Sleep Respiratory Disorders and Clinical Profile in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction   Sleep respiratory disorders (SRDs) are often found in patients with type 2 diabetes mellitus (T2DM).

Objective   The aim was to establish the prevalence of risk to develop an SRD using the Clinical Berlin Questionnaire (CBQ) and Epworth Sleepiness Scale (ESS) in patients with T2DM and verifying the correlation of anthropometric measurements and life quality (LQ) with ESS.

Methods   A descriptive and analytical study of a case series evaluating 208 patients with T2DM, submitted to clinical and biochemical evaluation and implementation of CBQ, ESS, and WHOQOL-bref to evaluate LQ.

Results   Mean age was 60.8 ± 8.8 years, and 65.4% were women. Most diabetics were overweight (36.1%), and 29.8% were class I obese. One-third had positive risk signals for a SRD, with 87.0 and 34.1% having high risk in CBQ and sleep disorders in ESS, respectively. There was a significant difference in the general LQ between the low- and high-risk groups in the CBQ.

Conclusion   In this scenario, it is noteworthy that the active search for sleep disorders must start from simple methods, such as application of protocols.

Keywords
► health evaluation
► epidemiology
► public health
► sleep disorders for excessive somnolence

Introduction

Type 2 diabetes mellitus (DM2) is a major chronic disease with high morbidity, mortality, and economic burden on public health.[1,2] Of the many risk factors associated with DM2, the most present in this population are long-term poor diet, smoking, physical inactivity, obesity, hypertension, and excessive alcohol consumption.[3,4]

Recent studies have investigated patients with DM2 in relation to central obesity, visceral adiposity, advancing age, and sleep-disordered breathing (SDB).[5–7] Individuals with DM2 commonly have SDB,[5] and obstructive sleep apnea (OSA) is one of the most common disorders identified as highly prevalent comorbidity in DM2.[5,8,9]

OSA is a respiratory disorder related to the physiologic changes during sleep and is characterized by recurrent episodes of partial or full collapse of upper airways, associated with intermittent hypoxemia and recurrent arousals from sleep.[10,11] The main symptoms are snoring, excessive daytime sleepiness, and apnea reported by observers. Characteristically, sleepiness occurs in monotonous situations, as assessed on the Epworth Sleepiness Scale (ESS).[12] Excessive daytime sleepiness can impair social and work activities of patients, reducing their quality of life[13] and contributing to an increase in the number of automobile accidents and occupational.[14,15]

Epidemiologic research with patients with OSA but without diabetes showed changes in glucose metabolism, including insulin resistance and glucose tolerance, independent of adiposity[16–18] and aging.[19]

Intrinsic sleep disorders include sleep apnea, difficulty in initiating or maintaining sleep, and restless legs. Extrinsic

disturbances are those related to environmental factors such as noise, listening to loud music, activity of reading, watching television, doing crafts, among others, as well as excessive intake of food and fluids before sleep, which consequently retard of its inception. The intrinsic and extrinsic sleep disorders alter the quality of life of the diabetic patient and play an important role in sleep quality.[5,8,9,13]

Therefore, the aim of this study is to establish the risk for developing SDB in patients with DM2 using the Clinical Berlin Questionnaire (CBQ) and the ESS, as well as to verify the correlation of anthropometric measurements and quality of life with ESS.

Methods

A descriptive and analytical study was conducted of a case series of patients with DM2, younger than 75 years old, residing in the urban area of Ijui/Rio Grande do Sul, registered in the county FHS (family health strategy) programs, from January 2010 to January 2013. This study was approved by the Research Ethics Committee No. 91/2010, and all participants signed an informed consent form.

According to data from the Brazilian Institute of Geography and Statistics,[20] the municipality of Ijui in 2010 had 78,915 inhabitants, occupying a territory of 689 km^2 located in the northwest region of the State of Rio Grande do Sul.

Exclusion criteria were patients with difficulty in understanding the proposed procedures, bedridden patients, and patients who were compromised during ambulation procedures.

