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Fasting Blood Glucose, Body Mass Index and Waist Circumference in Patients with Rheumatoid Arthritis

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Abstract

Background: The goal was to assess patterns of Fasting Blood Glucose (FBG), Body Mass Index (BMI), and Waist Circumference (WC) in Rheumatoid Arthritis (RA).

Methods: This was a cross-sectional study carried out on 142 RA patients. Demographics, disease characteristics, lifestyle factors, FBG, BMI, and WC were collected. A convenient sampling method was employed. Multivariable linear regression model and multivariable Generalized Additive Model (GAM) were built after application of backward elimination to explore the relationship between FBG/BMI/WC and risk factors. The predicted smooth functions and 95% confidence intervals were plotted in multivariable GAM models. P<0.05 was significant. All analyses used R Statistical Software.

Results: 82% of patients were females. Mean (SD) age was 52 (13) years. The prevalence of prediabetic FBG and diabetic FBG were 27% and 19%, respectively. A significant association was observed between FBG and adalimumab (β=0.77, 95%CI, 0.32 to 1.21, P=0.001), hydroxychloroquine (β=-11.19, 95%CI, -0.54 to -21.84, P=0.04) and wake-up time on weekends (β=-2.72, 95%CI, -5.26 to -0.17, P=0.04). The prevalence of overweight and obese BMI was 32% and 39%, respectively. Sleep duration on weekdays (EDF=1.37, P<0.04) and smoking (β=-0.17, P=0.04) were associated with BMI. The prevalence of abdominal obesity was 48% and it was associated with sleep duration on weekdays (EDF=2.00, P<0.005). Gender modified the relationship of sleep duration and BMI/WC.

Conclusion: In RA patients, adalimumab and late wake-up time on weekends were risk factors for FBG while hydroxychloroquine was protective. In female patients, sleep duration was associated with BMI and WC and smoking was associated with BMI.

Keywords: Rheumatoid arthritis; Fasting blood glucose; Body mass index; Waist circumference; sleep; Medications; Lifestyle

Introduction

Rheumatoid Arthritis (RA) is a disease that is characterized by inflammatory changes of the synovial tissues of joints [1,2]. It is the most common inflammatory arthritis and the major cause of disability in patients with rheumatologic disorders [3]. Abnormalities in the cellular and humoral immune systems lead to the production of autoantibodies that can form immune complexes within the joint space, attracting immune cells [4,5]. Joint pain, swelling, and destruction of cartilage and bone are the manifestations of inflammation. A hallmark of RA is synovial hyperplasia as the main contributor to the formation of invasive pannus [5,6].

Considering the inflammatory nature of RA, it is important to consider the relationship between RA and other conditions known to have inflammatory implications, like obesity and diabetes. Here we have sought to investigate the risk factors for markers of obesity including Body Mass Index (BMI) and Waist Circumference (WC) as well as markers of diabetes like Fasting Blood Glucose (FBG) among patients with RA. For the purposes of this study, the terms overweight (pre-obesity) and obesity refer to body mass index above 25 and 30 kg/m^2, respectively [7]. According to the World Health Organization (WHO), obesity has nearly tripled globally since 1975 and as of 2016, 39% of adults were overweight and 13% were obese [8]. Individuals who are overweight or obese tend to be more exposed to inflammation due to the secretion of inflammatory mediators from adipose tissue [9]. Importantly, it has also been reported that obesity is a documented risk factor for development of RA [10]. Additionally, obesity is known to be associated with worse measures of disease activity and is negatively associated with RA disease remission, independent of therapy used [11,12]. Thus, research not only indicates that an obesity increase the risk of RA, but that is also seems to worsen the prognoses of disease too. Waist circumference and BMI are both utilized as measures of obesity for this study, with waist circumference being more specific to abdominal obesity.

