate better HRQoL [12, 13].

Statistical analysis

The Raosoft sample size calculator was used to compute the sample size at 95% confidence interval (CI), 5% margin of error, and 50% response distribution. The overall sample size was determined to be 300 T1D and T2D patients after which Statistical Package for Social Sciences (SPSS 29.0, Chicago, USA) was used to conduct the statistical analysis [14]. The Shapiro-Wilk test was used to identify the pattern of data distribution, and it revealed that the data was not normally distributed. The significance of the differences between the Impact, Importance, and Weighted Impact ratings

was assessed using the Chi-Square test. The association that exists between the patient's demographic variables and average weighted impact score (AWIS) was determined using the Kruskal-Wallis test. All the analysis was done at a significance level $p < 0.05$.

Results

Baseline characteristics of the patients with diabetes

The study found mean age (in years ± SD) of the participants to be 55.49 ± 11.49 and approximately half of the population were male (n = 153, 51%). Most of the participants were married (96.7%). More than half of the study participants (57.7%) were urban residents. In terms of lifestyle factors, 25.7% of the participants were smokers, 12% were alcohol drinkers. It is noteworthy that a significant proportion of the participants were non-smokers (64.3%) and non-drinkers (78%). The mean duration of diabetes since diagnosis was 6.31 ± 5.58. According to family history, 16.3% of patient's parents had a previous history of diabetes. Other baseline characteristics are indicated in Table 1. The average value for HbA1c was found to be 9.879 ± 2.33 and the mean fasting and random glucose values (mg/dL) were found to be 220.72 ± 84.43 and 299.38 ± 94.67, respectively. With regard to diabetes complications, most patients had cardiovascular disease (25.3%), followed by nephropathy (5.3%), retinopathy (4.6%), neuropathy (3.6%) and about 3.2% patients had combined complications.

General quality of life in patients with diabetes

Table 2 depicts the overall QoL scores of diabetes patients. The data was analyzed using descriptive statistics.

Impact, importance and weighted impact scores of condition-specific domains of patients with diabetes

The HRQoL scores for the patients were assessed according to 19 condition-specific domains as shown in Supplementary Table 1. It was observed that diabetes demonstrated the greatest negative impact on "family life" (mean –2.12 ± 0.66) followed by "financial situation" (mean –1.95 ± 0.67) and least negative impact on "people's reaction" (mean –1.27 ± 0.50), "local or long-distance journeys" (mean –1.38 ± 0.77) and "holidays" (mean –1.39 ± 0.77). The most important domain was found to be "family life" (mean 2.33 ± 0.50) whereas the least important was "people's reaction" (mean 1.34 ± 0.56). After calculation of the weighted impact scores, family life (mean –5.18 ± 2.52), financial situation (mean –4.52 ± 2.43) and physical health (mean –4 ± 2.56) were found to be the most affected QoL domains, whereas the least affected QoL domain was reported to be people's reaction (mean –1.94 ± ± 1.62) as depicted in Figure 1.

Table 1. Baseline Characteristics of Patients with Diabetes (N = 300)

Baseline characteristics		Frequency n (%)
Gender	Male	153 (51)
Residence	Urban	173 (57.7)
	Rural	127 (42.3)
Smoking	Smoker	77 (25.7)
	Non-Smoker	193 (64.3)
	Ex-Smoker	30 (10)
Alcohol	Alcohol drinkers	36 (12)
	Non-drinkers	234 (78)
	Ex-drinkers	30 (10)
Marital status	Married	290 (96.7)
	Unmarried	4 (1.3)
	Divorced	1 (0.3)
	Widow	5 (1.7)
Education	Primary	218 (72.7)
	Secondary	35 (11.7)
	Tertiary	47 (15.7)
Family history	Father	13 (4.3)
	Mother	26 (8.7)
	Mother and Father	49 (16.3)
	Brother	11 (3.7)
	Sister	7 (2.3)
Family income (Rs)	≤ 5000	141 (47)
	5000–10 000	80 (26.7)
	> 10 000	79 (26.3)
Diabetes duration [years]	0–10	252 (84)
	11–20	42 (14)
	21–30	4 (2)

Table 2. Mean Scores of General Quality of Life for Patients with Diabetes Mellitus (N = 300)

General quality of life scores		
Statement I: My present quality of life is		Score range*
Mean ± SD	–1.13 ± 1.16	–3 to +3
Statement II: Quality of life without diabetes		
Mean ± SD	–1.66 ± 0.73	–3 to +1

*Better quality of life is indicated by lower negative ratings
–3 (extremely bad) to +3 (excellent); +2 (very good); +1 (good); 0 (neither good nor bad); –1 (bad); –2 (very bad)
–3 (very much better) to +1 (worst); –2 (much better); –1 (a little better) l and 0 (the same)
SD — standard deviation

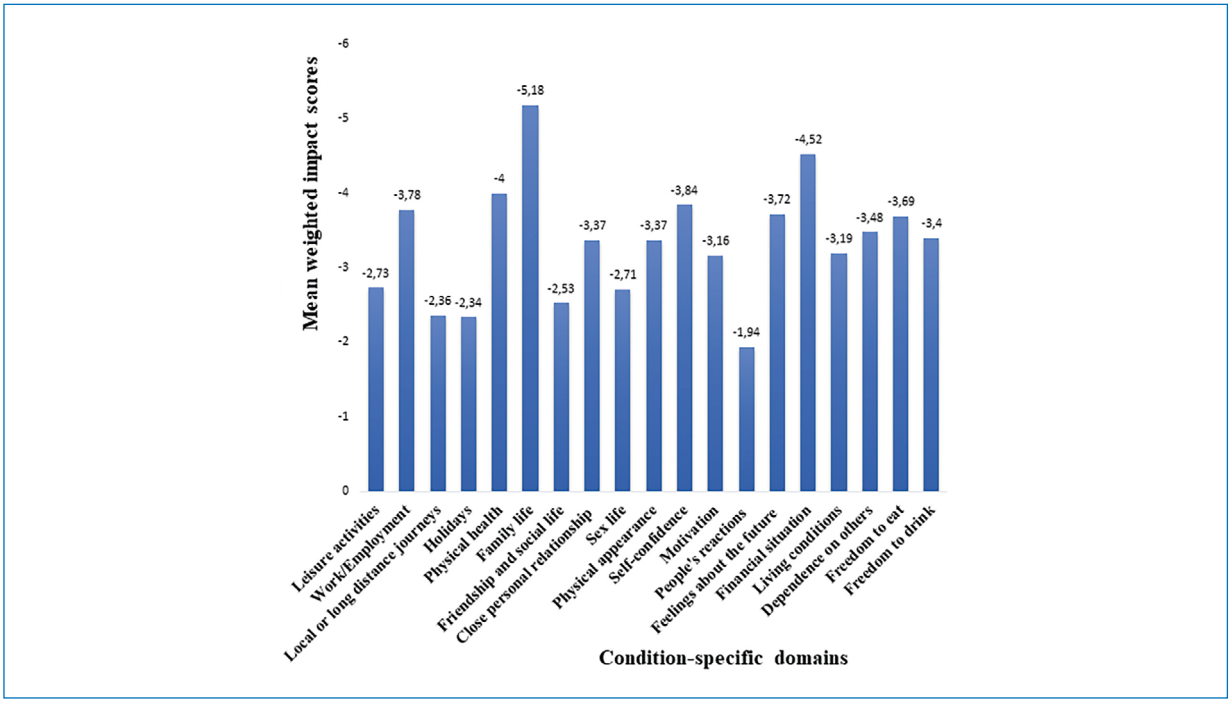

Figure 1. Overall Mean Weighted Impact Scores of Diabetes on the Individual Condition-Specific Life Domains

Association between patient demographic variables and average weighted impact scores

The link between patient demographic factors and average weighted impact scores demonstrated noteworthy significance for gender, residence, alcohol, marital status, education and family income which was analyzed by using the Kruskal-Wallis test at $p < 0.05$, as shown in Table 3.

Discussion

The present study determined that diabetes had a more detrimental impact on the present HRQoL, which was analogous to various other studies which revealed an identical negative influence of diabetes on the patient's HRQoL [15–23]. The mean AWI score of the total group of participants was –3.31, which was on the negative side of the QoL impact for diabetes. Also, majority of the patients rated their present QoL to be "bad" and thoughts that their QoL would be "a little better" if they did not have diabetes.

Diabetes had the greatest negative impact on the domain family life (–2.12) which was also found to be the most important domain which may be due to the fact that the Asian population including Indian people value family over self. These findings from the current study are consistent with the findings from the studies conducted in different countries [15–16]. The most affected domains with respect to WIS in the present study were family life (–5.18), financial situation (–4.52) and physical health (–4). These findings are in line with the studies conducted by Upadhyay et al. [12], Levterova et al. [16] and Jannoo et al. [17], respectively. However, a study by Kontoteza et al. [18] found the financial situation to be one of the least impacted domain.

On the other hand, the least impacted domain in the present study was found to be people's reactions (–1.27) followed by local or long-distance journeys (–1.38) and holidays (–1.39). The likely cause for this may stem from the elevated prevalence and frequency of diabetes, resulting in widespread awareness of the condition and a general absence of unfavorable attitudes towards individuals living with diabetes [19].

Interestingly, in this research, the domains that were most and least affected were identified to be family life and people's reaction, respectively, both before as well as after weighing. This information can aid in designing patient education materials by targeting the specific QoL areas that were most affected by diabetes for each person. In summary, the results of the present study rated the domain family life as the most impacted and important whereas people's reactions were rated as the least impacted and important, which is consist-

Table 3. Association between Patient Demographic Variables and Average Weighted Impact (AWI) Scores (N = 300)

Demographic variables		Frequency n (%)	AWI (mean ± SD)	Significance*
Gender	Male	153 (51)	–3.63 ± 1.54	0.000**
	Female	147 (49)	–2.98 ± 1.41	
Residence	Urban	173 (57.7)	–3.10 ± 1.48	0.006**
	Rural	127 (42.3)	–3.61 ± 1.51	
Smoking	Smoker	77 (25.7)	–3.54 ± 1.60	0.312
	Non-smoker	193 (64.3)	–3.25 ± 1.45	
	Ex-smoker	30 (10)	–3.14 ± 1.51	
Alcohol	Alcohol drinkers	36 (12)	–3.82 ± 1.49	0.019**
	Non-drinkers	234 (78)	–3.19 ± 1.52	
	Ex-drinkers	30 (10)	–3.68 ± 1.30	
Marital status	Married	290 (96.7)	–3.29 ± 1.47	0.000**
	Unmarried	4 (1.3)	–6.05 ± 0.67	
	Divorced	1 (0.3)	–6.21 ± 0	
	Widow	5 (1.7)	–1.77 ± 0.97	
Education	Primary	218 (72.7)	–3.03 ± 1.39	0.000**
	Secondary	35 (11.7)	–3.90 ± 1.58	
	Tertiary	47 (15.7)	–4.20 ± 1.53	
Family income (Rs)	≤ 5000	141 (47)	–3.05 ± 1.36	0.008**
	5000–10 000	80 (26.7)	–3.33 ± 1.56	
	> 10 000	79 (26.3)	–3.78 ± 1.60	

*Kruskal-Wallis test; **Significance at $p < 0.05$ (2-tailed test); SD — standard deviation

ent with various other studies conducted in different regions [16, 17, 19].

Major demographic variables associated with lower QoL were gender, residence, marital status, education and family income. These suggested that some socio-demographic and disease-specific predictors were likely to affect certain domains more than others which need to be considered in responding to patient's individual needs [15].

In our study, it was observed that male patients with diabetes had poorer HRQoL than female patients with respect to average weighted impact scores, which is identical to another study done by Komal et al. [20]; however, a study done by Gautam et al. found that female patients with diabetes had a comparatively poor QoL as male patients [21]. In the present study, it was found that rural population had a poorer effect on their HRQoL compared to urban population, which can be explained by the fact that urban living provides better access to healthcare facilities, thus helps in better disease management. These results were found to be similar to those from studies done by Naous et al. and Gvozdanovic et al. [22, 23].

The results of the present research demonstrated that measuring the HRQoL of diabetes patients using the ADDQoL questionnaire offered insightful information about the influence of diabetes on different facets of their day-to-day lives and highlighted the significance of addressing particular domains affected by diabetes to tailor patient education and improve overall well-being [18]. Like other studies, the current study is also not free from the study limitations. As the data collection was done only from one hospital (single center); therefore, the outcomes cannot be generalized to the entire population of the country. The cross-sectional approach of the study limits the development of causal links between variables by providing an overview of QoL at a certain point in time and fails to recognize variations in QoL over the course of time. Additionally, certain self-reported information such as diagnosis time frame and duration of diabetes may be subject to information bias because they depend upon the participant's thoughts.

Conclusions

DM stands as a prominent chronic ailment worldwide, carrying significant economic and social consequences. HRQoL offers a comprehensive outlook on a patient's physical, emotional, and social well-being. As per the results of our study, it was found that diabetes had a greater negative impact on present HRQoL. Also, the major demographic variables associated with lower HRQoL were found to be gender, residence, marital status, education and family income. Interestingly, in

our study, both before and after weighting, the most affected domain was found to be family life and the least affected domain was found to be people's reaction. Also, the majority of the patients rated their present QoL to be bad and thought that QoL would be a little better if they did not had diabetes. As we conclude this study, we acknowledge the invaluable contributions of every participant who shared their experiences, granting us profound insights into the complex tapestry of HRQoL in the face of diabetes.

Article information

Supplementary materials

The Supplementary materials for this article can be found at https://journals.viamedica.pl/clinical_diabetology/article/view/98812

Data availability statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Ethics approval

The questionnaire and methodology for this study was approved by the Human Research Ethics Committee of Jaipur National University Institute of Medical Science and Research Centre (No. JNUIMSRC/IEC/2022/97).

Consent to participate

Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Consent for publication was obtained from all the patients.

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Author contributions

Material preparation, data collection and analysis were performed by Gurusha Bahl and Tekchand Narang. The first draft of the manuscript was written by Gurusha Bahl and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conceptualization: Dinesh Kumar Upadhyay, Gurusha Bahl; Methodology: Dinesh Kumar Upadhyay, Gurusha Bahl; Software: Gurusha Bahl, Dinesh Kumar Upadhyay; Validation: Dinesh Kumar Upadhyay; Formal analysis: Tekchand Narang, Gurusha Bahl; Investigation: Tekchand Narang, Gurusha Bahl; Resources: Gurusha Bahl, Dinesh Kumar Upadhyay; Data curation: Gurusha Bahl, Tekchand Narang; Project administration: Gurusha Bahl, Tekchand Narang; Visualization: Gurusha Bahl, Tekchand Narang; Supervision: Dinesh Kumar Upadhyay; Writing – original draft preparation: Gurusha Bahl, Tekchand Narang; Writing – review and editing: Gurusha Bahl, Tekchand Narang

Conflict of interest

The authors declare no conflict of interest.

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Piyumi Kumari Weerawickrama[1], Chamila Weerasinghe[1], Anjana Sudarshani Fernando[1], Dilhara Sewwandi Karunarathna[2], Chaminda Garusinghe[3]

[1]Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defense University, Sri Lanka
[2]Department of Basic Sciences, Faculty of Allied Health Sciences, General Sir John Kotelawala Defense University, Sri Lanka
[3]Colombo South Teaching Hospital, Kalubowila, Sri Lanka

Prevalence of Cardiovascular Disease Risk Factors And Assessment of 10-Year Risk of Developing Cardiovascular Diseases in Premenopausal and Postmenopausal Women with Type 2 Diabetes: A Comparative Analysis

ABSTRACT

Objective: This study aimed to assess the prevalence of cardiovascular disease (CVD) risk factors and compare the performance of the World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction score and Framingham risk score (FRS) in predicting CVD risk among pre- and postmenopausal females.

Materials and methods: This cross-sectional study was conducted on a total of 293 female subjects with type 2 diabetes at Colombo South Teaching Hospital, Sri Lanka. The 10-year risk of developing CVD was calculated using WHO/ISH charts and FRSs and compared. The tools were validated through the use of elevated LDL-C levels, high diastolic blood pressure, high HbA1c and elevated fasting plasma glucose levels.