Initially the contact was made with the City Department of Health for approval of the research and to collect information on the total number of patients with DM2 enrolled in the FHS of the urban area. The sample size was calculated based on the data of the estimated population in 2009 in the city of Ijui; there was a 1.03% prevalence of DM2 in nine FHSs in the urban environment. StatCalc and Epi Info 3.5.3 software were used (CDC, Atlanta, USA). For a nonspecific outcome of 50%, 5% error, and confidence level of 95%, a sample of 269 patients was needed. In anticipation of losses, 5% was added to that number, totaling 283 patients with DM2.

The head nurse of each FHS conducted a meeting with community health workers to present the project. Patients to be evaluated were randomly drawn from the pool. Patients were invited to participate in the study during a home visit under monitoring of community health workers when possible. At this time, the research objectives were explained to the patient, and interviews and clinical exams were scheduled with patients who agreed to participate. This evaluation was performed at the Clinic of Physiotherapy and the clinical laboratory analysis, respectively.

Overall, 283 patients with DM2 fit the inclusion criteria, according to data collected from health professionals of the FHS from the records of the patients belonging to nine FHSs of the urban environment of the city of Ijui. Of these, 75 patients were excluded due to absence at the time of the visit, refusal of the patient to participate, not living at the informed

address, or not signing the informed consent, leaving a sample of 208 patients with DM2.

Interviews and tests were performed by trained professionals. Data were collected using a semistructured instrument. The independent variables were age (30 to 39, 40 to 49, 50 to 59, 60 to 69, and 70 to 75 years old); gender (female, male); and time since diagnosis of DM2 (in years).

The following anthropometric data were recorded: body mass (kg), height (m), waist circumference (cm), hip circumference (cm), waist-to-hip ratio, and neck circumference (cm) to evaluate muscular hypertrophy of the neck, in which women typically have a higher circumference of 38 cm and men a greater circumference of 40 cm. The waist-to-hip ratio was classified as Assessment Applied Body Composition (1996),[21] which ranks the waist-to-hip ratio according to gender and age as low, moderate, high, and very high levels. The body mass index (BMI; kg/m^2) was classified according to World Health Organization (2005).[22] Systemic arterial pressure (mm Hg) was also measured.[23]

At the end of the clinical evaluation, the date and time of blood collection from each patient were noted. Patients were instructed to fast for at least 12 hours following a standardized protocol. High-density lipoprotein (HDL), total cholesterol (TC), triglycerides (TGL), and glucose (Trinder enzymatic method) were determined.[24] The low-density lipoprotein (LDC) cholesterol was calculated using the Friedewald formula [LDL = TC (HDL + TG/5)].

Ddaytime sleepiness and the presence of risk for developing SDB were assessed by two protocols, the ESS and the CBQ. The ESS quantifies the propensity to sleep, subjectively, in a simple way, classifying the trend and possibility of napping from high to low in eight different situations of daily life; in addition, it is easy to use in clinical practice. Patients assigned values of 0 to 3 for each question, the maximum value being reached was 24 points. Values > 10 denote changes in sleep: the higher the score, the greater daytime sleepiness.[25,26]

The prevalence of SDB was assessed by the CBQ, which was specifically designed to identify the risk of the individual presenting SDB. It is used to assess the occurrence of risk factors for OSA, such as snoring, daytime sleepiness, and fatigue, as well as obesity and hypertension. It has a sensitivity of 86% and specificity of 77%, and although it does not capture all the necessary information about OSA, it can be a substitute for direct measurements of breathing during sleep and has been used in the identification of patients at risk for OSA.[27,28] It is divided into three categories: categories 1 and 2 are positive when the sum of the scores of all items is equal to or greater than 2, and category 3 denotes the presence of hypertension and/or obesity. Positivity in two or three categories defines high risk for OSA, and positivity in only one category or none defines a low risk as proposed by Vaz et al.[29]

Evaluation of quality of life was performed by means of the quality-of-life questionnaire WHOQOL abbreviated, a generic questionnaire validated for Portuguese with the domains of functional capacity, physical aspects, general health, social aspects, emotional aspect, and environment. The total score is the average of all domains. The comprehensive questionnaire was used because covers different aspects of the impact of the

disease in an individual's life. The closer to 100 points in the total score, the better.[30]

The Statistical Package for Social Sciences (SPSS; version 18.0; Chicago, Illinois, United States, USA) was used to process the data. Statistical analyses of all variables were tested for normality by the Kolmogorov-Smirnov test. The results were presented as average ± standard deviation for continuous variables, and categorical variables were expressed in absolute and relative frequency. The Mann-Whitney test was used for comparison of two independent groups with normal distributionused, considering $p < 0.05$ as statistically significance. To compare categorical variables we used the chi-square and Fisher exact tests. For correlation of the variables, the Spearman test was used. All tests were applied with a confidence interval of 95%.