Diabetes Mellitus (DM) is a chronic metabolic disease with several reported risk factors including obesity. Interestingly, RA has been reported as a risk factor of DM in prior studies [13,14]. However, another study reported that DM has protective effect against RA [15]. Further, it has been shown that RA is considered a risk factor for DM development, indicating a bidirectional relationship June exist [16]. Considering the conflicting findings within the literature, the relationship between DM and RA remains unclear, but it is important that we investigate what relationship, if any, June exist between the two because of their common inflammatory nature. Inflammation is known to have a role in both type I and type II DM and it has been shown to be a mediator of insulin resistance [17].

The relationship between FBG/WC/BMI and RA has yet to be fully elucidated and considering the potential ways in which these conditions June be increasing the risk of developing another condition or worsen the prognoses, it is essential that we work to clarify the dynamics at play. The current study was conducted to assess the patterns of FBG, BMI, and WC in patients with rheumatoid arthritis and to clarify the potential associated risk factors.

Methods

Population

This cross-sectional study was carried out in a medical university affiliated clinic during the summertime. The study protocol was approved by the university's Committee of Ethics. The methods were carried out in accordance with relevant guidelines and regulations. All participants signed a written consent form. Patients with rheumatoid arthritis were consecutively enrolled (convenience sampling method). Demographics, smoking, mood status, social activity, sleep duration, sleep quality, physical activity, diet, disease duration, and symptoms were inquired and recorded. Physical examination and laboratory data were conducted and recorded. Sleep quality was evaluated by mini-sleep Questionnaire [18]. Extra questions were devoted to measure all aspects of sleep quality and quantity (Table 1). Mood was evaluated according to Gallup Well-being Index [19]. Diet status was assessed using modified Gallup Diet Questionnaire. Physical activity was inquired based on a modified question from Brunel lifestyle physical activity questionnaire [20]. Smoking pattern was assessed as well. FBG was defined as prediabetic when it was between 100 and 125 mg/dL. FBG was defined as diabetic when it was >125 mg/dL. BMI was defined as normal, overweight, obese I, obese II and obese II when it was 18.5-24.99, 25-29.99, 30-34.99, 35-39.99 and ≥ 40 kg/m^2, respectively. Abdominal obesity was defined as a WC greater than 88 cm in females and 102 cm in males.

Lifestyle factors	Question	Time or days per week
Quantity of sleep	What time did you usually go to bed on weekdays?	
	How long did it take to fall asleep?	
	What time did you usually go to bed on weekends?	
	What time did you usually get out of bed on weekdays?	
	]What time did you usually get out of bed on weekends?	
	How many hours did you sleep every night on weekdays?	
	How many hours did you sleep every night on weekends?	
	How many hours did you get a nap on weekdays?	
	How many hours did you get a nap on weekends?	
Sleep quality	How many days per week do you have difficulties falling asleep?	/7
	How many days per week do you wake up too early?	/7
	How many days per week do you use Hypnotic medications (sleep aids)?	/7
	How many days per week do you fall asleep during the day?	/7
	How many days per week do you feel tired upon waking up in the morning?	/7
	How many days per week do you snore?	/7
	How many days per week do you experience mid-sleep awakenings?	/7
	How many days per week do you experience headaches on awakening?	/7
	How many days per week do you experience excessive daytime sleepiness?	/7
	How many days per week do you experience excessive movement during sleep?	/7
	Total Score of Sleep Quality out of 70	/70
Mood	How many days per week do you experience no energy to get things done?	/7

	How many days per week do you experience sadness?	/7
	How many days per week do you experience worry?	/7
	How many days per week do you experience anger?	/7
	How many days per week do you experience physical pain?	/7
	Total Score of Mood Status out of 35	/35
Diet	How many days per week do you eat fast food?	/7
	How many days per week did you eat red meat?	/7
	How many days per week do you eat fish/ omega 3?	/7
	How many days per week do you eat 4-5 servings of fruits/vegetables?	/7
	How many days per week did you take vitamin D tablet?	/7
	How many days per week did you take Magnesium tablet?	/7
	Total Score of Diet out of 42	/42
Physical activity	How many days per week in a normal week do you engage in at least 30-minute pre-planned physical activity?	/7
Social activity	How many days per week did you participate in a social, cultural, or support group that you belong to?	/7
Smoking	Do you smoke?	
Behavior	If yes, how many cigarettes do you smoke per day?	
Self-rated wellness and health	How much do you rate your wellness and health out of 10; 10 being the healthiest and 0 being the unhealthiest?	/10

Table 1: Lifestyle questionnaire and the calculating method of corresponding scores.