Results: Among the study population, 25.9%, 54.9%, 50.8%, 98.0% and 0% had dyslipidemia, hypertension, obesity/overweight, central obesity, and smoking, respectively. The CVD risk was significantly greater among postmenopausal women than premenopausal women ($p < 0.05$). The FRS identified 23.2%, 48.8%, 20.8% and 7.2% of women as low risk (< 10%), moderate risk (10–19.9%), high risk (20–29.9%) and very high risk (≥ 30%), respectively, whereas the WHO/ISH identified 78.8%, 14.3%, 2.0% and 4.8%, respectively. There was a significant discrepancy in the agreement between the two tools (k value = 0.068, $p < 0.05$). WHO/ISH charts revealed that the majority of women with elevated LDL-C levels (80.2%) were low-risk individuals, while FRSs identified the majority of women with raised LDL-C levels (92.2%) as moderate/high risk.

Conclusions: There was a significant discrepancy in the performance of the WHO/ISH and FRS. WHO/ISH underestimates CVD risk, while the FRS identifies high-risk women who require therapeutic interventions.

(Clin Diabetol 2024; 13, 2: 93–100)

Keywords: cardiovascular diseases, type 2 diabetes, menopausal women, Framingham risk score (FRS), World Health Organization/International Society of Hypertension Risk Prediction Chans (WHO/ISH risk prediction charts)

Address for correspondence:
Piyumi Kumari Weerawickrama
e-mail: piyumik45@gmail.com
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Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality and account for one-third of deaths worldwide [1]. In Sri Lanka, the incidence of CVD has rapidly increased during the past few decades, and CVD has become the leading cause of death during the last 40 years [2]. Therefore, CVDs place heavy social and economic burdens on Sri Lanka. Type 2 diabetes (T2D) is considered a prime risk factor for developing CVDs which has been proven by many studies [3, 4]. T2D is the most prevalent type of diabetes in the world [5]. It is associated with relative insulin deficiency and peripheral insulin resistance [6]. The global prevalence of diabetes has increased rapidly over the past few decades [5], and T2D is one of the major noncommunicable diseases leading to death in the Sri Lankan population [2]. Cardiovascular diseases are considered leading causes of mortality and morbidity among patients with T2D in Sri Lanka [7]. Endothelial damage and dysfunction due to hyperglycemia are the major pathological causes of CVD development in T2D patients. Cardiovascular diseases represent one-third of all deaths among women, and women with T2D have a greater risk of mortality than men [8]. It is well known that estrogen plays a protective role against cardiovascular complications in nonmenopausal women compared to men [9]. However, oxidative stress induced by hyperglycemia alters the effects of estrogen on endothelial estrogen receptors and thereby reduces the beneficial effect of estrogen hormones in women with T2D [10]. Therefore, assessing the risk of CVD development in patients with T2D is mandatory to initiate primary preventive strategies.

Several risk assessment tools, including the Framingham risk score (FRS), the United Kingdom Prospective Diabetes Study (UKPDS) risk engine and the World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction chart, have been developed over the past two decades. Although several studies have been conducted worldwide to assess the efficacy of these risk assessment tools, a limited number of studies have been conducted in Sri Lanka. However, the performance of various CVD risk assessment tools among Sri Lankans may not be the same as that of other well-studied populations. Moreover, in Sri Lanka, the performance of CVD risk assessment tools in postmenopausal women with T2D has not yet been studied. The Ministry of Health, Sri Lanka, recommends WHO/ISH as a cost-effective method for assessing the risk of developing CVD within 10 years in the primary care setting. However, a study conducted in the southern province of Sri Lanka proved that both the UKPDS risk engine and the WHO/ISH method have poor sensitivity as screening tools for assessing CVD risk among T2D patients in Sri Lanka [11]. The FRS has been used as a valid risk assessment tool in different Asian countries in recent years [12, 13]. The sensitivity of the FRS as a risk assessment tool for screening CVD risk among patients with diabetes has not yet been studied in Sri Lanka. In addition, neither the FRS nor the WHO/ISH method are diabetes-specific risk assessment tools; hence, it is important to determine the local applicability of these risk assessment tools for assessing CVD risk in women with T2D in Sri Lanka.

Methods

Study population

This cross-sectional study was conducted at the Diabetes and Endocrinology Clinic at Colombo South Teaching Hospital (CSTH). A total of 343 female patients aged between 40 and 79 years with T2D who attended the clinic between October 2021 and February 2022 were recruited for the study. Patients with type 1 diabetes; other chronic severe illnesses, such as cancer and thyroid dysfunction; a history of CVD complications (stable and unstable angina; myocardial infarction; heart failure; coronary artery bypass graft; coronary angioplasty/stenting; and stroke); pregnant or lactating women; and estrogen replacement therapy and hysterectomy women were excluded from the study. An information sheet was provided regarding the study to all participants in their preferred languages (English, Sinhala or Tamil), and written informed consent was subsequently obtained from the patients prior to the study. The present study was approved by the ethical review committee of CSTH.

Data collection

Data related to sociodemographic and clinical characteristics, such as age, reproductive data, family history of DM and CVD, smoking status and diabetes duration, were collected using interviewer-administered questionnaires and medical records. Biochemical data such as fasting plasma glucose (FPG), total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and HbA1c were obtained from routine clinical investigations conducted at the biochemistry laboratory at CSTH. Anthropometric data, including height, weight, waist circumference and hip circumference, were measured by trained investigators according to WHO guidelines. Blood pressure measurements, including systolic blood pressure (SBP) and diastolic blood pressure (DBP), were collected by medical officers at the clinic. We classified the 293 patients into premenopausal (n = 71), postmenopausal (< 5 years; n = 56) and postmenopausal

(≥ 5 years; n = 166) groups based on their menopausal status and time since menopause.

CVD risk factors

Subjects were classified as dyslipidemic if the following criteria were met: total cholesterol level ≥ 240 mg/dL, LDL-C level ≥ 130 mg/dL, triglycerides level > 150 mg/dL and HDL-C level < 40 mg/dL. In addition, individuals on lipid-lowering medications were also considered to have dyslipidemia [14]. Hypertension was defined as an SBP ≥ 140 mmHg, a DBP ≥ 90 mmHg, and a known hypertensive status or use of antihypertensive drugs [15]. Overweight was defined as a body mass index (BMI) ≥ 25 kg/m^2, and obesity was defined as a BMI ≥ 30 kg/m^2 [16]. Central obesity in women was defined as a waist circumference (WC) > 80 cm and/or a waist–hip ratio (WHR) ≥ 0.85 cm as a substantially increased risk of CVD [17]. CVD risk was calculated using the FRS and WHO/ISH risk prediction tools.

Two risk assessment tools, namely, the female FRS and WHO/ISH risk prediction charts, were used to predict the 10-year risk of CVD in premenopausal and postmenopausal women with T2D. The WHO/ISH risk prediction charts for Southeast Asian epidemiological subregion B (SEAR B) were used to estimate CVD risk. The individuals were categorized into five risk categories by WHO/ISH risk prediction charts: low risk (< 10%), 10–20%, 20–30%, 30–40% and ≥ 40%. Five parameters, namely, age, total cholesterol (TC) level, SBP, smoking status and diabetes status (yes or no), were used to determine an individual's risk category by the color of each parameter corresponding to the cell on the chart. The level of risk was coded by color [18]. The calculation of CVD risk by the female FRS was based on six parameters, namely, age, TC level, HDL-C level, SBP, smoking status and diabetes status (yes or no). According to the female FRS, a risk point was given for each risk factor category, and the FRS was calculated after summing the risk points for each risk factor. CVD risk percentage (%) was estimated according to the total points [19].

Comparison of two risk assessment tools

To compare the performance of the two risk assessment tools, the patients were categorized into four groups based on WHO/ISH risk prediction chart categorization and the FRS corresponding risk percentage: low risk (< 10%), moderate risk (10–19.9%), high risk (20–29.9%), and very high risk (≥ 30%). The proportions of patients at different risk levels according to the FRS and WHO/ISH risk prediction charts were compared. Agreement in risk categorization with two prediction tools was compared using Cohen's kappa coefficient (κ).

Validity of two risk assessment tools

Elevated LDL-C levels, high DBP, high FPG and elevated HbA1c are important modifiable CVD risk factors in patients with T2D. However, LDL-C, DBP, FPG and HbA1c were not considered CVD risk factors according to either risk assessment tool. Therefore, to compare the validity of the two risk assessment tools, the proportions of patients with elevated LDL-C (≥ 100 mg/dL), high DBP (> 90 mmHg), FPG (≥ 126 mg/dL) and HbA1c (> 7.0%) requiring therapeutic intervention in the four risk categories were estimated for both risk assessment tools [20]. Cut-off values were taken as recommended by the American Diabetes Association (ADA) [21]. The sensitivity and specificity of each risk assessment tool for identifying elevated LDL-C, DBP, FPG and HbA1c levels requiring therapeutic intervention were subsequently calculated.

Statistical analysis

The study population was classified into three categories based on menopausal status and time since menopause: premenopausal and postmenopausal. SPSS ver. 26 (SPSS, Inc., Chicago, IL, USA) was used to analyze the data statistically. All the data are expressed as the mean ± standard deviation (SD) or percentage. One-way ANOVA (for continuous variables) and the chi-square test (for categorical variables) were used to compare the data between different groups. Non-parametric tests were used when the data were not normally distributed.

Results and discussion

This study assessed CVD risk in female patients with T2D using WHO/ISH risk prediction charts and the FRS. WHO/ISH risk prediction charts have been recommended as easy and cost-effective risk assessment tools for predicting future CVD risk. Studies conducted in several countries, including a few South Asian countries, to assess the sensitivity and validity of the FRS have shown that the FRS is more sensitive in predicting future CVD risk [12, 13]. However, the performance of the FRS as a CVD risk assessment tool for predicting future CVD risk among women with T2D has not yet been studied in Sri Lanka.

Demographic and clinical characteristics among women with T2D

All the sociodemographic and clinical characteristics are summarized in Table 1. The variables considered are age, family history of diabetes, family history of CVD, diabetes mellitus duration, weight, BMI,WHR, FPG, total cholesterol, LDL-C, triglyceride, HDL, TC/HDL ratio, LDL/HDL ratio and smoking.

Table 1. Demographic and Clinical Characteristics of Women with T2D in the Three Groups According to Reproductive Status

Variable	Total	Group			P-value*
	n = 293	Premenopausal (n = 71)	Postmenopausal < 5 y (n = 56)	Postmenopausal ≥ 5 y (n = 166)	
Age [years]	55.05 ± 7.56	45.82 ± 4.5[bc]	53.61 ± 4.04[ac]	53.61 ± 4.04[ab]	< 0.001
Family history of diabetes (%)	185 (63.1%)	50 (70.4%)	30 (53.6%)	105 (63.3%)	0.135
Family history of CVD	97 (33.1%)	27 (38.0%)	15 (26.8%)	55 (33.1%)	0.364
Diabetes duration [months]	119.11± 91.15	82.96± 85.94[c]	105.65± 82.81[c]	138.17±91.16[ab]	< 0.001
Weight [kg]	60.96 ± 12.00	62.50 ± 12.50	60.37 ± 8.64	60.50 ± 12.75	0.487
BMI	26.22 ± 5.57	26.54 ± 4.24	25.95 ± 3.56	26.18 ± 5.01	0.697
WHR	0.94 ± 0.05	0.93 ± 0.04	0.94 ± 0.04	0.94 ± 0.05	0.710
FPG [mg/dL]	144.00 ± 57.10	159.66 ± 61.92[c]	145.30 ± 57.77	136.87 ± 53.61[a]	0.014
Total cholesterol [mg/dL]	176.70 ± 43.38	185.86 ± 47.02	177.83 ± 45.56	172.42 ± 40.57	0.070
LDL–C [mg/dL]	99.19 ± 36.89	108.60 ± 41.10[c]	99.04 ± 39.93	95.19 ± 33.24[a]	0.024
TG [mg/dL]	137.82 ± 59.48	149.31 ± 64.68	143.44 ± 59.97	131.36 ± 56.36	0.103
HDL [mg/dL]	49.85 ± 14.99	46.66 ± 8.92	50.30 ± 10.96	51.06 ± 17.83	0.110
TC/HDL ratio	3.69 ± 1.00	4.05 ± 1.02[bc]	3.62 ± 0.97[a]	3.55 ± 0.96[a]	< 0.001
LDL/HDL ratio	2.08 ± 0.83	2.38 ± 0.93[bc]	2.02 ± 0.87[a]	1.97 ± 0.76[a]	< 0.001
Hypoglycemic agents (oral drugs)	283 (93.6%)	69 (97.2%)	55 (98.2%)	159 (95.8%)	0.677
Hypoglycemic agent (insulin injection)	85 (29%)	18 (25.4%)	13 (23.2%)	54 (32.5%)	0.236
Antihypertensive	185 (63.1%)	29 (40.8%)	33 (58.9%)	123 (74.1%)	<0.001
Lipid modulators	232 (79.2%)	44 (62.0%)	43 (76.8%)	145 (87.3%)	<0.001
Smoking	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

[a]Compared with the premenopausal group, p < 0.05; [b]Compared with the postmenopausal < 5 y group, p < 0.05; [c]Compared with the postmenopausal ≥ 5 y group, p < 0.05; *Compared among groups; BMI — body mass index; CVD — cardiovascular disease; FPG — fasting plasma glucose; HDL — high--density lipoprotein; LDL — low-density lipoprotein; TC — total cholesterol; TG — triglycerides; WHR — waist-hip ratio

CVD risk factors among women with T2D

According to the present study findings, the prevalence of dyslipidemia, increased LDL cholesterol levels, hypertriglyceridemia, low HDL cholesterol, hypertension, obesity and overweight, central obesity and smoking among T2D patients were 25.9%, 41.3%, 33.1%, 19.5%, 54.9%, 50.8%, 98% and 0%, respectively. The prevalence of elevated LDL cholesterol levels, hypertriglyceridemia, hypertension, obesity/overweight and central obesity was high among the studied population, but the majority of the patients were receiving hypotensive drugs (63.1%) and lipid modulators (79.2%). This discrepancy may be attributed to multiple factors, including poor adherence to therapeutic agents, inappropriate dietary habits, sedentary lifestyles and poor clinical attention due to the COVID-19 pandemic. It is well known that the hormone estrogen plays a protective role in preventing CVD events in healthy nonmenopausal women by controlling LDL cholesterol levels [22]. However, according to the current study, the incidence of dyslipidemia, elevated LDL cholesterol, hypertriglyceridemia and low HDL cholesterol was considerably greater among premenopausal women than among postmenopausal women (Fig. 1). This may be due to elimination of the beneficial effect of estrogen due to metabolic changes of T2D [10] which is further aggravated by the poor adherence to therapeutic agents and inappropriate lifestyle and due to COVID-19 lockdown period.

Comparison of the two assessment tools

This study showed that the WHO/ISH risk prediction chart categorized the majority of subjects in the low-risk category (78.8%), while the FRS categorized only 23.2% in the low-risk category. However, in the high-risk subgroup (≥ 30%), both tools were consistent and identified a similar proportion of patients (4.8% [14/293] vs. 7.2% [21/293]) (Tab. 2).