Results

We evaluated 208 diabetic patients, living in the urban area of the municipality of Ijuí in the period 2010 to 2013, corresponding to 73.5% of the population sample calculated (success rate). Sixty-four individuals were not included in the study for the following reasons: absence at the time of the visit; refusal to participate; not at the address provided; or refusal to sign the consent form.

Among the patients studied, 65.4% (136/208) were women, with a mean age of 60.8 ± 8.8 years. The median time from diagnosis of T2DM was 8.1 ± 6.9 years, waist-to-hip ratio was 1.0 ± 0.1, systolic blood pressure as 134.9 ± 16.1 mm Hg, and diastolic was 84.9 ± 14.5 mm Hg were higher averages in men, and BMI (32.1 ± 6.4 kg/m^2), hip circumference (107.8 ± 13.0 cm), and plasma glucose (127.2 ± 54.4 mg/dL) were higher in women. The variables waist circumference, time of diagnosis of DM2, systolic and diastolic blood pressure, and plasma glucose did not differ statistically ($p > 0.05$; ►Table 1).

►Table 2 shows that most subjects were classified as overweight (36.1%) and obese class I (29.8%), aged between 60 and 69 years old (46.6%), with abnormal waist circumference (81.3%), and 54.3% had stress. For waist-to-hip ratio, 92.4% of women were rated as having very high risk and 33.9% of men had high ratio and 48.2%, too high. Only one-third of the men had normal neck circumference, and in the women, normal and altered values were similar. Nearly three-quarters of the sample reported not exercising regularly.

►Table 3 shows that 29.8% of the subjects had positive signs of risk for SDB, 18.3% of the women and 11.5% of the men. In the sample, 80.0 and 34.1% had a high risk in CBQ and sleep disturbance in ESS, respectively. Most overweight (32.2%) and class I obese (30.0%) women showed normal ESS, and the class II obese (30.4%) women showed changes in sleep. Men showed the same proportion in both classifications of ESS. Class I obese women (30.3%) had a high risk in CBQ, as did overweight (45.2%) and obesity class I (35.5%) men. BMI showed a statistically significant difference in CBQ ($p = 0.025$) between low and high risk. ESS showed a significant difference in neck circumference ($p = 0.018$) between the normal classification and sleep disturbance. Both ESS and the CBQ showed most women to have changes in waist circumferences, regardless of the classification in the scale and questionnaire. In men, there is dispersion between the measurements of the normal waist and changed the ESS, CBQ in most individuals with a high risk for DSB also possessed increased waist circumference (►Table 4).

►Table 5 shows that patients with mean changes in ESS classification and high-risk CBQ had lower average in the quality of life compared with diabetics with normal

Table 1 Clinical profile of individuals with type 2 diabetes mellitus

Variables	Women (n = 136), average ± SD	Men (n = 72), average ± SD	p^b
Age (y)	59.7 ± 9.0	62.7 ± 8.2	<0.05
Body mass (kg)	77.5 ± 16.5	83.3 ± 13.1	<0.05
Height (cm)	155.5 ± 6.3	169.1 ± 6.5	<0.001
BMI (kg/m^2)	32.1 ± 6.4	29.1 ± 4.2	<0.001
Waist circumference (cm)	104.6 ± 14.4	104.6 ± 11.3	0.89
Hip circumference (cm)	107.8 ± 13.0	102.7 ± 9.8	<0.05
RC/Q	0.97 ± 0.1	1.0 ± 0.1	<0.001
Neck circumference (cm)	38.1 ± 3.6	41.4 ± 3.4	<0.001
TDDM2 (y)	7.1 ± 6.8	8.1 ± 6.9	0.24
PAS (mm Hg)	131.3 ± 16.0	134.9 ± 16.1	0.10
PAD (mm Hg)	81.2 ± 12.2	84.9 ± 14.5	0.09
Glucose (mg/dL)[a]	127.2 ± 54.4	124.0 ± 48.4	0.95