Data analysis

Descriptive analyses were used to determine the frequency distributions of demographics, lifestyle factors, symptoms and signs and laboratory data. T-test was applied to compare the continuous variables. Model assumptions were assessed by investigating the normality of residuals, homoscedasticity, and residual symmetry. Univariable associations of outcome variables and other variables were carried out through linear and nonlinear regression analyses. FBG, BMI, and WC were treated as outcome variables, independently. Multivariable generalized additive model with backward elimination was executed to determine the nonlinear associations of continuous variables and the outcomes. In case of finding no nonlinear association, multivariable linear regression model with backward elimination was built to determine the linear associations of variables and the outcomes. Both models were adjusted for confounders including age, sex, diet, mood, sleep, physical activity, social activity, smoking, disease characteristics and medications. Data analyses were conducted using RA P-value of <0.05 was considered significant.

Results

The sample size was 142 patients and the age range of the patients was 21-82 years. About 82% were women. The mean (SD) age was 52 (13) years. The mean and the range of FBG, BMI, WC and other characteristics of patients are presented in Table 2. The average BMI was 28.86, which is in the overweight range (Table 2); 29% of patients had normal BMI, 32% were overweight and 39% were obese. Abdominal obesity (WC>88 cm in females and >102 cm in males) was observed in 48% of patients. Additionally, the mean FBG was in prediabetic range; 54% of patients had normal FBG, 27% were prediabetic (100 ≤ FBG ≤ 125), and 19% were diabetic (FBG>125)(Table 3).

Patients' characteristics	Minimum	Maximum	Mean	SD
Age	21	82	52.32	13.05
Nutrition score	9	46	22.35	6.44

Pre-planned physical activity, days per week	0	7	0.27	1.26
Sleep duration, weekdays, hours	3	12	7.54	1.46
Sleep duration, weekends, hours	4	12	8.6	1.75
Sleep quality Score	3	63	29.4	12.05
Falling sleep, minutes	0	60	31.09	21.08
Nap duration, weekdays, minutes	0	60	19.74	17.87
Nap duration, weekends, minutes	0	180	48.02	31.93
Mood score	0	35	18.64	9.4
Smoking, pack-year	0	40	1.63	7.77
Social activity score	0	7	0.3	1.35
Waist circumference, cm	60	195	90.88	19.24
Body Mass Index, kg/m^2	18.71	72.19	28.86	6.82
Fasting Blood Glucose, mg/dl	76	264	107.88	32.98
Disease duration, years	1	50	7.98	8.82
Number of tender Joints	0	23	4.42	4.55
Number of swollen Joints	0	20	3.99	4.26
Hemoglobin, mg/dl	9.2	30	12.76	2.12

Table 2: Mean, Standard Deviation (SD) and range of continuous variables.

Participants' Characteristics		**Fasting blood glucose**			
		Normal, n=77 (54%)	**Prediabetic, n=38 (27%)**	**Diabetic, n=27 (19%)**	**p**
Age, Years, Mean (SD)		51.4 (12.3)	52.6 (12.2)	54.4 (16.1)	0.6
Sex, n (%)	Male	12 (46%)	10 (38.5%)	4 (15.5%)	0.3
	Female	65 (56%)	28 (24%)	23 (20%)	
Sleep duration, weekdays, hours, mean (SD)		7.6 (1.4)	7.5 (1.7)	7.4 (1.0)	0.9
Sleep duration, weekends, hours, mean (SD)		8.6 (1.7)	9.0 (2.0)	8.1 (1.4)	0.15
Time to bed, weekdays, PM		22:48	22:54	22:30	0.3
Time to bed, weekends, PM		23:53	24:00:00	23:40	0.4
Time to fall asleep, minutes, mean (SD)		33 (21)	29 (21)	29 (19)	0.6
Time to get out of bed, weekdays, AM		06:13	06:14	05:43	0.15
Time to get out of bed, Weekends, AM		07:26	07:48	06:23	0.02
Nap duration, weekdays, Minutes, Mean (SD)		19.5 (18.1)	22.5 (19.6)	16.4 (14.2)	0.4