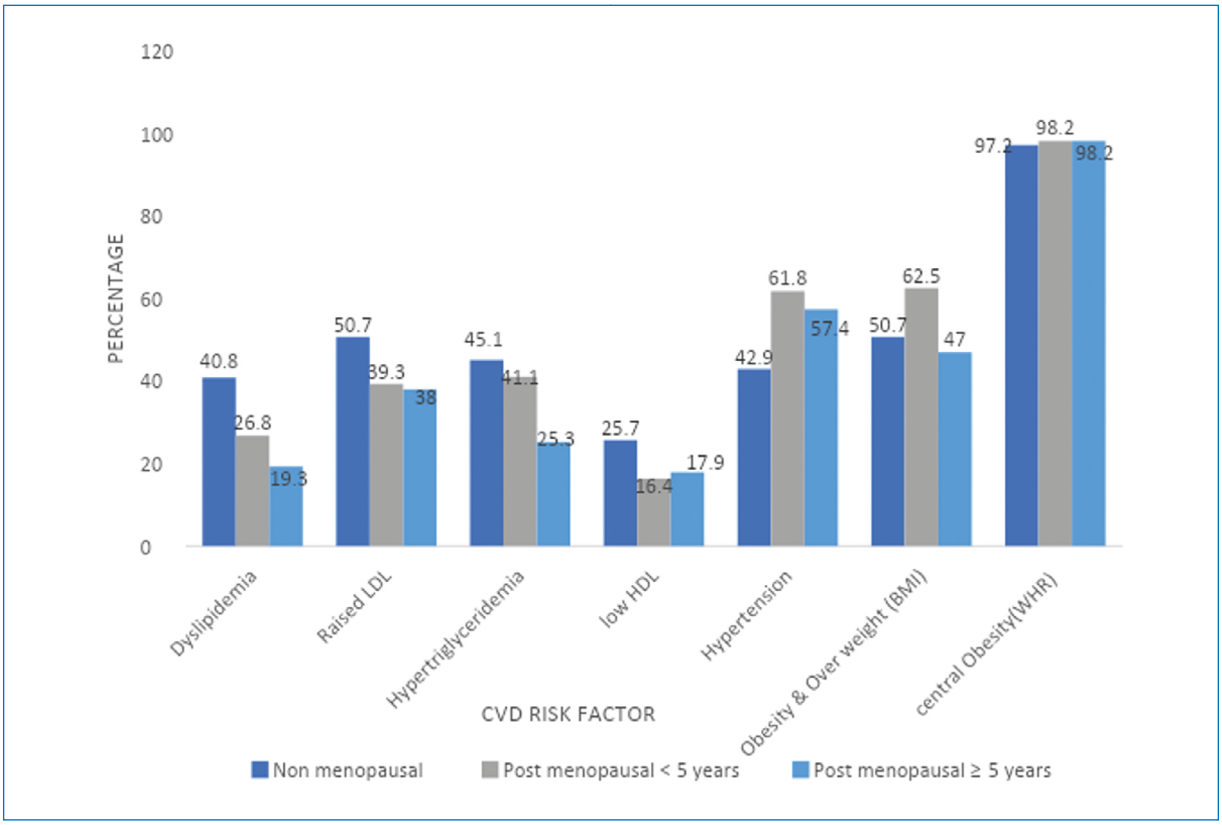

Figure 1. Prevalence of CVD Risk Factors among Women with T2D in One of Three Reproductive States
BMI — body mass index; CVD — cardiovascular disease; HDL — high-density lipoprotein; LDL — low-density lipoprotein; T2D — type 2 diabetes; WHR — waist–hip ratio

Table 2. Comparison of the Categorization of Women with T2D according to the FRS and WHO/ISH Risk Tools

Category	WHO/ISH		FRS	
	Frequency	Percent	Frequency	Percent
Low risk (< 10%)	231	78.8%	68	32.2%
Moderate risk (10–19.9%)	42	14.3%	143	48.8%
High risk (20–29.9%)	6	2.0%	61	20.8%
Very high risk (≥ 30%)	14	4.8%	21	7.2%
Total	293	100%	293	100%

FRS — Framingham risk score; ISH — International Society of Hypertension; T2D — type 2 diabetes; WHO — World Health Organization

The FRS categorizes the highest proportion (48.8%) of subjects in the moderate-risk category. Similarly, a study conducted in Sri Lanka revealed that according to WHO/ISH data, the highest proportion of patients were categorized in the low-risk category [20]. Similarly, several studies have reported that a greater proportion of patients are categorized in the low-risk subgroup according to the WHO/ISH criteria than according to other risk prediction tools. [23–25]. Thus, the categorization of a high proportion of women as having low cardiac risk may be mainly due to the poor ability of WHO/ISH charts to identify high-risk individuals. Even though WHO/ISH charts are considered a cost-effective tool for assessing future CVD risk in developing countries, these charts might underestimate the CVD risk of women with T2D irrespective of their reproductive stage. As reported in the present study, the FRS categorizes most patients in the moderate risk category. Selvarajah et al., 2014 [25], recommended the FRS to assess CVD risk in women in Malaysia and reported that

Table 3. Validation of the WHO/ISH and FRS Charts by LDL, DBP, FPG and HbA1c Levels

	LDL (> 100 mg/dL)		DBP (> 90 mmHg)		FPG (> 126 mg/dL)		HbA1c (> 7.5%)	
	WHO/ISH (%)	FRS (%)	WHO/ISH (%)	FRS (%)	WHO/ISH (%)	FRS (%)	WHO/ISH (%)	FRS (%)
Low risk (< 10%)	80.2	14.0	81.2	7.1	79.2	26.2	65.9	17.1
Moderate risk (10–19.9%)	14.9	56.2	10.6	49.4	12.9	49.0	22.0	61.0
High risk (≥ 20%)	5	36	8.2	43.5	7.9	24.8	9	22.0
Sensitivity	20	86	19	93	21	74	34	83
Specificity	78	30	86	30	78	16	79	36

DBP — diastolic blood pressure; FPG — fasting plasma glucose; FRS — Framingham risk score; HbA1c — glycated hemoglobin; ISH — International Society of Hypertension; LDL — low-density lipoprotein; WHO — World Health Organization

the FRS can be used to categorize high-risk patients more accurately than can the WHO/ISH risk prediction charts. Most of the studies conducted on the FRS have shown that it accurately categorizes CVD risk among the population. However, few studies have concluded that the FRS overestimates CVD risk [26]. According to the current study, there was a significant disagreement between WHO/ISH risk prediction charts and the FRS in predicting future CVD risk, as the kappa value was 0.068 ($p < 0.05$). This finding was supported by several other studies conducted among the Asian population [24, 25, 27].

Validation of the two assessment tools

The present study validated the use of risk prediction tools by demonstrating that individuals with elevated LDL, high DBP, high FPG and high HbA1c need therapeutic intervention (Tab. 3). The WHO/ISH risk prediction charts failed to identify the majority of the patients with elevated LDL, high FPG, high DBP and poor control of blood glucose (high HbA1c) as high--risk individuals, while the FRS categorized the majority of individuals as moderate/high risk. WHO/ISH charts had poor sensitivity and high specificity for all four validation methods. Thus, if the therapeutic interventions are decided alone by WHO/ISH charts, most of the women who require therapeutic interventions will be advised against the treatment. These findings are comparable to the results of a study conducted in Sri Lanka. [20]. In contrast, the present study revealed that the FRS is able to categorize the majority of patients with CVD risk factors into moderate (10–19.9%) and high risk (≥ 20%) categories by indicating the need for therapeutic intervention, unlike the WHO/ISH, which completely underestimates high-risk subjects into the low-risk category. The sensitivity of the FRS for all four validation methods was high, but the specificity was low. Even though the FRS showed better performance than did the WHO/ISH score, six risk factors were common to both risk prediction tools. Thus, the high sensitivity of the FRS could be attributed to the use of a more comprehensive CVD risk definition and the inclusion of HDL cholesterol levels for risk calculations. This could be further explained by the high prevalence of women with low HDL cholesterol among the studied population. In this study, it was revealed that CVD risk is significantly greater among postmenopausal women than among premenopausal women. Moreover, Yang et al. [28] reported that postmenopausal women had a significantly greater risk of both fatal and nonfatal CVD compared with premenopausal women. This study has several limitations. The present study was conducted in a cohort of women with T2D registered at the Diabetes and Endocrinology Clinic at CSTH. Thus, the findings cannot be generalized to other groups in Sri Lanka, as the study was based on data from a single center. Neither tool we utilized to assess CVD risk among women with T2D was specifically designed to assess CVD risk among diabetes patients.

Conclusions and future directions

Even though the majority of patients in the study population were receiving therapeutic interventions, the prevalence of major CVD risk factors was high among the studied women with T2D. Close monitoring and proper adherence to treatment modalities along with appropriate lifestyle changes will reduce the prevalence of CVD risk factors. The CVD risk is higher in women who experienced menopause than in premenopausal women. Further studies on sex hormone levels are recommended to determine the mechanism underlying the high CVD risk among postmenopausal women. There is a significant discrepancy between WHO/ISH risk prediction charts and the FRS in predict-

ing CVD risk among women with T2D. The WHO/ISH risk prediction charts underestimate high-risk women, while the FRS is able to identify high-risk women who require therapeutic interventions. The FRS can be used to predict CVD risk and initiate therapeutic interventions in the clinical setting. However, the tool must be validated by large-scale multicenter studies with greater numbers of participants. In addition, a sensitive, cost-effective tool specific for T2D, which can easily be used in a low-resource setting to accurately identify high-risk individuals, should be identified or designed for the female population with diabetes, considering reproductive risk factors.

Article information

Ethical consideration

This study was approved by the ethical review committee of Colombo South Teaching Hospital, Kalubowila, Sri Lanka, and followed the guidelines of the Declaration of Helsinki.

Data availability

The raw quantitative datasets used to support the findings of this study are deidentified participant data and are available from the corresponding author upon reasonable request. Please contact Ms. PK Weerawickrama.

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Author contributions

This manuscript is a revised and updated version of the final year thesis of PK Weerawickrama, WMCP Weerasinghe, and IKAS Fernando. AMDS Karunarathna, Chaminda Garusinghe, PK Weerawickrama, WMCP Weerasinghe and IKAS Fernando participated in the design and conception of the study. PK Weerawickrama, WMCP Weerasinghe & IKAS Fernando conducted the study and acquired the data. PK Weerawickrama, WMCP Weerasinghe and IKAS Fernando entered the data into the statistical software and cross-checked for any errors. AMDS Karunarathna & PK Weerawickrama analyzed the data, performed the statistical analysis and, together with Chaminda Garusinghe, contributed to the data interpretation. AMDS Karunarathna and PK_Weerawickrama wrote the paper. All the authors participated in reviewing and revising the manuscript and approved the final version. PK Weerawickrama is responsible for the integrity of the work as a whole and serves as guarantor of this work.

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Conflict of interest

The authors declare no conflict of interest.

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Shuichi Okada[1], Kazuya Okada[2], Junichi Okada[3], Koji Kikkawa[1], Eijiro Yamada[4], Tsugumichi Saito[4], Tetsuro Andou[1], Kihachi Ohshima[1]

[1]Hidaka Hospital, Gunma, Japan
[2]Department of Orthopedic Surgery, Tone Chuo Hospital, Numata, Gunma, Japan
[3]Department of Medicine, Division of Endocrinology, Albert Einstein College of Medicine, New York, United States
[4]Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Gunma, Japan

Inverse Correlation between Free Triiodothyronine to Free Thyroxine Ratio and Dietary Sodium Intake in Patients with Type 2 Diabetes Taking Dipeptidyl Peptidase 4 Inhibitors: A Retrospective Cohort Study

ABSTRACT

Objective: This clinical study investigated the hypothesis that patients with type 2 diabetes (T2D), who consume more dietary sodium while taking dipeptidyl peptidase 4 inhibitors (DPP4is), would demonstrate increased iodothyronine deiodinase-2 activity, elevating the free triiodothyronine to free thyroxine ratio.

Materials and methods: This study included 157 patients with T2D. Dietary salt intake was estimated following Tanaka's formula. Pearson's correlation coefficients were calculated to estimate the linear correlations between variables.

Results: The DPP4i and non-DPP4i groups included 58 (female/male = 15/43) and 99 participants (female/male = 37/62), respectively. The patient characteristics of the DPP4i versus non-DPP4i groups were as follows: mean age (years): 70.2 ± 10.7 versus 68.3 ± 11.7; mean T2D duration (years):16.8 ± 10.9 versus 16.5 ± 12.7; mean thyroid-stimulating hormone (μU/mL): 2.04 ± ± 1.75 versus 2.036 ± 1.381; mean free triiodothyronine (FT3) (pg/mL): 2.792 ± 0.378 versus 2.741 ± 0.402; free thyroxine (FT4) (ng/dL): 1.08 ± 0.216 versus 1.134 ± 0.237; FT3/FT4 ratio: 2.569 ± 0.487 versus 2.486 ± 0.486; sodium intake (g/day): 10.4 ± 2.911 versus 10.41 ± 2.671. The free triiodothyronine to free thyroxine ratio was inversely correlated with dietary sodium intake in the DPP4i group (r = −0.444) but demonstrated no correlation with dietary sodium intake in the non-DPP4i group (r = −0.153).

Conclusions: The results are different from those of mouse adipose tissue, but DPP4is may affect iodothyronine deiodinase-2 activity in patients with T2D under certain conditions. Clinicians should pay close attention to DPP4i intake and dietary sodium consumption when estimating the iodothyronine deiodinase activity of patients with T2D. (Clin Diabetol 2024; 13, 2: 101–105)

Keywords: type 2 diabetes, iodothyronine deiodinase-2, free triiodothyronine to free thyroxine ratio, sodium intake, dipeptidyl peptidase 4 inhibitor

Address for correspondence:
Shuichi Okada
Hidaka Hospital, 886 Nakao-machi, Takasaki, Gunma 370-0001, Japan,
e-mail: okadash1823@gmail.com,
phone: +81-27-362-6201
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Introduction

Liraglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), increases type 2 iodothyronine deiodinase (DIO2) activity without significantly up-regulating its mRNA levels in mouse adipose tissue [1]. A study revealed that oral sodium loading increases endogenous glucagon-like peptide-1 (GLP-1) levels in humans [2], whereas our previous study demonstrated that patients with type 2 diabetes (T2D) who received increased dietary sodium intake exhibited improved dipeptidyl peptidase 4 inhibitors (DPP4i) effects on glycemic control [3].

The free triiodothyronine (FT3) to free thyroxine (FT4) ratio (FT3/FT4 ratio) is considered an index of type 1 iodothyronine deiodinase (DIO1) and DIO2 activities [4–6]. Therefore, this clinical study investigated the hypothesis that patients with T2D consuming more dietary sodium while taking DPP4i would demonstrate increased DIO activities, causing elevated FT3/FT4 ratio.

Materials and methods

Participants

The Institutional Review Board of Hidaka Hospital approved our study protocol that conformed to the principles stated in the Declaration of Helsinki (1964) (#336). Each participant signed written informed consent.

We excluded participants who had ever been diagnosed with hypertension with or without antihypertensive medication because they were instructed to reduce dietary sodium intake. Additionally, changes were not made to the prescriptions during the observation period. Moreover, this study excluded participants with an estimated glomerular filtration rate of < 45 mL/min/1.73 m^2 as well as those taking GLP-1 RA because the ligand level to the GLP-1 receptor reached a nonphysiologically high level.

Thus, this study included 157 patients with T2D and no previously diagnosed hypertension who visited our hospital from December 2021 to December 2022.

Estimation of the dietary sodium intake

Dietary salt intake was estimated according to Tanaka's formula [7]. Tanaka's formula is a method for estimating 24-h sodium excretion using urine samples at any time. It is used to evaluate salt intake in patients with hypertension and for salt reduction guidance.

Specifically, first, calculate the 24-h urinary creatinine excretion (mg/day) from the formula {[weight (kg) × 14.89] + [height (cm) × 16.14] (age × 2.043) 2244.45. Afterward, calculate the 24-h urinary Na excretion (mEq/day) by {21.98 × [urinary Na (mEq/L) at any time ÷ urinary creatinine (mg/dL) at any time ÷ ÷ 10 × 24-hour urinary creatinine excretion] ^ 0.392}. Finally, the estimated daily salt intake (g/day) was calculated from {24-hour urine Na divided by 17}.

Sample size

The sample size was calculated, considering a statistical power of 0.80, a of 0.05, and an effect size of 0.361. The resulting sample sizes were individuals for the outcomes. Therefore, our study required 58 samples for the DPP4i group.

Statistical analysis

All statistical data were analyzed using Statistical Package for the Social Sciences software (version 10.0, SPSS Inc., Chicago, IL, USA). All numerical values are expressed as means ± SD. Dunnett's test was used for multiple comparisons of variables. Analysis of variance and Wilcoxon rank-sum test were used to compare continuous variables by group for non-normally distributed data. We calculated Pearson's correlation coefficients to estimate the linear correlation between variables. All tests for significance and the resulting p-values were two-sided, with a level of significance set at 5%.