Abbreviations: PAD: diastolic blood pressure; PAS: systolic blood pressure; RC/Q: waist-to-hip ratio; SD, standard deviation; TDDM2: time to diagnosis of type 2 diabetes mellitus.
[a]Women (n = 92) and men (n = 50).
[b]Mann-Whitney test.

Table 2 Categorical variables by gender in individuals with diabetes mellitus type 2

	Women, n (%)	Men, n (%)
BMI		
Normal weight (<24.9 kg/m^2)	15 (11.0)	10 (13.9)
Overweight (25–29.9 kg/m^2)	41 (30.1)	34 (47.2)
Obese class I (30–34.9 kg/m^2)	39 (28.7)	23 (31.9)
Obese class II (35–39.9 kg/m^2)	24 (17.6)	4 (5.6)
Obese class III (>40 kg/m^2)	17 (12.5)	1 (1.4)
Age (y)		
30–39	2 (1.5)	0 (0)
40–49	21 (15.4)	5 (6.9)
50–59	33 (24.3)	16 (22.2)
60–69	62 (45.6)	35 (48.6)
70–75	18 (13.2)	16 (22.2)
Waist circumference		
Normal	9 (6.6)	30 (41.7)
Changed (men > 102 cm; women > 88 cm)	127 (93.4)	42 (58.3)
RC/Q[a]		
Low	2 (1.7)	1 (1.8)
Moderate	2 (1.7)	9 (16.1)
High	5 (4.2)	19 (33.9)
Very high	109 (92.4)	27 (48.2)
Neck circumference		
Normal	69 (50.7)	25 (34.7)
Changed (men > 40 cm; women > 38 cm)	67 (49.3)	47 (65.3)
Stress		
Yes	76 (55.9)	37 (51.4)
No	60 (44.1)	35 (48.6)
Regular physical exercise (3 × /wk)[b]		
Yes	37 (28.9)	18 (25.7)
No	91 (71.1)	52 (74.3)

Abbreviations: BMI, body mass index; RC/Q, waist-to-hip ratio.

[a]Risk classification according to gender and age (applied body composition assessment, 1996), women (n = 118) and men (n = 56), because the age range of 70 to 75 years has no waist-to-hip ratio classification according to above-mentioned reference.

[b]Women (n = 128) and men (n = 70).

classification in ESS and low risk in CBQ; however, there was a statistically significant difference only in the general area of quality of life between the low- and high-risk groups in CBQ.

No statistically significant correlation was observed between ESS and anthropometric measures and domains of the questionnaire of quality-of-life WHOQOL abbreviated.

Discussion

This study found a considerable prevalence of SDB characteristics in patients with DM2, ~30% of the sample, in both genders. This finding is consistent with results obtained in Western anterior study[8] that detected SDB in 36% of diabetic patients and disagrees with an Oriental[31] study in which 77.5% of Japanese diabetic patients had SDB.

Despite this evidence, these data do not provide a diagnosis of OSA to research participants; the ESS and CBQ questionnaires were used as a tool to verify positive signs of qualifications for SDB. One limitation of the evaluation with questionnaires is that its accuracy depends on patients' truthfulness of the answers, and subjective self-assessment may present incongruity between scales and polysomnography. Polysomnography is considered the gold standard test for the diagnosis of OSAS, because it allows monitoring of sleep stages; however, polysomnography is a costly and laborious examination. Thus, the clinical interview and the initial screening of patients with suspected SDB is a useful, accessible, and easy-to-use tool among health professionals.[32]

In this study, 34.1% of patients with diabetes showed sleep disturbance as verified by ESS, which quantifies the propensity for sleep and sleepiness in different day-to-day situations. Geloneze et al argued that sleep disruption and hypoxia caused by OSA affect the quality of sleep, causing daytime sleepiness.[33]

Most of the sample showed some level of obesity, with 36.1% overweight and 52% classified as obese class I, II, or III. There is a relationship between obesity and OSA; ~70% of patients with OSA are obese, and obesity is the only risk factor that is important and reversible.[34] This relationship is explained by changes that obesity has on the respiratory system in pulmonary function and decreased ability to work.[35] These findings demonstrate the relevance of direct actions by the FHSs for the guidance of individuals and the importance of physical activity and a healthy diet, both for the prevention of DM2 and other comorbidities to improve quality of life.