Nap duration, weekends, Minutes, Mean (SD)		49.7 (31.9)	54.6 (36.0)	33.8 (20.7)	0.03
Snore, days per week		2.2 (3.1)	2.2 (3.1)	4.1 (3.3)	0.02
Sleep Quality Score, Mean (SD)		27.3 (11.2)	29.7 (11.1)	35.1 (14.0)	0.01
Mood score, Mean (SD)		18.3 (9.5)	18.9 (9.3)	19.2 (9.5)	0.9
Diet score, Mean (SD)		23.3 (6.0)	21.5 (6.1)	20.8 (7.7)	0.15
Pre-planned physical activity, minutes per Week, Mean (SD)		24 (90)	0	16 (79)	0.3
Sociocultural activity, mean (SD)		0.47 (1.6)	0	0.26 (1.3)	0.2
Smoking, pack-year, mean (SD)		2.1 (8.9)	1.1 (6.5)	1.1 (5.8)	0.7
Disease duration, years, mean (SD)		8.6 (9.5)	6.1 (5.3)	8.7 (10.5)	0.1
Visual analog scale of pain, Out of 100		42.0 (32.9)	48.7 (36.5)	36.5 (33.1)	0.4
Tender joints, n, Mean (SD)		3.8 (4.2)	4.9 (5.5)	5.4 (4.0)	0.2
Swollen joints, n, Mean (SD)		4.0 (4.3)	3.6 (4.1)	4.6 (4.4)	0.7
Disease activity score-28, Mean (SD)		3.9 (1.5)	4.2 (1.6)	4.1 (1.3)	0.6
Functional capacity, n (%)	Normal in all activities	37 (26.1%)	11 (7.7%)	11 (7.7%)	0.9
	Limited in vocational activities	26 (18.3%)	16 (11.3%)	8 (5.6%)	
	Limited in vocational and avocational activities	9 (6.3%)	7 (4.9%)	8 (5.6%)	
	Limited in All Activities	5 (3.5%)	4 (2.8%)	0	
Body mass index	Normal, (18.5-24.99 kg/m^2)	26 (18.3%)	8 (5.6%)	7 (4.9%)	0.3
	Overweight, (25-29.99 kg/m^2)	26 (18.3%)	13 (9.2%)	7 (4.9%)	
	Obese I (30-34.99 kg/m^2)	16 (11.3%)	11 (7.7%)	5 (3.5%)	
	Obese II (35-39.99 kg/m^2)	6 (4.2%)	6 (4.2%)	7 (4.9%)	
	Obese III (≥ 40 kg/m^2)	3 (2.1%)	0	1 (0.7%)	
Waist circumference, cm		88.5 (21)	93.5 (16)	93.7 (18)	0.3
Abdominal Obesity, n (%)		31 (21.8%)	21 (14.8%)	16 (11.3%)	0.1
Hypothyroidism, n (%)		13 (9.1%)	6 (4.2%)	1 (0.7%)	0.2
Laboratory Findings					
Hemoglobin, mg/dl		13 (2.5)	12.7 (1.6)	12.3 (1.6)	0.4
Platelets, cells/L		2,73,715	2,70,500	2,54,125	0.6
White Blood Cells, cells/L		8,080	8,436	7,571	0.6
Lymphocytes, cell/L		6,236	2,844	2,743	0.6
Erythrocyte sedimentation rate, mm/hr		27	25	22	0.6
C-Reactive Protein, mg/L		11	13	11	0.8
Positive Anti-MCV, n (%)		12 (8.5%)	9 (6.3%)	5 (3.5%)	0.6