Results

Participant characteristics

The majority of the subjects were male, accounting for 74.1% and 62.6% of the DPP4i (N = 58) and non-DPP4i groups (N = 99), respectively. The patient characteristics in the DPP4i and non-DPP4i groups were as follows: mean age (years): 70.2 ± 10.7 versus 68.3 ± ± 11.7; mean T2D duration (years): 16.8 ± 10.9 versus 16.5 ± 12.7; mean body mass index (kg/m^2): 24.5 ± 3.4 versus 24.7 ± 16.2; mean systolic blood pressure (mmHg): 133.2 ± 15.6 versus 134.1 ± 16.2; mean diastolic blood pressure (mmHg): 71.3 ± 11.7 versus 72.3 ± 11.0; mean serum creatinine level (mg/dL): 0.90 ± 0.28 versus 0.85 ± 0.32; mean casual triglyceride level (mg/dL): 152.1 ± 86.7 versus 164.1 ± 98.5; mean high-density lipoprotein cholesterol level (mg/dL): 53.0 ± 12.7 versus 60.2 ± 19.0; mean low-density lipoprotein cholesterol level (mg/dL): 105.6 ± 30.5 versus 111.7 ± 32.6; mean casual plasma glucose level (mg/dL): 163.6 ± 50.1 versus 153.6 ± 56.6; mean glycated hemoglobin level (%): 6.7 ± 1.0 versus 6.8 ± 0.8; mean thyroid-stimulating hormone (TSH) (μU/mL): 2.04 ± 1.75 versus 2.036 ± 1.381; mean free triiodothyronine (FT3) (pg/mL): 2.792 ± 0.378 versus 2.741 ± 0.402; mean free thyroxine (FT4) (ng/dL): 1.08 ± 0.216 versus 1.134 ± 0.237; FT3/FT4 ratio: 2.569 ± 0.487 versus 2.486 ± 0.486; sodium intake (g/day): 10.4 ± 2.911 versus 10.41 ± 2.671. The dif-

ference in characteristics between the two groups is statistically not significant.

Proportion of patients prescribed antidiabetic medications

Among those in the DPP4i and non-DPP4i groups, sodium-glucose cotransporter 2 inhibitors (SGLT2is) were prescribed to 42.4% and 46.6%, glinides to 22.2% and 13.8%, sulfonylureas to 22.2% and 8.6%, α-glucosidase inhibitors to 11.1% and 6.9%, thiazolidinediones to 1.0% and 0%, to biguanides 30.3% and 20.7%, and GLP-1 receptor analogs (GLP-1 RAs) to 0.0% and 0.0%. Insulin was administered in 10.0% and 25.9% and imeglimin in 12.1% and 6.9% of the DPP4i and non-DPP4i groups, respectively.

Proportion of patients prescribed DPP4i

Sitagliptin, vildagliptin, linagliptin, teneligliptin, alogliptin, and anagliptin were administered in 58.0%, 18.0%, 16.0%, 4.0%, 2.0%, and 2.0% of patients, respectively. Statins were prescribed in 37.4% and 25.8% of the patients and proton-pump inhibitors in 3.0% and 3.2% of the DPP4i and non-DPP4i groups, respectively.

Analysis of multiple comparisons for factors affecting the FT3/FT4 ratio

Table 1 shows that sodium intake was independently associated with the FT3/FT4 ratio but not associated with TSH, FT3, and FT4 levels in the DPP4i group. Conversely, sodium intake was not associated with TSH, FT3, FT4, and FT3/FT4 ratios in the non-DPP4i group.

Relationship between the FT3/FT4 ratio and dietary sodium intake in the DPP4i and non-DPP4i groups

Figure 1 shows the regression coefficients for the univariate linear regression analysis between the FT3/FT4 ratio and dietary sodium intake in the DPP4i and non-DPP4i groups. The FT3/FT4 ratio was inversely correlated with dietary sodium intake in the DPP4i group ($r = -0.444$) (Fig. 1A) but not in the non-DPP4i group ($r = -0.153$) (Fig. 1B).

Discussion

Thyroid hormone deiodinases consist of a dynamic system whose components synergistically act to ultimately maintain thyroid hormone signaling to the greatest extent possible in the serum and intracellular environment, thereby supporting thyroid function concerning various demands of the organism in physiological and pathological contexts [8]. The FT3/FT4 ratio is an index of DIO1 and DIO2 activities [4–6].

Studies have revealed that liraglutide, a GLP-1 RA, increases DIO2 activity in mice [1]. However, oral sodium loading increases endogenous GLP-1 levels in humans [2]. Consistent with these results, we previously revealed that patients with T2D who had increased dietary sodium intake demonstrated heightened DPP4i

Table 1. Participant Characteristics

	DPP4i group	Non-DPP4i group
N	58	99
Gender [F/M]	15/43	37/62
Age [years]	70.2 ± 10.7	68.3 ± 11.7
Type 2 diabetes duration [years]	16.8 ± 10.9	16.5 ± 12.7
Body mass index [kg/m^2]	24.5 ± 3.4	24.7 ± 16.2
Systolic blood pressure [mmHg]	133.2 ± 15.6	134.1 ± 16.2
Diastolic blood pressure [mmHg]	71.3 ± 11.7	72.3 ± 11.0
Serum creatinine [mg/dL]	0.90 ± 0.28	0.85 ± 0.32
Casual triglyceride [mg/dL]	152.1 ± 86.7	164.1 ± 98.5
High-density lipoprotein cholesterol [mg/dL]	53.0 ± 12.7	60.2 ± 19.0
Low-density lipoprotein cholesterol [mg/dL]	105.6 ± 30.5	111.7 ± 32.6
Casual plasma glucose [mg/dL]	163.6 ± 50.1	153.6 ± 56.6
Glycated hemoglobin [%]	6.7 ± 1.0	6.8 ± 0.8
Thyroid stimulating hormone [mU/mL]	2.04 ± 1.75	2.036 ± 1.381
Free triiodothyronine [pg/mL]	2.792 ± 0.378	2.741 ± 0.402
Free thyroxine [ng/dL]	1.08 ± 0.216	1.134 ± 0.237
Free triiodothyronine to free thyroxine ratio	2.569 ± 0.487	2.486 ± 0.486
Sodium intake [g/day]	10.4 ± 2.911	10.41 ± 2.671

All numerical values are expressed as means ± standard deviation; DPP4i — dipeptidyl peptidase 4 inhibitor

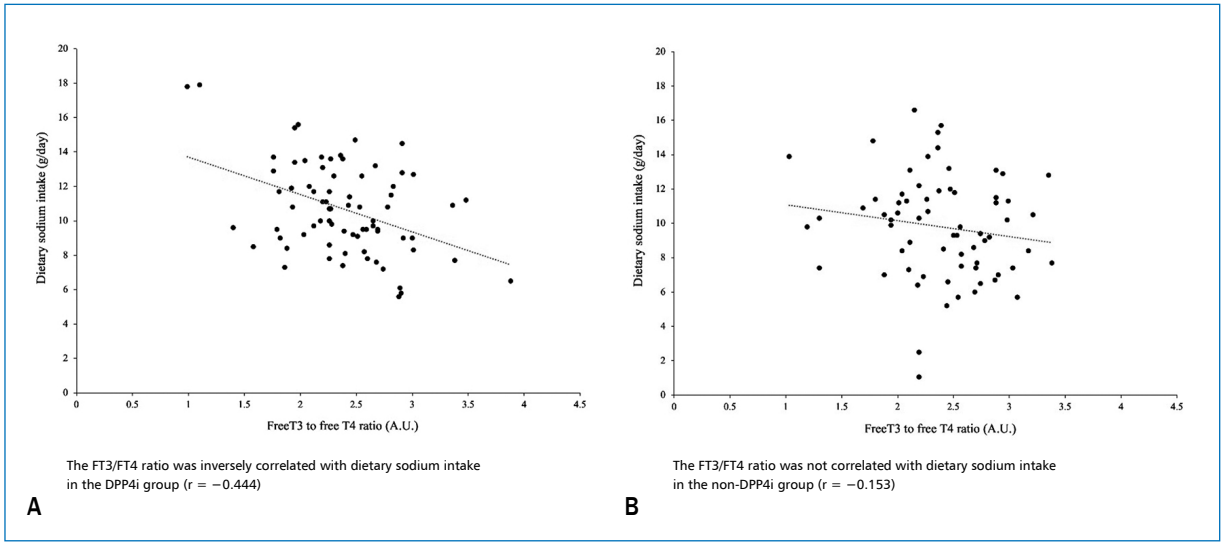

Figure 1. Relationship between the Free Triiodothyronine to Free Thyroxine Ratio (FT3/FT4 Ratio) and Dietary Sodium Intake in **A**. the DPP4 Inhibitor (DPP4i) and **B.** Non-DPP4i Groups. DPP4 — dipeptidyl peptidase 4

Table 2. Multiple Regression Analysis of the Relationship between Sodium Intake and Associated Thyroid Hormones

	DPP4i group		non-DPP4i group	
	p-value	r-value	p-value	r-value
Thyroid stimulating hormone	0.822	0.023	0.644	0.067
Free triiodothyronine	0.483	−0.062	0.343	−0.118
Free thyroxine	0.324	0.148	0.455	0.067
Free triiodothyronine to free thyroxine ratio	0.011	−0.444	0.011	−0.153

r represents the correlation coefficient; DPP4i — dipeptidyl peptidase 4 inhibitor

effects on glycemic control, based on which we assumed that dietary sodium intake affects endogenous GLP-1 levels and activity [3]. Thus, DPP4 may affect DIO2 activity under certain conditions. Therefore, the current clinical study aimed to investigate the hypothesis that patients with T2D, who consume more dietary sodium while taking DPP4is, would exhibit increased DIO2 activities, causing elevated FT3/FT4 ratios. However, contrary to our hypothesis, the FT3/FT4 ratio was inversely correlated with dietary sodium intake in the DPP4i group (r = −0.444) but not correlated in the non-DPP4i group (r = −0.153). Our results indicate differences between humans and mice as well as DIO2 measurement.

The clinical significance of this study

Clinicians need to determine the blood TSH and T4 levels and do not directly measure T3 to assess thyroid function [9]. However, a recent study has revealed that subclinical variation in the hypothalamic–pituitary–thyroid–axis effector hormone T3 is a crucial and overlooked factor connecting socioeconomic forces, human biology, and aging [9]. Importantly, T4 and TSH levels are poorly associated with free T3 levels. Alternatively, TSH and T4 may not be accurate surrogates of free T3. Thus, measuring T3 levels is recommended in addition to T4 and TSH levels. However, deiodinase produced T3 from T4 [4–6], thus determining a new factor that affects deiodinase activity is important. Concomitant with this line of thought, whether or not dietary sodium intake and DPP4i affect deiodinase activity (FT3 to FT4 ratio) becomes a clinically important issue.

Our study has limitations that warrant further discussion. First, we did not measure GLP-1 levels because we did not obtain blood samples. Second, the sample size was small (N = 157), with limited differences in ethnicity, age, and weight. Therefore, our results are not completely generalizable. Thus, future studies that include a larger

cohort with a wider range of demographic characteristics are warranted to confirm our results. Altogether, our results revealed that clinicians should pay close attention to DPP4i intake and dietary sodium consumption when estimating DIO2 activities in patients with T2D.

Article information

Data availability statement

The datasets generated or analyzed in the current study are available from the corresponding author upon reasonable request.

Ethics statement

The ethics committees at Hidaka Hospital approved our study, which conformed to the Declaration of Helsinki (as #355).

Author contributions

Shuichi Okada, Koji Kikkawa, and Kihachi Ohshima took care of the patient. Shuichi Okada, Kazuya Okada, Koji Kikkawa, Junichi Okada, Eijiro Yamada, Tsugumichi Saito, Tetsuro Andou, and Kihachi Ohshima attended the clinical conferences and made important suggestions for differential diagnosis and therapeutic strategy. Shuichi Okada and Junichi Okada prepared the manuscript.

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Conflict of interest

The authors declare no conflict of interest.

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Vanda Sargautiene[1, 2], Didzis Gavars[2], Renate Ligere[1]
[1]Faculty of Medicine, University of Latvia, Riga, Latvia
[2]E. Gulbis Laboratory, Riga, Latvia

Fecal Calprotectin, Serum Ferritin, and C-Reactive Protein Levels in Individuals with Inflammatory Bowel Disease Concomitant with Type 2 Diabetes: A Retrospective Study

ABSTRACT

Objective: The current study aims to conduct comparative analysis of C-reactive protein (CRP), serum ferritin (SF), and fecal calprotectin (CALP) levels in individuals presenting with both inflammatory bowel disease (IBD) and type 2 diabetes (T2D) in contrast to those with IBD without T2D.

Materials and methods: This retrospective analysis of a laboratory database included 2274 unique individuals diagnosed with IBD categorized into two cohorts: 2125 IBD patients without T2D, and 149 IBD patients with T2D. The differences between groups on a continuous measure were determined using non-parametric Mann-Whitney U test.

Results: The study involved 925 male and 1200 female IBD patients without T2D, with mean ages of 41.6 ± ± 15.1 years for males and 47.1 ± 17.4 years for females. The second cohort involved 51 males and 98 females with IBD and T2D, with mean ages of 58.1 ± ± 13.9 years for males and 64.2 ± 12.1 years for females. Individuals with comorbid IBD and T2D demonstrated elevated levels of CRP and SF compared to those affected by IBD without T2D, with statistical significance observed ($p < 0.05$). An increase in CALP values was found in females afflicted with both IBD and T2D when compared to individuals with IBD without comorbid T2D ($p < 0.01$); however, such an increase was not noted in males.

Conclusions: These findings underscore the need for further research on gender-specific differences and the potential presence of additional inflammatory conditions in individuals with IBD and T2D. (Clin Diabetol 2024; 13, 2: 106–115)

Keywords: type 2 diabetes (T2D), inflammatory bowel disease (IBD), comorbidities, C-reactive protein (CRP), ferritin, fecal calprotectin

Introduction

A recent Danish population-based cohort study revealed an increased risk of type 2 diabetes (T2D) development in individuals with both subtypes of inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), linked to prolonged intestinal inflammation [1]. It has also been suggested that there is a coexistence of IBD and T2D and that a potential link between these two conditions may arise due to dysbiosis of the gut microbiota, disruption of the epithelial barrier and inflammatory processes [2]. Another large IBD cohort study indicates a potential link between T2D in IBD and heightened severity of the disease, elevated utilization of 5-aminosalicylic

Address for correspondence:
Vanda Sargautiene
e-mail: vandasarg@outlook.com
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acid (5-ASA), and increased instances of IBD-related hospitalizations [3].

Fecal calprotectin (CALP) is frequently employed to identify disease activity in IBD [4–6]; its elevated levels have also been seen in individuals with insulin resistance, as well as in individuals with other low-grade chronic inflammatory conditions such as obesity and T2D [7]. Nevertheless, to the best of our knowledge, a comparative analysis of CALP levels in patients with IBD, both with and without T2D, has not been conducted to date.

Routine monitoring of inflammatory biomarkers is recommended for the aforementioned health conditions, as their elevated levels may signal the activity and progression of disease in IBD [4, 9–10], along with potential complications linked to T2D [11]. CRP, a sensitive marker of inflammation, and ferritin, functioning as an iron storage protein and acute phase reactant during inflammation, are frequently elevated in both IBD and T2D [8, 12–14]. Serum ferritin (SF) has been noted as serving as an early indicator of atherosclerosis in a cohort of hypertensive patients with diverse levels of glucose tolerance [15]. An association was observed also between HbA1c and the levels of SF and CRP in individuals with T2D [16].

In light of the fact, that IBD occurs in episodes of inflammation in the gastrointestinal tract, varying in intensity and duration, interspersed with periods of remission [17, 18], whereas in T2D, inflammation tends to persist chronically and systemically, contributing to the development of lasting complications associated with diabetes [19]. Uncertainties persist regarding whether differences in the values of inflammatory biomarkers are discernible among individuals with IBD, with or without concomitant T2D.

Thus, the objective of this retrospective investigation was to conduct comparative analysis of CRP, SF, and CALP levels in individuals presenting with both IBD and T2D in contrast to those with IBD without T2D.

Materials and methods

Study design and participants

This retrospective analysis of a database contrasts laboratory findings between individuals diagnosed with IBD and comorbid T2D against those with IBD without T2D. The studied dataset, comprising laboratory tests and disease records, comes from Latvia's clinical laboratory, "E. Gulbis Laboratory" (EGL), situated in Riga, Latvia. EGL holds accreditation in accordance with international standards LVS EN ISO/IEC 17025 and LVS EN ISO 15189:2013, thereby ensuring the international recognition of their test results. Adherence to rigorous quality control protocols guarantees precise medical test results, mitigating measurement bias and ensuring measurement accuracy. All laboratory tests included in this study adhered to the respective analysis and reagent manufacturers' guidelines.

The laboratory has established branches and offers its services to healthcare providers and patients throughout all areas of Latvia, thereby mitigating the potential bias arising from patients selected from specific regions.

Data generation relied on the EGL database, which documents and stores clinical data obtained during patient laboratory visits. All patient data used in this study were subjected to de-identified measures to protect privacy.