Most diabetic patients showed a change in waist circumference associated with obesity. Waist circumference is an important risk factor for OSA; it is as a better predictor than BMI, as it is one of the indices of body circumference that identifies people with standard central or visceral obesity, which causes higher risk from obesity-related problems regardless of BMI.[36] Waist circumference is associated with apnea more often than other forms of obesity.[37] Carneiro et al found increased waist circumference to be a predictor for OSA even in individuals who were not obese.[38]

In the present study, there was a statistically significant difference in neck circumference between normal classification and sleep disturbance ESS. The change of this parameter influences the rating scale being considered in this study (changes in neck circumference values exceeding 38 and 40 cm for women and men, respectively). However, a previous study estimated the cutoff at 40 cm in both genders.[39] It is assumed that the marked deposition of fat and soft tissue surrounding this region or the upper airways is responsible

Table 3 ESS by gender in individuals with diabetes mellitus type 2

Variables	ESS normal			ESS sleep change		
	Women, n (%)	Men, n (%)	Total, n (%)	Women, n (%)	Men, n (%)	Total, n (%)
CBQ low risk	9 (6.6)	9 (12.5)	18 (8.6)	8 (5.9)	1 (1.4)	9 (4.3)
QCB high risk	81 (59.6)	38 (52.8)	119 (57.2)	38 (27.9)	24 (33.3)	62 (29.8)

Abbreviations: CBQ, Clinical Berlin Questionnaire; ESS, Epworth Sleep Scale.

for apnea in obese patients,[37] thus making it an important measure in patients with symptoms of SDB.

The quality of life showed no correlation with the ESS; however, the study of Silva and Leite found a negative impact on the quality of life of SDB and found an association between SDB and worse quality of life in children with obstructive sleep disorders.[40]

The treatment of OSA decreases insulin resistance.[38] Therefore it is essential to investigate the impact of various pathologies associated with DM2 on glucose control to develop preventive and therapeutic strategies to halt and/or minimize the negative effects to this population.[41]

Although the correct diagnosis and treatment of OSA are determined by overnight polysomnography, a history of snoring accompanied by fellow apnea and excessive daytime sleepiness should raise clinical suspicion for SDB.[42] Thus, the present study is important because it assessed the presence of factors that raise suspicion for diagnosis of SDB in patients with DM2, highlighting the importance of research of SDB in diabetic patients, especially when obesity is associated. Polysomnography should be required for these patients.

The present study had limitations concerning to the clinical diagnosis of SDB. Therefore, we suggest future studies provide polysomnography in patients with suspected SDB in screening with the scale and the questionnaire to prove the effectiveness of protocols as the primary form of possible diagnosis of SDB.

Table 4 ESS and CBQ as the anthropometric measurements of patients with diabetes mellitus type 2