Inclusion criteria

The study enrolled individuals aged 18 years and older who had been registered at the EGL laboratory over a five-year period, from January 1, 2015, to December 31, 2019, and who had been diagnosed with IBD. Diagnoses were identified using the International Classification of Diseases 10 (ICD-10) codes for Ulcerative Colitis (UC) (K51.XX) and Crohn's Disease (CD) (K50.XX). From the cohort of individuals diagnosed with IBD, a subset was identified comprising individuals concurrently diagnosed with T2D, as determined by the ICD-10 code E.11.XX. Accordingly, patients suffering from IBD were divided into two subgroups depending on the presence or absence of T2D.

To ensure the distinctiveness of each patient, a unique identification number was assigned to them during their initial visit to the EGL laboratory. This identifier remained unchanged for all subsequent analyses, facilitating the accurate tracking and differentiation of individual patients within the study.

Ethical approval

The study was designed in accordance with the principles enshrined in the Declaration of Helsinki and was approved by the Research Ethics Committee of the Institute of Cardiology and Regenerative Medicine of the University of Latvia. Patient consent was waived due to all patient data used in this study was anonymized before its use.

Data collection

Laboratory data [20] was extracted from database using specific criteria and filters. Initially, individuals aged 18 and above with IBD were identified within a 5-year timeframe, based on their registration and completion of laboratory blood tests. Each patient in the database was assigned a unique identifier during

their initial visit, ensuring anonymity while enabling continuous tracking across subsequent visits. The investigation focused on analyzing patient demographics (age, gender) and laboratory parameters CRP, SF, CALP. All specified laboratory tests conducted on these subgroups during the specified period were considered.

Statistical data analysis

The age of patient was expressed as a mean of ages recorded at the date of laboratory analysis and assigned to the determined age groups.

Descriptive statistics were described as number of patients for categorical parameters and mean (standard deviation; SD), 95% confidential intervals (95% CI) for distributed continuous parameters.

The Lilliefors test (a modified Kolmogorov-Smirnov test), an empirical distribution function (EDF) omnibus test for the composite hypothesis of normality [21], as well as visual informal assessment of normality methods (quantile-quantile plots, QQplot) were used to test for normality. Measurement data distributed in a non – normal manner was expressed as the median, Inter Quartile Range (IQR). Minimum required sample size to test difference between two groups was calculated by "pwrss" package for R [22]. The differences between two independent groups on a continuous measure were determined using non-parametric Mann-Whitney U test. A p-value of below 0.05 was considered statistically significant.

Tests wherein the outliers were detected and eliminated comprised values which lied outside the boxplot 25^{th} and 75^{th} percentiles multiplied by 1.5 range IQR (from 25^{th} percentile – 1.5* IQR to 75^{th} percentile + 1.5* IQR [23]. Data sets wherein outliers were eliminated did not pass any further modification and proceeded directly in tests.

The outcome of the Mann-Whitney test encompasses a standardized Z-score. Subsequently to the execution of the Mann-Whitney U test on the dataset, the Z-score was utilized for the computation of the correlation coefficient denoted as 'r.' The explication of the derived 'r' value aligns with the interpretation conventions applied to Pearson's correlation coefficient ('r') [24]. The r values were interpreted as follows 0.10–0.29 (small effect), 0.30–0.49 (moderate effect) and ≥ 0.50 (large effect).

Statistical analysis was conducted in R [25]. Figures and data were processed using R packages [26–28]. RStudio [29] was used for Integrated Development Environment for R.

Results

Subject characteristics

Among the 2274 unique individuals diagnosed with IBD, 149 had concomitant T2D. The average age varied between genders in the study, with female patients (n = 1298) having an average age of 48 years, while male patients (n = 976) had an average age of 42 years. A comprehensive delineation of age groups among enrolled patients with IBD, classified according to the presence or absence of T2D, is illustrated in Figure 1.

The study comprised 925 male and 1200 female IBD patients without T2D, with mean ages of 41.6 ± 15.1 years (95% CI, 40.60–42.55) for males and 47.1 ± 17.4 years (95% CI, 46.10–48.10) for females.

For IBD patients with T2D, 51 males and 98 females were included, with mean ages of 58.1 ± 13.9 years (95% CI, 54.21–62.06) for males and 64.2 ± 12.1 years (95% CI, 61.80–66.70) for females.

Comparison of serum C-reactive protein values between IBD patients with and without T2D

Regular CRP aids in identifying high-risk individuals and guiding appropriate interventions in IBD and T2D.

In this study, 27,102 CRP analyses were performed on a cohort of 2,126 unique patients diagnosed with IBD without T2D, and 2,862 CRP analyses were carried out on a subgroup of 149 unique IBD patients with concomitant T2D. Graphical representation of the statistics and detailed processed data is plotted in Figure 2.

Our study revealed a statistically significant difference in all CRP values between cohorts ($p < 0.05$), indicating higher CRP levels in patients with IBD and comorbid T2D compared to those with IBD without T2D, median [IQR] CRP 3.10 [1.00–8.88] and 1.50 [0.40–5.70] respectively. The difference persisted after adjusting for outliers, emphasizing higher CRP levels in IBD patients with T2D compared to those without T2D ($p < 0.01$).

A more detailed examination based on gender indicated that within a group of 1200 female patients diagnosed with IBD and without T2D, a total of 15,718 CRP analyses were conducted, yielding a median [IQR] of 1.50 [0.40–5.90]. In a distinct cohort of 98 females diagnosed with both IBD and T2D, a total of 1,797 CRP analyses were carried out, revealing a median [IQR] of 3.70 [1.50–9.20]. Despite small (0.16) effect size, there were significant differences in CRP values in females between IBD subgroups with and without T2D, with a p-value of < 0.01; 95% CI (–1.50; –1.20).

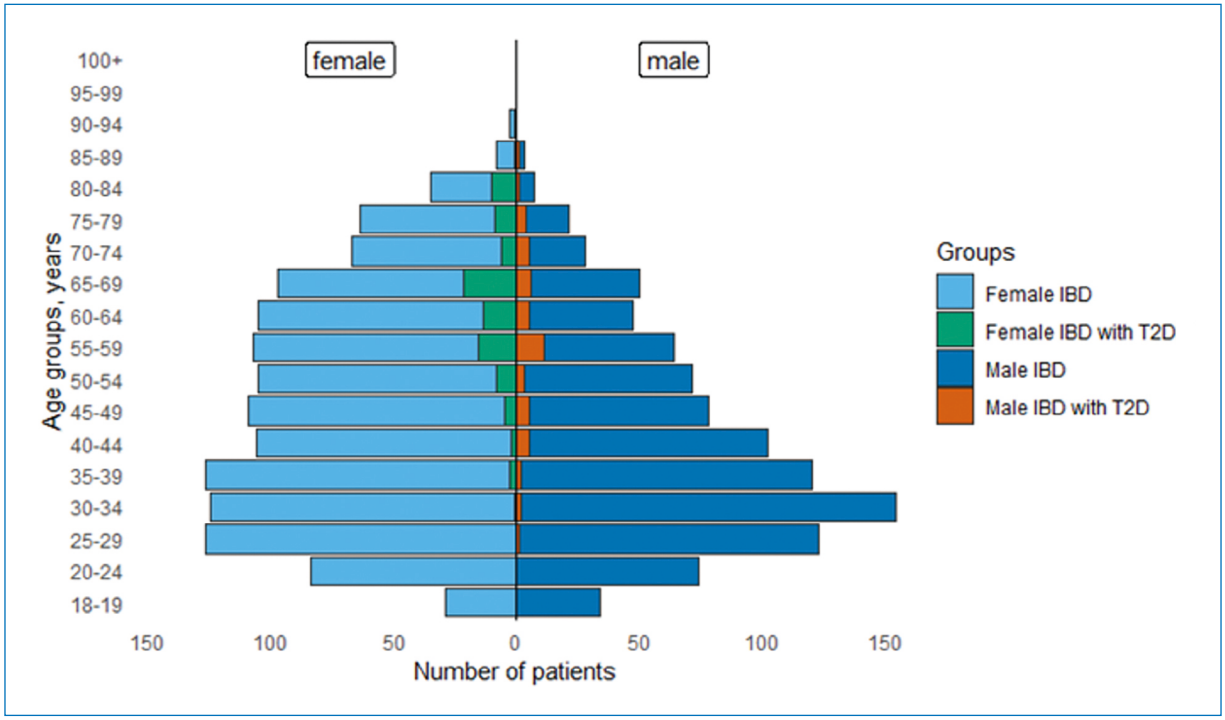

Figure 1. The Total Count of IBD Patients Included in the Study, Categorized Based on Age Groups (Years) and the Presence or Absence of T2D as a Comorbidity
IBD — inflammatory bowel disease; T2D — type 2 diabetes

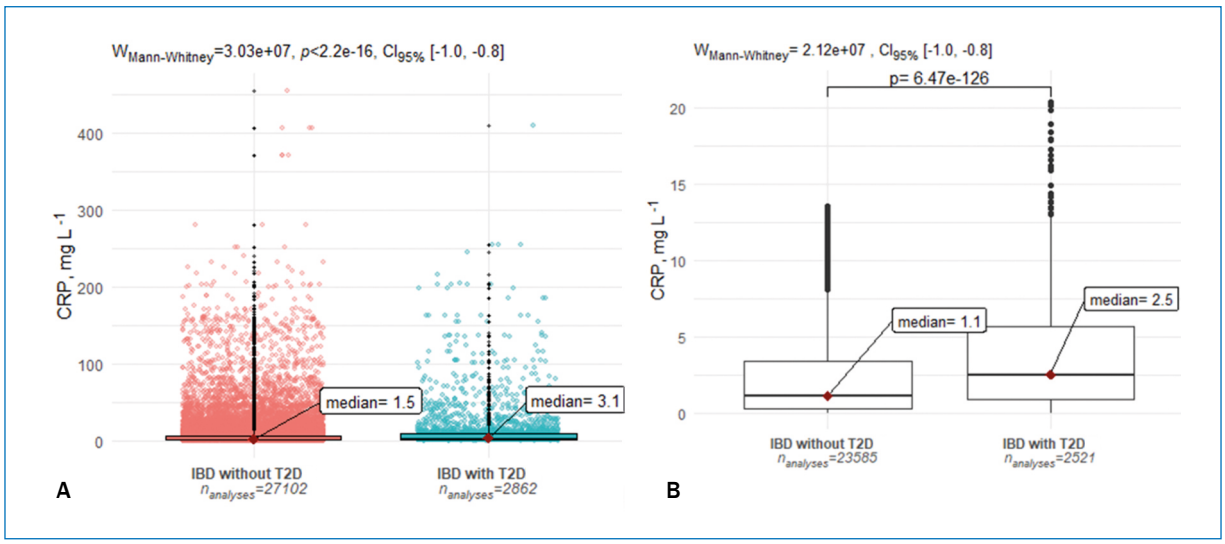

Figure 2. Comparison of Serum CRP Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: IBD patients without T2D and IBD patients with T2D. The complete set of obtained CRP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CRP — C-reactive protein; CI — confidence interval; IBD — inflammatory bowel disease; T2D — type 2 diabetes

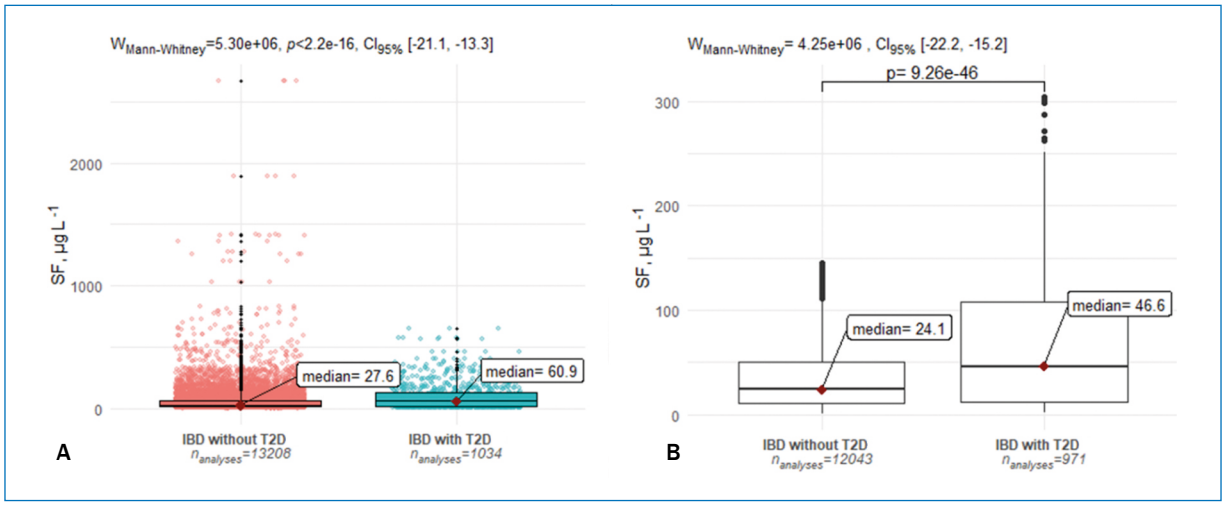

Figure 3. Comparison of SF Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: IBD patients without T2D and IBD patients with T2D. The complete set of obtained CRP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CRP — C-reactive protein; CI — confidence interval; IBD — inflammatory bowel disease; SF —serum ferritin; T2D — type 2 diabetes

Similarly, in 925 male patients with IBD and without T2D, a total of 11 384 CRP analyses were conducted, with a median [IQR] of 1.50 [0.40–5.90]. Among 51 males with IBD and T2D, a total of 1065 CRP analyses were performed, yielding a median [IQR] of 2.00 [0.70–7.40]. Analogously to the observations in females, noteworthy distinctions in CRP values among males across IBD groups with and without T2D were identified, with a p-value of < 0.01 and a 95% CI of (–0.40; –0.10). The effect size was calculated to be 0.04, indicating a small magnitude of impact.

Comparison of serum ferritin values between IBD patients with and without T2D

Similar to the CRP analysis, an elevation in SF levels was observed among patients with IBD and comorbid T2D. The conducted investigation encompassed 13 208 observations within the cohort of 2125 distinct IBD patients without T2D, median [IQR] 27.60 [11.80–65.30]. In the subset of 149 unique patients with IBD and comorbid T2D, there were 1034 observations of SF, median [IQR] 60.90 [12.50–130.00]. Graphical representation of the statistics and detailed processed data is plotted in Figure 3.

Our investigation unveiled a statistically significant differences in all SF values across cohorts ($p < 0.01$), signifying elevated SF levels in individuals with both IBD and comorbid T2D in comparison to those diagnosed with IBD without T2D. This finding persisted after adjusting for outliers, emphasizing higher SF levels in IBD patients with T2D compared to those without T2D ($p < 0.005$).

A more thorough analysis focused on gender revealed that among a cohort of 1200 female IBD patients without T2D, a total of 9105 SF analyses were carried out, resulting in a median [IQR] of 22.40 [10.30–49.50]. In a distinct cohort of 98 females diagnosed with both IBD and T2D, 710 SF analyses were carried out, revealing a median [IQR] of 71.60 [15.43–142.75]. Despite small (0.15) effect size, there were significant differences in SF values in females between IBD subgroups with and without T2D, with a $p < 0.01$; 95% CI (–30.30; –21.20).

Similarly, within a subset of 925 male patients diagnosed with IBD without T2D, a comprehensive 4103 SF analyses were undertaken, revealing a median [IQR] of 47.30 [18.20–108.00]. Among 51 males with IBD and T2D, 324 SF analyses were performed, yielding a median [IQR] of 56.00 [11.40–107.00]. Analogously to the observations in females, noteworthy distinctions in SF values among males across IBD groups with and without T2D were identified, with a *p*-value of < 0.01 and a 95% CI of (–3.10; –5.40). The effect size was calculated to be 0.01, indicating a small magnitude of impact.