	ESS					CBQ				
	Normal		Sleep change			Low risk		High risk		
	Women, n (%)	Men, n (%)	Women, n (%)	Men, n (%)	χ^2	Women, n (%)	Men, n (%)	Women, n (%)	Men, n (%)	χ^2
BMI					0.070[b]					0.025[b]
Normal weight	13 (14.4)	8 (17.0)	2 (4.3)	2 (8.0)		3 (17.6)	2 (20.0)	12 (10.1)	8 (12.9)	
Overweight	29 (32.2)	21 (44.7)	12 (26.1)	13 (52.0)		10 (58.8)	6 (60.0)	31 (26.1)	28 (45.2)	
Obese class I	27 (30.0)	15 (31.9)	12 (26.1)	38 (32.0)		3 (17.6)	1 (10.0)	36 (30.3)	22 (35.5)	
Obese class II	10 (11.1)	3 (6.4)	14 (30.4)	1 (4.0)		0 (0)	1 (10.0)	24 (20.2)	3 (4.8)	
Obese class III	11 (12.2)	0 (0)	6 (13.0)	1 (4.0)		1 (5.9)	0 (0)	16 (13.4)	1 (1.6)	
RC/Q[a]					0.648[c]					0.465[b]
Low	2 (2.6)	1 (2.6)	0 (0)	0 (0)		1 (6.7)	0 (0.0)	1 (1.0)	1 (2.0)	
Moderate	2 (2.6)	4 (10.5)	0 (0)	5 (27.8)		0 (0)	2 (28.6)	2 (1.9)	7 (14.3)	
High	3 (3.9)	13 (34.2)	2 (4.9)	6 (33.3)		2 (13.3)	1 (14.4)	4 (2.9)	18 (36.7)	
Very high	70 (90.9)	20 (52.6)	39 (95.1)	7 (38.9)		12 (80.0)	4 (57.1)	97 (94.2)	23 (46.9)	
Neck circumference					0.018[b]					0.115[c]
Normal	50 (55.6)	20 (42.6)	19 (41.3)	5 (20.0)		12 (70.6)	4 (40.0)	57 (47.9)	21 (33.9)	
Changed	40 (44.4)	27 (57.4)	27 (58.7)	20 (80.0)		5 (29.4)	6 (60.0)	62 (52.1)	41 (66.1)	
Waist circumference					0.386[b]					0.620[c]
Normal	8 (8.9)	19 (40.4)	1 (2.2)	11 (44.0)		2 (11.8)	4 (40.0)	6 (5.7)	7 (5.9)	
Changed	82 (91.1)	28 (59.6)	45 (97.8)	14 (56.0)		15 (88.2)	6 (60.0)	100 (94.3)	112 (91.1)	

Abbreviations: BMI, body mass index; CBQ, Clinical Berlin Questionnaire; ESS, Epworth Sleep Scale; RC/Q, waist-to-hip ratio.
[a]In RC/Q, 34 individuals (women = 18; men = 16) did not participate because the analysis does not have classification by age group as the applied body composition assessment (1996).
[b]Chi-square test.
[c]Fisher exact test.

Table 5 Comparison between the averages of the WHOQOL-bref according to the Epworth Sleep Scale and the Clinical Berlin Questionnaire

Domains of the QOL questionnaire WHOQOL-bref	Epworth Sleep Scale			Clinical Berlin Questionnaire		
	Normal ($n = 135$)	Changed ($n = 73$)	p^a	Low risk ($n = 31$)	High risk ($n = 177$)	p^a
General	84.8 ± 17.7	84.6 ± 16.1	0.85	91.5 ± 11.2	83.7 ± 17.6	0.02[b]
Physical	83.7 ± 9.4	81.1 ± 10.6	0.12	83.8 ± 7.6	82.6 ± 10.2	0.64
Psychological	84.6 ± 9.6	81.9 ± 9.6	0.08	86.5 ± 9.7	83.3 ± 9.7	0.15
Social	96.9 ± 17.7	93.6 ± 17.5	0.24	97.8 ± 15.1	95.4 ± 18.1	0.99
Environmental	87.6 ± 11.3	87.2 ± 10.9	0.63	89.0 ± 10.1	87.2 ± 11.3	0.46

Abbreviations: QOL: quality of life; WHOQOL-bref.

[a]Mann-Whitney test.

[b]$p < 0.05$.

Conclusion

Based on the obtained data, it is estimated by CBQ that 29.8% of patients with DM2 have positive signs for SDB; one-third of the sample demonstrated sleep alteration by ESS, featuring one of the most frequent symptoms of individuals with sleep disorders. The majority of the sample was female, overweight and class I obese, of advanced age, and with changes of anthropometric measurements. In this scenario, respiratory sleep disorders should be assessed, from simple methods such as the application of protocols, to restore the quality of life with appropriate treatment and avoid possible consequences of this disorder.

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