Comparison of fecal calprotectin values between IBD patients with and without T2D

For a more comprehensive examination of the inflammatory state among the studied IBD subgroups,

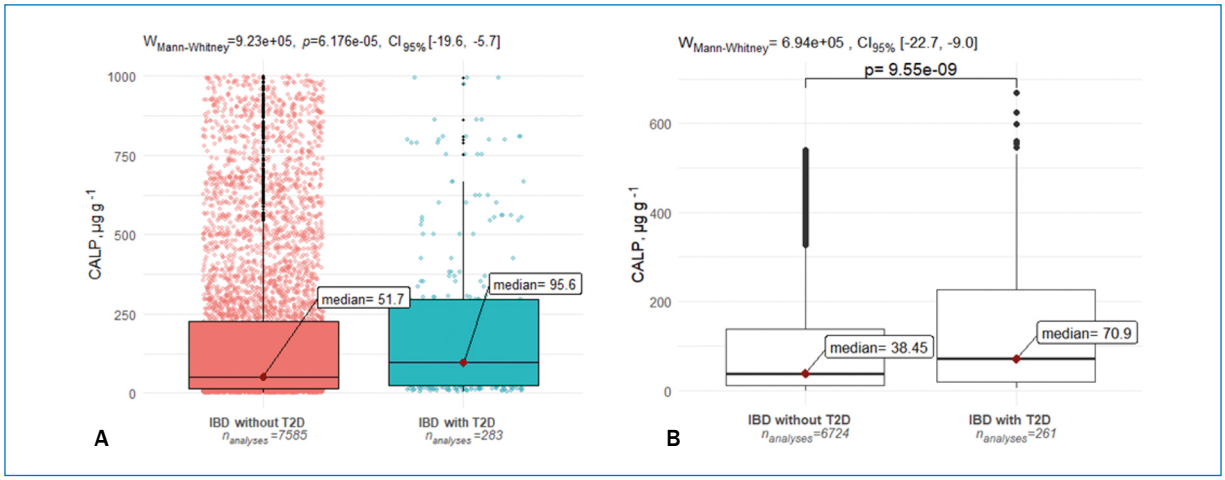

Figure 4. Comparison of Fecal Calprotectin (CALP) Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: one comprising individuals diagnosed with IBD without T2D and the other consisting of individuals with IBD alongside T2D as a comorbidity. The complete set of obtained CALP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CI — confidence interval; IBD — inflammatory bowel disease; T2D — type 2 diabetes

we incorporated fecal CALP, a commonly utilized marker for assessing disease activity in individuals with IBD [5, 7].

In our investigation, elevated CALP levels were noted in individuals with IBD and comorbid T2D. The conducted investigation encompassed 7585 observations within the cohort of 2125 unique IBD patients without T2D, median [IQR] 51.70 [14.20–225.10] μg/g. In the subset of 149 unique patients with IBD and comorbid T2D, there were 283 observations of CALP, median [IQR] 95.60 [23.70–296.00] μg/g.

Graphical representation of the statistics and detailed processed data is plotted in Figure 4.

Our study revealed a statistically significant difference in CALP values between cohorts ($p < 0.005$), indicating higher CALP levels in patients with IBD and comorbid T2D compared to those with IBD alone. This finding persisted after adjusting for outliers, emphasizing higher CALP levels in IBD patients with T2D compared to those without T2D ($p < 0.05$).

A more detailed examination based on gender indicated that within a group of 1200 female patients diagnosed with IBD and without T2D, a total of 4103 CALP analyses were conducted, yielding a median [IQR] of 48.90 [13.90–233.00] μg/g. In a distinct cohort of 98 females diagnosed with IBD and T2D, 185 CALP analyses were carried out, revealing a median [IQR] of 167.30 [27.10–301.30] μg/g. Despite small (0.08) effect size, there were significant differences in CALP values in females between IBD subgroups with and without T2D, with a p-value of < 0.01; 95% CI (–56.50; –12.90).

Similarly, in 925 male patients with IBD and without T2D, 3482 CALP analyses were conducted, with a median [IQR] of 53.40 [14.63–220.00] μg/g. Among 51 males with IBD and T2D, a total of 98 CALP analyses were performed, yielding a median [IQR] of 36.90 [16.80–134.00] μg/g. Small effect size (0.003) was observed, and no statistically significant differences in CALP values among males were found between IBD subgroups with and without T2D, with a p-value of 0.85 and a 95% CI of (–6.30; 11.70).

Discussion

According to Latvian health statistics for 2022 [30], 92 187 residents, representing 4.9% of the population, were diagnosed with T2D. In our study, 6.6 % of patients with IBD had T2D as co-morbidity, which is 33% higher than the prevalence of T2D in the general population.

Although a recent study indicates that genetic predisposition to T2D is linked to a reduced likelihood of IBD [31], findings from a Danish nationwide cohort population study suggest an elevated susceptibility to T2D among individuals afflicted with both forms of IBD [1]. It is imperative not to overlook the potential negative impacts of T2D on IBD, as T2D in IBD may be associated with worse disease severity [3]. Hence, despite the absence of a genetic links between the two conditions, further investigations should delve into lifestyle factors, the impact of medications, the composition of intestinal microbiota, and other pertinent variables to elucidate their interplay in comorbid conditions.

The findings from our investigation indicate that 81% of females with IBD and comorbid T2D fall within the age range of 55–94 years, in contrast to only 34% of IBD females without T2D within the same age group. Likewise, among male individuals diagnosed with IBD and comorbid T2D, 65% were situated in the age category exceeding 55 years, contrasting with the inclusion of only 20% of IBD-afflicted female without T2D in the same age bracket. These results are consistent with the official statistical information reported by The Centre for Disease Prevention and Control of Latvia [30], where the prevalence data for T2D in 2022 revealed that 89% of T2D patients fall within the age category of 55 and older [30].

Our cohort of IBD patients with T2D had a limited representation of individuals below the age of 55. However, an alternative study indicates that in younger individuals with a relatively low risk of metabolic diseases, IBD significantly contributes to the pathogenesis of T2D, which underscores the importance of healthcare practitioners being vigilant for potential diabetes development in this population [32].

Our investigation provided a thorough comparative analysis of inflammatory biomarkers, including CRP, SF, and CALP, conducted over a 5-year period in patients with IBD.

Fecal CALP is commonly employed to assess disease activity in individuals with IBD [5]. An elevated CALP level surpassing 250 μg/g is associated with mucosal disease activity, while a threshold of 150 μg/g may prove beneficial in identifying individuals undergoing mucosal healing; conversely, a negative CALP value below 100 μg/g may suggest histological healing [6].

To our knowledge, there are no previous studies comparing the differences in CALP values between IBD people with and without T2D. Although the study results showed statistical differences in CALP values among study groups, a more detailed analysis by gender showed increased CALP values among female subjects with comorbid IBD and T2D, while no such increase was observed in male subgroup. The increased CALP levels in females with concurrent IBD and T2D may suggest a multifaceted origin related to intestinal inflammation and microbiota dysbiosis. A recent study [33], using a novel ex vivo assay demonstrated microbiome-dependent variations in calprotectin metabolism sensitive to amino acid levels. Further exploration into intestinal microbiota composition, its relationship with CALP levels, and the potential impact of gut microbiome on calprotectin metabolism could enhance our comprehension of these interconnections.

Furthermore, there is a need for scientific focus and additional investigations into CALP levels in females with T2D, particularly within the context of gynecological conditions like polycystic ovary syndrome (PCOS), which is recognized for its higher prevalence in individuals with T2D [34]. Consistent with earlier research, a strong correlation was observed between serum calprotectin and fecal calprotectin in individuals with IBD [35]. Studies on females with PCOS suggested that serum calprotectin might be a valuable diagnostic indicator, especially in cases linked to insulin resistance [36]. However, the relationship to fecal calprotectin remains uncertain, requiring additional investigations for a comprehensive understanding.

Our study findings indicated heightened CRP and SF values in IBD patients with comorbid T2D, $p < 0.05$. These results align with those of another large cohort study on IBD [3], wherein individuals with IBD and T2D exhibited increased occurrences of elevated C-reactive protein levels. In people diagnosed with T2D, CRP concentrations typically vary from 4.49 to 16.48 mg/L [37, 38]. In the context of our investigation, the median [IQR] CRP values in IBD patients with T2D were observed to be 3.10 [1.00–8.88] mg/L. CRP levels above 100 mg/L may suggest the presence of infection, rheumatologic diseases, malignancy and various inflammatory conditions, and multiple diagnoses [39]. For those experiencing acute systemic inflammatory response syndromes, the CRP levels can range much higher, reaching from 31.08 to 226.1 mg/L [37]. The latest cross-sectional analysis, conducted among adults aged 50 and above, revealed that individuals diagnosed with Metabolic Syndrome (MetS) exhibited a 34% higher probability of developing atherosclerotic cardiovascular disease (CVD) for every 1 mg/L increase in serum high sensitivity C-reactive protein levels [40]. MetS results from imbalances in calorie intake, energy expenditure, genetic/epigenetic factors, sedentary behavior, diet quality, and gut microbiome composition [41]. Thus, these factors might play a role in the increased CRP levels detected in our study's participants with both IBD and T2D, indicating a potential link with CVD. Consequently, further research investigating the concurrent factors that worsen the condition of IBD is warranted.

In our study, the SF median [IQR] values in patients with IBD, both with and without T2D, were observed to be 60.90 [12.50–130.00] and 27.60 [11.80–65.30] μg/L, respectively. Elevated levels of SF were observed in both male and female patients with IBD who also had comorbid T2D when compared to the IBD group without T2D. SF is a recognized acute-phase reactant, indicative of both acute and chronic inflammation in various systemic diseases [15]. Serving as a biomarker for disease progression, SF independently predicts

diverse clinical outcomes in different patient settings [15]. Moreover, an elevated SF levels, stemming from inflammation, may lead to misleading false-negative outcomes in the diagnosis of iron deficiency (ID), emphasizing the utility of incorporating CRP levels to discern individuals with concurrent inflammation [42].

Therefore, in patients with IBD, the diagnosis of ID is advised through the application of specific thresholds for SF and CRP, including SF threshold of < 30 μg/L in the absence of inflammation (CRP < 5mg/L), and SF threshold of < 100 μg/L in the presence of inflammation (CRP > 5mg/L) [4, 43]. However, SF thresholds to identify ID, iron overload, or low-grade inflammation in distinct subgroups of individuals with T2D remain uncertain [44].

Further research is warranted to explore the potential impact of probiotics, prebiotics, and synbiotics in regulating gut microbiota and their potential implications for inflammation, particularly in comorbid conditions such as IBD and T2D.

Clinical implications and future research directions

The clinical implications derived from the findings of this preliminary investigation suggest that individuals concurrently affected by IBD and T2D tend to exhibit elevated levels of inflammatory biomarkers compared to those solely affected by IBD without comorbid T2D. These findings underscore the necessity for additional prospective studies aimed at investigating gender-specific variances and potential concurrent inflammatory conditions that could exacerbate IBD. Furthermore, the findings underscore the necessity for developing inflammation management strategies tailored to individuals with concurrent conditions such as IBD and T2D. Such strategies should consider the unique physiological and inflammatory profiles of patients with comorbidities to optimize their clinical care and outcomes.

Study limitations

Our study has its limitations, mostly due its retrospective character of analysis. This study was conducted in a single medical laboratory, so analyzes of general data and laboratory tests specific to hospitalized patients with severe illness, complications such as blood loss, or recent surgeries are not available.

There was no possibility to obtain some missing information, such as duration of illness or medications used. The assignment of IBD and T2D diagnoses in the laboratory database was based on ICD-10 codes provided by referring physicians for laboratory tests, but the confirmation of IBD diagnoses through endoscopies or radiological examinations is unknown.

The study findings indicate small effect sizes, which, for clinical significance, warrant validation through additional prospective studies before strong definitive conclusions can be drawn regarding their application in clinical practice.

Despite the retrospective design limitations, our study's strengths lie in the robustness of the biomedical test data sourced from Latvia's largest accredited laboratory, which maintains branches across all regions of the country. Adherence to stringent quality control measures makes it possible to compare this laboratory data with results from other tests and laboratories.

Further studies, employing precise patient selection and subgrouping individuals into categories such as those with Crohn's disease and ulcerative colitis, along with a separate group of patients with T2D without IBD, would be beneficial for understanding baseline variations in biomarkers attributable to each condition independently.

Conclusions

The results obtained from the present preliminary investigation indicate that individuals with comorbidities, such as IBD and T2D exhibit heightened levels of CRP, SF, when compared to individuals affected by IBD without comorbid T2D. An increase in CALP values was identified in females afflicted with both IBD and T2D when compared to individuals with IBD without comorbid T2D; however, such an increase was not noted in males. The potential for worsening inflammatory status in IBD when coexisting with T2D requires consideration, and individualized approach. These findings underscore the need for further prospective studies on gender-specific differences and the potential presence of additional inflammatory conditions, as well as the development of inflammation management strategies for individuals with comorbidities such as IBD and T2D.

Article information

Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Research Ethics Committee of the Institute of Cardiology and Regenerative Medicine of the University of Latvia (LU KRMI ZP sēde 17.11.2020). Ethical review and approval were waived for this study because all patient data used in this study were subjected to pseudo-depersonalization measures to protect privacy. Patient consent

was waived because all patient data used in this study were subjected to pseudo-depersonalization measures to protect privacy.

Author contributions

Conceptualization, V.S and D.G.; methodology, V.S.; software, V.S. and D.G. validation, V.S., D.G. and R.L.; formal analysis, V.S.; investigation, V.S.; data curation, D.G.; writing — original draft preparation, V.S.; writing — review and editing, D.G.,R.L.; visualization, V.S.; supervision, D.G.,R.L. All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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Basem Abbas Ahmed Al Ubaidi[1], Khatoon Jaffar Abdulla[2], Noora Ahmed Al Jenaidi[2], Hussain Abdulla Ali[2], Eman Merza Marhoon[2], Hajar Merza Matar[3], Hawra Ali Shakeeb[4]

[1]Consultant Family Physician (retired)

[2]Sheikh Sabah Health Center, Ministry of Health, Manama, Bahrain

[3]MISR University for Science and Technology, Giza, Egypt

[4]Department of Pathology, Salmaniya Medical Complex, Ministry of Health, Manama, Bahrain

Self-Care Management and Glycemic Control Among Patients with Type 2 Diabetes in Bahrain: A Cross-Sectional Study

ABSTRACT

Objective: This study aimed to evaluate the impact of self-care management on glycemic control in type 2 diabetes patients within primary care facilities in the Kingdom of Bahrain.

Materials and methods: It was a cross-sectional study that enrolled a cohort of 400 individuals diagnosed with type 2 diabetes. Data collection included the administration of the Diabetes Mellitus Self-Management Questionnaire (DSMQ). Statistical analysis was conducted using SPSS software version 24.0. The Chi-square test was employed to compare optimal scores in relation to diabetes self-care, while the Kruskal-Wallis test was utilized to assess the impact of patients' activities, as indicated by DSMQ items, on parameters reflecting HbA1c levels. Additionally, the Spearman rank correlation test was applied to examine the association between knowledge of DSMQ items and HbA1c levels. A statistical significance threshold was set at $p < 0.05$.

Results: The study involved participants with a mean age of 55.6 ± 9.3 years (mean ± standard deviation). Notably, there was a significant negative correlation between DSMQ-16 scores and HbA1c levels ($p = 0.026$). Similarly, a significant negative correlation was observed between dietary control and HbA1c levels ($p = 0.017$). Among the various socio-demographic variables examined, only the duration of diabetes exhibited a significant association with the overall self-care score for diabetes ($p = 0.045$).

Conclusions: The study underscores the paramount importance of dietary control in attaining favorable glycemic outcomes in individuals with diabetes. It emphasizes the crucial role of healthcare providers in delivering precise and comprehensive dietary guidance to all diabetes patients. (Clin Diabetol 2024; 13, 2: 116–123)

Keywords: Bahrain, cross-sectional study, Diabetes Self-Management Questionnaire (DSMQ), HbA1c, type 2 diabetes

Address for correspondence:
Dr. Khatoon Jaffar Abdulla
Consultant Family Physician, Sheikh Sabah Health Center,
Ministry of Health, Manama, Bahrain
e-mail: KAhmed2@health.gov.bh

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Introduction

Type 2 diabetes (T2D) is the most prevalent and clinically significant metabolic disorder, which has recently become a global pandemic and is increasing the healthcare burden worldwide [1]. T2D prevalence has been highest in the countries experiencing rapid epidemiologic transitions, especially in Asia, the Middle East, and North Africa [2]. According to a previous study, the Arab countries with the highest incidence of T2D are the Kingdom of Saudi Arabia (31.6%), Oman (29%), Kuwait (25.4%), Bahrain (25%), and the United Arab Emirates (25%) [3].

According to the American Diabetes Association (ADA), one of the most important strategies for managing diabetes is glycemic control [4]. In clinical practice, optimal long-term control is difficult to achieve as the causes for poor glycemic control in patients with T2D are complex. Patient- and healthcare provider-related factors may both lead to poor glycemic control [5].

Self-care in diabetes has been termed an evolutionary process of increasing knowledge or awareness by learning to cope with the complex nature of diabetes in a social context [6]. According to the ADA Standards of Medical Care in Diabetes, to attain adequate glycemic control, patients must engage in dedicated self-care behaviors across multiple domains, including increase activity levels, change eating patterns, comply with medication regimens, perform self-monitoring of blood glucose, and monitor carbohydrate intake [6, 7]. To reduce diabetes-related morbidity and mortality, patients must follow self-care management [6]. In the Gulf countries, good glycemic control ranges between 11% and 41% and in Bahrain it was found that only 14.8% of patients attending diabetic clinic had good glycemic control [4, 8]. Traditional/cultural lifestyle restrictions in Gulf countries contribute to sedentary behavior which ultimately increases the prevalence of diabetes [4]. Previous research reported age, medication, self-efficacy, and self-care as predictors of glycemic control [9, 10], and very few studies have been conducted in Bahrain among patients with T2D to correlate self-care management with glycemic control. This study evaluated multiple domains of self-care by using Diabetes Mellitus Self-Management Questionnaire (DSMQ). Considering the high prevalence of diabetes and lack of diabetes self-care in Bahrain [3, 11], and with an aim to create awareness, the current study was designed to determine the effect of self-care management (SCM) on glycemic control in patients with T2D at primary care facilities in the Kingdom of Bahrain.

Materials and methods

Study design and population

The present cross-sectional study was conducted at a primary care center in the Kingdom of Bahrain (eight primary centers were included: Sheikh Sabah Health Center in Um Alhassam, Manama; Hamad Town Health Center in Hamad Town; Isa Town Health Center in Isa Town; Naim Health Center in Naim, Manama; Jidhafs Health Center in Jidhafs; Dair Health Center in Dair, Muharraq; Sitra Health Center in Sitra; North Muharraq Health Center in Muharraq) from February 2023 to May 2023. The research assistant screened the potential participant for eligibility using the following inclusion criteria: Adults aged between 25 and 70 years and diagnosed with T2D at least one year before the commencement of data collection. Adults who were newly diagnosed with T2D, known to have type 1 diabetes (T1D), and diagnosed with mental and/or physical disabilities were excluded from the study.

Ethical considerations

Ethical clearance was obtained from the Institutional Research and Ethics Committee in primary care under serial number 17-11-2022 before the commencement of the study. Prior to data collection, a researcher ensured that participants were fully informed about the purpose of the questionnaire, the research objectives, and how their data would be used. The participants clearly explained their voluntary participation and their right to withdraw at any time without consequences and to sign informed consent before participation.

The researcher guaranteed the anonymity of data collected, its storage, transmission, and disposing methods to protect participants' confidentiality. A channel was established for participants to provide feedback on any questionnaire inquiry or raise concerns about the research process. The researcher envisioned that the research would provide significant benefits to the health center or the broader community and ensured measures to minimize potential harm to participants, both physical and emotional.

Data collection

DSMQ was designed to assess self-care activities that can predict glycemic control [12]. Data was collected using DSMQ questionnaire. Sociodemographic information about the participants, such as age, sex, marital status, income, level of education, and duration of diabetes was collected.

Anthropometric measurements of the patients, such as weight in kilograms (kg), height in centimeters (cm), and body mass index (BMI) were recorded. The

weight was measured with the patient wearing light clothing and no shoes. Height was measured using a standard height board with the participant wearing no shoes. BMI was calculated as weight in kg divided by height in meters squared. BMI was categorized as normal (19–25 kg/m^2), overweight (26–30 kg/m^2), and obese (≥ 30 kg/m^2) [13].

Most recent laboratory results for HbA1c were noted. Glycemic status was categorized as 'good glycemic control' (HbA1c ≤ 7%), 'moderate glycemic control' (HbA1c 7.1–9.0%), and 'poor glycemic control' (HbA1c > 9.0%) [14].

Further, DSMQ was used which consisted of 16 questions and was freely available online. DSMQ has excellent psychometric properties [12]. The questionnaire presents itself as an effective tool that provides reliable and valid information on diabetes self-care and evaluates four well-defined specific self-care activities related to glycemic control.

The DSMQ-16 is a tool that evaluates patients' knowledge, attitudes, and behaviors pertaining to diabetes self-management. This tool consists of 16 items, employs a 4-point Likert scale for responses, with options ranging from 0 (no) to 3 (yes, definitely) [12–15].

In the current research, the Arabic version of the Diabetes Self-Management Questionnaire (A-DSMQ) was employed which was developed by Kaddech et al. in 2022 [16]. The DSMQ score was categorized as optimal and sub-optimal self-care of diabetes according to the DSMQ — user information and scoring guide. The questionnaire allows for a 'Sum Scale' score to be calculated and the estimation of four subscale scores [12]. Subscale scores were calculated by summing the scores of the four items in each subscale, with a range of 0–12. The subscales were labelled 'Glucose Management' (items 1, 4, 6, 10, 12), 'Dietary Control' (items 2, 5, 9, 13), 'Physical Activity' (items 8, 11, 15), and 'Health-Care Use' (items 3, 7, 14) based on their contents. Participants rated themselves on a scale ranging from 0 to 3, where 0: It does not apply to me; 1: It applies to me to some degree; 2: It applies to me to a considerable degree and 3: It applies to me very much. Some patients also responded to the options "blood sugar measurement is not required as a part of my treatment" and "diabetes medication/insulin is not required as a part of my treatment" [12].

Statistical analysis

Sample size calculation

The sample size was calculated using the formula, $n = t^2 \times p(1-p)/m^2$. The resulting sample size was 384.16. Further, sample size was rounded up to 400. The sample size was established by the number of people diagnosed with T2DM, a 95% confidence interval (CI), a 5% tolerated error, and a design effect of 2.

SPSS software version 24.0 (IBM, Meadville, PA) was used to analyze the data. The DSMQ score was expressed as the mean with a standard deviation. The suboptimal score in each domain was expressed as a percentage. The Chi-square test was used to compare optimal diabetes self-care scores across socioeconomic variables. To compare optimal scores on self-care of diabetes between different socio-demographic variables, Chi-square test was computed. However, when the assumptions of Chi-square test failed in more than two-by-two table, appropriate rows were combined and assessed. Shapiro-Wilk test and Kruskal-Wallis test were used to determine the normality of data and the effect of the patient's DSMQ item activities on HbA1c parameters, respectively. Spearman rank correlation test was used to determine the relationship between assessments of knowledge about DSMQ items and HbA1c. In this study, a p-value less than or equal to 0.05 was considered statistically significant.

Results

This study included 400 patients (216 males and 184 females) with a mean ± SD age of 55.6 ± 9.3 years. About 47% of the patients were obese. As per WHO, ranges of BMI are classified as normal BMI (18.5 to 24.9), overweight (BMI ≥ 25 kg/m^2), obesity (BMI ≥ 30 kg/m^2) and severe obesity (BMI ≥ 40 kg/m^2) [17]. Most participants were educated up to the secondary school level (44.2%). In our study, the patient's HbA1c control level rates for good, moderate, and poor were 42.5%, 43.8%, and 13.8%, respectively. Most of the patients had moderate glycemic control (HbA1c) 7.7 ± 3.3 (mean ± SD). The duration of diabetes observed was 11.4 ± 8.0 (mean ± SD) years. Most of the patients (45.0%) had an income of less than 500 Bahraini Dinars (BD) (Tab. 1).

The majority of patients responded as, 'It applies to me (Score 0)' for the following questions: "I check my blood sugar levels with care and attention" (34%); "I keep all doctors' appointments recommended for my diabetes treatment" (88.7%); "I take my diabetes medication (e. g. insulin, tablets) as prescribed" (84.7%); "I strictly follow the dietary recommendations given by my doctor or diabetes specialist" (39.5%) (Suppl. Tab. 1).

Average DSMQ score on self-care for diabetes

The overall mean DSMQ score was 6.9 ± 1.4 points, which is higher than the sub-optimal score (> 6 points) [15]. The average scores on the subscale domains of glucose management, dietary control,

Table 1. Baseline Characteristic of the Study Subjects

Variable	Category	Frequency (%)
Age [years]	Mean ± SD	55.6 ± 9.3
Gender		
	Male	216 (54.0%)
	Female	184 (46.0%)
Marital Status		
	Single	28 (7.0%)
	Married	337 (84.2%)
	Divorced/Separated	13 (3.3%)
	Widow	22 (5.5%)
BMI	Mean ± SD	31.4 ± 6.2 kg/m^2
BMI		
	19–25	73 (18.3%)
	26–30	138 (34.4%)
	> 30	189 (47.3%)
Level of education		
	Not literate	11 (2.8%)
	Less than secondary	76 (19.0%)
	Secondary	177 (44.2%)
	College/University	122 (30.5%)
	Postgraduate	14 (3.5%)
HbA1c [%]	Mean ± SD	7.7 ± 3.3
HbA1c		
	Good control	170 (42.5%)
	Moderate control	175 (43.8%)
	Poor control	55 (13.8%)
Duration of diabetes [years]	Mean ± SD	11.4 ± 8.0
Duration of diabetes		
	≤ 10 years	235 (58.8%)
	>10 years	165 (41.2%)
Monthly income category		
	Less than 500 BD	180 (45.0%)
	500–1000 BD	172 (43.0%)
	> 1000 BD	48 (12.0%)

BD — Bahraini dinars; BMI — body mass index; HbA1c — glycated hemoglobin; SD — standard deviation

physical activity, and health care use, respectively, were 7.0 ± 2.0, 6.5 ± 2.0, 6.4 ± 2.7, and 7.8 ± 1.9. All domains scored higher than suboptimal level (> 6 points).

Distribution of score by the self-care of diabetes

The proportions of patients with optimal (> 6.0) and suboptimal (≤ 6.0) DSMQ score were 73.5% and 26.5%, respectively. Optimal and suboptimal scores for the glucose control domain were achieved by 60.4% and 39.6% of respondents, respectively. The optimal and sub-optimal scores for dietary control were achieved by 53.5% and 46.5%, respectively, and the physical activity scores were achieved by 54.5% and 45.5% of respondents, respectively. The optimal and sub-optimal scores for healthcare use were 85.7% and 14.3% in respondents, respectively.

Table 2 illustrates the correlation and comparison of DSMQ self-care activities with HbA1c levels. A significant negative correlation was noted between DSMQ-16 and HbA1c levels ($p = 0.026$), and for dietary control and HbA1c levels ($p = 0.017$). Cronbach's α coefficient for DSMQ-16 was 0.70 which is acceptable.

A significant negative correlation was observed between, "I strictly follow the dietary recommendations given by my doctor or diabetes specialist" and HbA1c levels ($p = 0.018$), and similarly for "My diabetes self-care is poor" and HbA1clevels ($p = 0.006$) (Suppl. Tab. 2).

Association between demographic profile and total score of self-care of diabetes

In the context of a study which examined the sub-optimal scores in diabetes self-care, an investigation was undertaken to assess potential associations with sociodemographic variables. Notably, the analysis revealed that males exhibited a lower score (53.5%) in contrast to females (28.8%). However, it is noteworthy that this observed disparity did not reach statistical significance ($p = 0.335$).

Moreover, an exploration of BMI categories uncovered varying rates of sub-optimal scores. Specifically, 19.2% of individuals within the 19–25 kg/m^2 category displayed sub-optimal scores, while 23.9% and 31.2% within the 26–30 and >30 kg/m^2 categories, respectively, exhibited similar sub-optimal scores. It is important to highlight that the proportional differences among these BMI categories did not attain statistical significance ($p = 0.098$).

For duration of diabetes, 30.2% of patients had a sub-optimal score for ≤ 10 years as compared to 21.2% of patients > 10 years which was statistically significant ($p = 0.045$). According to the Kruskal-Wallis test, there were no statistically significant differences between patient groups with 'good glycemic control' (HbA1c ≤ 7%), 'moderate glycemic control' (HbA1c 7.1–9.0%), and 'poor glycemic control' (HbA1c > 9.0%) in both the DSMQ sum scale scores and subscale scores (Tab. 3).

The DSMQ sum scale score was positively correlated with the duration of diabetes ($p = 0.009$). However, a negative correlation was noted for BMI ($p = 0.005$) and HbA1c levels ($p = 0.026$). For subscales, glucose management was positively correlated with the dura-

Table 2. Correlation and Comparison of DSMQ Self-Care Activities with HbA1c Levels

	Correlation		Comparison	
	Correlation coefficient	P-value	Mean (SD)	Cronbach alpha
DSMQ-16	–0.111	0.026*	6.9 (1.4)	0.70
Glucose management	–0.003	0.955	7.0 (2.0)	0.72
Dietary control	–0.120	0.017*	6.5 (2.0)	0.68
Physical activity	–0.098	0.051	6.4 (2.7)	0.68
Health-care use	–0.079	0.115	6.9 (1.9)	0.75

*Indicates statistical significance (note: Cronbach alpha is 0.7, which is considered respectable reliability)
DSMQ — Diabetes Self-Management Questionnaire; HbA1c — glycated hemoglobin; SD — standard deviation

Table 3. Comparison of the DSMQ Self-Care Activities in Patients with HbA1c Level

	HbA1c ≤ 7%	HbA1c 7.1–9.0%	HbA1c > 9.0%	P-value
DSMQ-16	7.08 (6.04, 8.13)	6.88 (6.04, 7.92)	6.67 (5.48, 7.71)	0.080^{K}
Glucose management	6.67 (5.69, 8.67)	7.33 (5.33, 8.67)	6.67 (6.00, 8.00)	0.863^{K}
Dietary control	6.67 (5.63, 8.33)	6.67 (5.00, 7.50)	5.83 (5.00, 8.33)	0.058^{K}
Physical activity	6.67 (4.44, 8.89)	6.67 (4.44, 7.78)	5.56 (4.44, 7.78)	0.148^{K}
Health-care use	7.78 (6.67, 10.00)	7.78 (6.67, 8.89)	7.78 (6.67, 8.89)	0.287^{K}

DSMQ — Diabetes Self-Management Questionnaire; HbA1c — glycated hemoglobin; K — Kruskal Wallis test

Table 4. Correlation of DSMQ Scales and Patient Characteristics

	Correlation Coefficient (P-value)				
	DSMQ sum scale	Glucose management	Dietary control	Physical activity	Health-care use
Age	0.026 (0.625)	–0.004 (0.945)	0.115 (**0.031***)	–0.010 (0.851)	–0.098 (0.067)
Gender	0.062 (0.212)	–0.037 (0.455)	0.030 (0.547)	0.202 (< 0.001*)	0.004 (0.934)
BMI	–0.140 (**0.005***)	0.036 (0.467)	–0.218 (< 0.001*)	–0.183 (< 0.001*)	0.020 (0.686)
Duration of diabetes	0.131 (0.009*)	0.141 (0.005*)	0.095 (0.057)	0.068 (0.172)	–0.066 (0.189)
HbA1c level	–0.111 (0.026*)	–0.003 (0.955)	–0.120 (0.017*)	–0.98 (0.051)	–0.079 (0.115)

*Indicates statistical significance
BMI — body mass index; DSMQ — Diabetes Self-Management Questionnaire; HbA1c — glycated hemoglobin

tion of diabetes ($p = 0.005$). Dietary control was positively correlated with age ($p = 0.031$) and negatively correlated with BMI ($p < 0.001$). Physical activity was positively correlated with gender ($p < 0.001$) and negatively correlated with BMI ($p < 0.001$) (Tab. 4).

Discussion

The burden of T2D in Bahrain is steadily increasing due to population growth, urbanization, lack of physical activity and unhealthy diet [18, 19]. Considering the main goal of diabetes management is glycemic control [20], this study estimated the effect of self-care management on glycemic control in patients with T2D at primary care in the Kingdom of Bahrain.

A total of 400 patients with T2D were included in this study, and the mean age of the participants was found to be 55.6 years. This finding aligned with Alawainati et al. [21] who conducted the study on Bahraini population. Research consistently indicates that the prevalence of T2D rises with advancing age [22]. The study population consisted of approximately equal percentages of males (54%) and females (46%). These findings are consistent with Midhet et al. [23] (male: 48.1%; female: 51.9%) but a meta-analysis on prevalence of DM in Saudi conducted by Jarrar et al. [24] reported contrasting findings on gender distribution.

Most participants were married (84.2%), obese (47.3%), and completed their education up to secondary level (44.2%). These findings agree with Saad et al. [13] where most of the participants were married (93.5%), obese (43.1%), and studied up to secondary level (32.5%). The reason for this could be that diabe-

tes affects older people more than young people, thus most patients were married. Obesity could be due to unhealthy eating habits [18, 22, 25]. Lower education levels may be associated with higher diabetes incidence, as individuals with lower education may not be aware of the signs and symptoms of diabetes.

In the current study, 42.5% of participants had good control, and 13.8% had poor control of HbA1c levels. The previous study conducted by Al Ubaidi et al. [26], among Bahraini population reported that 57.91% patients had controlled HbA1c levels, which is similar to the findings of the current study. In contrast, a study by D'Souza et al. [10] reported that 32% of participants had moderate glycemic control and 65% of participants had poor glycemic control. The diverging results of these studies may be due to the behavior of patients regarding self-care management.

The present study reported higher score than the suboptimal level (> 6 points) for all the domains. A maximum sub-optimal score was noted for dietary control followed by physical activity and glucose management. Similar findings were reported by Bukhsh et al. [27], where majority of the study participants had poor knowledge regarding diet and physical activity. In contrast, study by Totesora et al. [28] reported least sub-optimal score for dietary control and maximum was found in glucose management, followed by physical activity. The analysis showed that there was a significant negative correlation between DSMQ-16 ($p = 0.026$), dietary control ($p = 0.017$) and HbA1c levels. Similarly, a study conducted by Alodhayani et al. [29] reported a weak negative correlation between dietary control, physical activity and HbA1c levels. This may be attributed to the unhealthy diet consumption in Eastern Mediterranean region [9, 30]. The negative correlations found between dietary control and HbA1c levels, as well as between physical activity and HbA1c levels demonstrate the clinical significance of lifestyle factors in diabetes care. A decline in dietary control and physical activity is related with an increase in HbA1c levels, signifying poorer long-term blood sugar control.

Patients with diabetes for more than ten years were more likely to have poor self-care scores than those with diabetes for less than ten years. Similarly, Ko et al. [31], reported that a longer duration of diabetes resulted in a lower adherence to self-care activities and poorer glycemic control. The relationship between diabetes duration and diabetes self-management was weak and inversely proportional, which means that as diabetes duration increases, diabetes self-management and control decrease and thus become less effective [32].

Our study has few limitations that merit consideration. First, the use of a convenience sampling method may limit the generalizability of our findings, as those who volunteered may not fully represent the diversity of the entire Bahraini population with T2D. Second, the omission of comprehensive covariate adjustment in our analysis, including variables such as age, gender, duration of diabetes, BMI, educational level, and income, restricts our ability to fully account for potential confounding effects. Third, the cross-sectional design prohibits the establishment of causal relationships, and the reliance on self-reported data, particularly in the assessment of self-care management, introduces the potential for recall and social desirability biases. Fourth, the analysis of nominal variables, such as gender, using traditional correlation methods presents challenges due to linearity assumptions, and while biserial correlation would be ideal, software constraints limited its implementation. Lastly, while our study focuses on the Bahraini population, variations in socioeconomic status, cultural diversity, and healthcare access may limit the generalizability of our findings across all segments of the population. These limitations underscore the need for cautious interpretation and highlight avenues for future research with more comprehensive datasets and study designs.

Despite these limitations, this study has several advantages, including a large sample size, assessing multiple domains of self-care and their correlation with glycemic control, providing a comprehensive understanding of the factors influencing diabetes management in the primary care setting. The reliability analysis of the DSMQ scale demonstrated respectable internal consistency, adding rigor to the study's measurements.

Further research should consider longitudinal designs to investigate the dynamics of self-care behaviors and their effect on glycemic control over time. The impact of cultural and social factors on self-care behaviors in Bahrain, considering the diverse population can also be examined. Efforts should be directed towards investigating strategies for the seamless integration of self-care support within the healthcare system, with the aim of enhancing patient outcomes. Additionally, there is a need to explore the influence of healthcare provider training on diabetes management, as such investigations hold promise for advancing our comprehension of effective strategies in this domain, ultimately leading to improved diabetes care.

Conclusions

DSMQ-16 serves as a robust instrument for the evaluation of diabetes self-management behaviors.

DSMQ along with demographic data and relevant variables provided an effective measurement of self-care management. This instrument provides valuable insights for guiding interventions aimed at improving diabetes care.

Our findings confirmed that self-care activity adherence had a significant influence on glycemic control. Diabetes duration and non-adherence to diabetes self-care management behaviors were linked to poor glycemic control. The findings also highlight the need to improve patient and healthcare provider involvement in self-care management practice, as well as patient empowerment. Developing programs on self-care management in T2D is noteworthy; therefore, more research is needed on factors associated with T2D patients' self-care management practices.

Article information

Supplementary material

The Supplementary materials for this article can be found at https://journals.viamedica.pl/clinical_diabetology/article/view/98550

Ethics statement

Ethical clearance was obtained from the Institutional Research and Ethics Committee in primary care under serial number 17-11-2022 before the commencement of the study. Prior to data collection, a researcher ensured that participants were fully informed about the purpose of the questionnaire, the research objectives, and how their data would be used. The participants clearly explained their voluntary participation and their right to withdraw at any time without consequences and to sign informed consent before participation.

Author contributions

Basem Abbas Ahmed Al Ubaidi, Khatoon Jaffar Abdulla contributed to the study design, data collection and implementation of the research. Noora Ahmed Al Jenaidi, Hussain Abdulla Ali and Eman Merza Marhoon contributed to data analysis and interpretation. Hajar Merza Matar and Hawra Ali Shakeeb aided in interpreting the results and worked on the manuscript. All the authors discussed the results, revised the articled and approved the final version of manuscript for submission.

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Conflict of interest

The authors declare no conflict of interest.

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Małgorzata Górska-Ciebiada[1], Maciej Ciebiada[2]
[1]Department of Propaedeutics of Lifestyle Diseases, Medical University of Lodz, Poland
[2]Department of General and Oncological Pneumology, Medical University of Lodz, Poland

Depressive Symptoms, Cognitive Function and Vitamin D Levels in the Oldest-Old Patients with Type 2 Diabetes

Introduction

The oldest-old population (aged 85 or older) is growing fast and there is a need to improve geriatric care. Many individuals in later life experience diabetes mellitus (DM) and depression; and both could be risk factors for dementia and mild cognitive impairment (MCI) [1]. Depression and diabetes have recently become a focus of research [1, 2]. The present study explores the association between the level of vitamin D, which regulates the nervous system and brain [3], and the prevalence of depressive symptoms, MCI and their comorbidity in patients aged ≥ 85 years with type 2 diabetes (T2D).

Methods

A cross-sectional study was conducted among T2D patients aged 85 or older, recruited from an outpatient diabetology clinic. The participants were assessed with the Montreal Cognitive Assessment (MoCA) for MCI and the Geriatric Depression Scale (GDS-30). The serum levels of 25-hydroxyvitamin D were assessed using ELISA. Detailed data was collected including sociodemographic, clinical, and biochemical parameters. Comparison between groups was done using ANOVA, followed by post-hoc test. Statistica 13.1 (StatSoft, Poland) was used for analysis.

Results

Clinical data were collected from 81 T2D patients, (73.6% female; mean age 87.3 ± 2.6 years). MCI was diagnosed in 21 (25.9%) subjects, depressive symptoms in 12 (14.8%); comorbid cognitive impairment and depression in 16 (19.8%). Thirty-two (39.5%) subjects had no psychiatric problems. The patients with comorbid cognitive impairment and depression were significantly more likely to be female ($p < 0.001$), single ($p = 0.003$), smokers ($p = 0.04$), older ($p = 0.03$), with a higher number of co-morbidities ($p < 0.001$), retinopathy ($p = 0.006$), hyperlipidemia ($p < 0.001$), cardiovascular diseases ($p < 0.001$), and with higher HbA1c level (67 ± 18.5 mmol/L, $p < 0.001$), compared to controls.

ANOVA followed by a *post hoc* test found serum 25-hydroxyvitamin D level was significantly decreased in patients with depressive symptoms (16.48 ± 5.12 ng/mL, $p = 0.025$) and MCI subjects (16.54 ± 3.98 ng/mL, $p = 0.002$) compared to controls (22.28 ± 5.92 ng/mL). The lowest concentration was noted in patients with diabetes who had comorbid MCI and depressive symptoms (14.12 ± 3.29 ng/mL, $p < 0.001$) (Fig. 1).

Correlation analysis showed a significant negative relationship between vitamin D and HbA1c levels in the comorbid cognitive impairment and depression

Address for correspondence:
dr hab. n. med. prof. UM Małgorzata Górska-Ciebiada,
The Department of Propaedeutics of Lifestyle Diseases,
Medical University of Lodz
63 Jaracza Street, 90-251 Lodz, Poland
Tel: +48 42 2725978
e-mail: malgorzata.gorska-ciebiada@umed.lodz.pl
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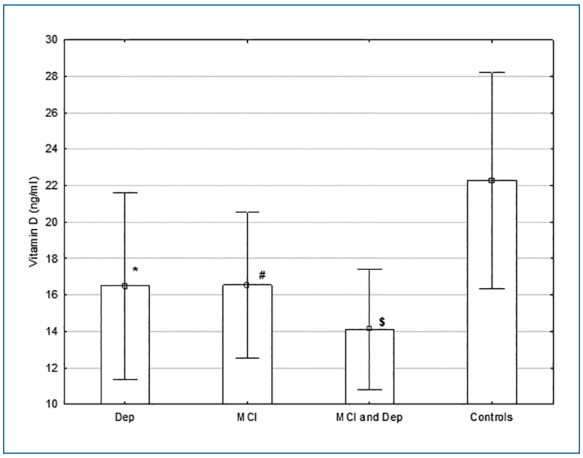

Figure 1. Serum 25-Hydroxyvitamin D Levels (ng/mL) in the Oldest-Old Patients with Type 2 Diabetes
Dep — patients with depressive symptoms; MCI — patients with mild cognitive impairment; MCI and Dep — patients with comorbid depressive symptoms and MCI; Controls — patients without depressive symptoms and MCI
Values are expressed by mean ± standard deviation; * # $ indicate difference between groups and controls, respectively. The ANOVA test followed by *post-hoc* test was used to test for significant differences. A p-value of less than 0.05 was considered statistically significant.

group ($r = -0.83$, $p < 0.001$), the depressive group ($r = -0.74$, $p = 0.006$), and in controls ($r = -0.63$, $p < 0.001$). In patients with comorbid cognitive impairment and depression, 25-hydroxyvitamin D level negatively correlated with GDS-30 score ($r = -0.87$, $p < 0.001$) and positively correlated with MoCA score ($r = 0.81$, $p < 0.001$).

Discussion

Our data indicates comorbidity of MCI, depression and diabetes in the diabetic population over 85 years. Our study showed that lower vitamin D levels were associated with a higher prevalence of MCI and depressive symptoms, as well as higher HbA1c levels, lower MoCA scores and a higher GDS-30 score. In line with other studies [4, 5] we propose that vitamin D may be a potential protective factor for cognitive impairment and comorbid depression in patients with type 2 diabetes. Further prospective studies are needed to evaluate the influence of vitamin D supplementation on the development of dementia or depression in the oldest-old population.

Article information

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki, and approved by the independent local Ethics Committee of Medical University of Lodz

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Conflict of interest

The authors declare no conflict of interest.

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Alif Ramli[1, 2], Fredie Robinson[1], Mohd Hafizuddin Ahmad[1], Balachandar S. Sayapathi[3], Carol Lim Kai Joo[3], Syakeel Muhammad[3], Nirmal Kaur[4], Anisah Jantim[4], Ismail Lasa[5], Norimah Yusof[6]

[1]Department of Public Health Medicine, Faculty of Medical and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia
[2]Medical Care Quality Section, Medical Development Division, Ministry of Health Malaysia, Putrajaya, Malaysia
[3]Penampang Area Health Office, Sabah, Malaysia
[4]Sabah State Health Department, Sabah, Malaysia
[5]Selangor State Health Department, Selangor, Malaysia
[6]Universiti Malaya, Kuala Lumpur, Malaysia

Factors Associated with Diabetes Complications among People with Type 2 Diabetes in Sabah, Malaysia: A Cross-Sectional Study

Introduction

The rising prevalence of type 2 diabetes (T2D) and diabetes complication result in substantial healthcare expenses, particularly given the considerable government subsidies provided to the healthcare system in Malaysia [1]. It is essential to periodically research diabetes complications and related variables to identify evolving trends and devise a plan of action. The objective of this study was to determine the prevalence and factors associated with diabetes complications among people with T2D in Sabah, Malaysia.

Address for correspondence:
Fredie Robinson, PhD
Department of Public Health Medicine, Faculty of Medical and Health Sciences, Universiti Malaysia Sabah, 88400 UMS Road, Kota Kinabalu, Sabah, Malaysia;
e-mail: freddie@ums.edu.my
phone: + 60168324477
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Methods

This cross-sectional study was carried out at six primary healthcare clinics in Kota Kinabalu and Penampang areas in West Coast Division, Sabah from April 2023 to July 2023. A total of 287 patients with suboptimally controlled T2D (HbA1c > 6.5%) who met inclusion criteria (diagnosed with T2D, ≥ 18 years old, on T2D medications and HbA1c > 6.5%) and provided written consent were included in the analysis. Demographic and medical data were obtained from the patients' medical records. This study received ethical approval from the Ministry of Health Malaysia's Medical Review and Ethics Committee (ethical approval: NMRR-ID-23-0097-XP1(IIR)).

The diabetes complication in this study refers to having at least one of the diabetes-related complications that had been identified by physicians and recorded in patients' medical records, which include retinopathy, stroke, ischemic heart disease, nephropathy, and diabetes-related foot problems. The definition of diabetes complications in this study was in line with the latest Sixth Clinical Practice Guidelines for the Management of Type 2 Diabetes Mellitus by the Ministry of Health Malaysia [2].

Table 1. Multivariable Analysis of the Association of Diabetes Complications with Age, Marital Status, Diabetes Duration and Polypharmacy

Variable	Multivariable logistic regression OR (95% CI), p-value
Age [years]	1.044 (1.003–1.087), p = 0.034[a]
Marital status	
Married	1
Unmarried	2.674 (1.174–6.092), p = 0.019[a]
Diabetes duration [years]	1.065 (1.002–1.132), p = 0.042[a]
Polypharmacy	
No	1
Yes	4.612 (1.637–12.997), p = 0.004[a]

[a]p-value < 0.05; CI — confidence interval; OR — odds ratio

Multiple logistic regression models were used to estimate odds ratio (OR) [and 95% confidence interval (CI)] for diabetes complications using SPSS version 28.

Results

Trained medical officers identified and briefed 420 potential eligible study participants who attended the participating healthcare clinics about taking part in this study. One hundred thirty-three individuals were excluded who refused to participate in the study or did not meet the criteria. A total of 287 participants with T2D were included in this study (mean age = 53.31 years, female = 54.4%, mean diabetes duration = 6.23 years). The prevalence of diabetes complications was 12.9%. Most participants were Dusun-Kadazan ethnicity (41.1%), with education level of secondary and below (96.5%), and overweight [mean body mass index (BMI) = 29.65]. Age (OR = 1.044, 95% CI: 1.003–1.087), unmarried (OR = 2.674, 95% CI: 1.174–6.092), diabetes duration (OR = 1.065, 95% CI: 1.002–1.132) and polypharmacy (OR = 4.612, 95% CI: 1.637–12.997) were associated with increased risk of diabetes complications (Tab. 1) after adjusting for age, marital status, diabetes duration and polypharmacy.

Discussion

Factors associated with diabetes complications among people with T2D is age, unmarried status, diabetes duration and polypharmacy. The findings of this study are comparable to other studies [3, 4]. Similarly, a study done in China documented that the odds of vascular complications was higher in unmarried patients than in married patients (OR = 1.41, 95% CI: 1.12–1.77) [3]. This information could be useful in developing methods for managing and preventing diabetes complications such as an effective intervention to improve glycemic control incorporating health education on self-care management.

The limitations of this study include small sample size, and due to the nature of the cross-sectional study, the findings may not be generalizable and not suitable to examine cause-and-effect relationships.

Article information

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Conflict of interest

The authors declare no conflict of interest.

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