Positive Anti-CCP, n (%)	9 (6.3%)	6 (4.2%)	4 (2.8%)	0.8
Blood Urea Nitrogen, mg/dl	25 (12)	26 (12)	31 (17)	0.15
Creatinine, mg/dl	1.22	0.89	1.59	0.25
Aspartate Aminotransferase (AST), IU/L	18	21	20	0.08
Alanine Transaminase (ALT), IU/L	19	24	22	0.09
Medications				
Prednisolone, mg, Mean (SD)	7.1 (4.1)	7.9 (3.2)	7.3 (3.1)	0.6
Methotrexate, n (%)	59 (41.5%)	36 (25.4%)	23 (16.2%)	0.049
Hydroxychloroquine, n (%)	36 (46.8%)	13 (34.2%)	6 (22.2%)	0.06
Sulfasalazine, n (%)	23 (16.2%)	11 (7.7%)	6 (4.2%)	0.7
Leflunomide, n (%)	14 (9.9%)	12 (8.5%)	8 (5.6%)	0.2
Cyclosporin, n (%)	1 (0.7%)	0	0	0.6
Adalimumab, n (%)	3 (2.1%)	4 (2.8%)	7 (4.9%)	0.004

Table 3: Comparison of the patients stratified by FBG.

Characteristics of patients stratified according to three categories of FBG are presented in Table 3. There were no significant differences among the three groups in terms of age, sex, diet, mood, physical activity, social activity, smoking, disease characteristics, and laboratory findings. Sleep quality score, snore days per week, time to get out of bed on weekends, and nap duration on weekends were significantly different among the three groups of FBG.

All patients were on corticosteroids except 4% who were in remission and were not taking any medications. The maximum dose of prednisolone was 15 mg/day and the minimum dose was 1.75 mg/day. Most patients received combination therapy with prednisolone, hydroxychloroquine and methotrexate (Table 2). Other less frequent prescribed Disease-Modifying Antirheumatic Drugs (DMARD) were sulfasalazine, leflunomide, and cyclosporin A. Biologic therapy was given in the absence of response to conventional DMARD, which was predominantly adalimumab (Table 3). Frequency distributions of most medications were similar among the three groups of FBG except methotrexate and adalimumab (Table 3).

Generalized Additive Model (GAM) [21] was applied to assess the nonlinear association between the outcome (FBG, BMI or WC) and the continuous variables. The multivariable GAM model was adjusted for age, sex, diet, mood, sleep, physical activity, social activity, smoking, disease characteristics and medications. The final model showed no significant nonlinear associations between FBG and continuous variables. Then, multivariable linear regression model [22] along with backward elimination was used to find the most significant factors associated with FBG. The findings are presented in Table 4. Four variables were left in the final multivariable regression model, of which the following three were significantly associated with FBG: Time to get out of bed on weekends, hydroxychloroquine use, and adalimumab use (Table 4). Mean (SD) FBG in 14 patients who received adalimumab was 134 (49) mg/dl whereas in 128 patients who didn't receive adalimumab, it was 105 (29) mg/dl (P=0.001). Mean (SD) FBG in 55 patients who received hydroxychloroquine was 101 (28) mg/dl whereas in 87 patients who didn't receive hydroxychloroquine was 112 (35) mg/dl (P=0.046).

Predictors	**Univariable linear regression**				**Multivariable linear regression**	
	B	**(95% CI)**		**P**	**β (95% CI)**	**P**
Age, years	0.14	-0.28	0.56	0.5	0.32 (-0.09 to 0.72)	0.1
Wake-up time on weekends	-2.57	-5.23	0.09	0.059	-2.72 (-5.26 to -0.17)	0.04
Hydroxychloroquine use	-11.32	-0.2	-22.43	0.04	-11.19 (-0.54 to -21.84)	0.04
Adalimumab use	0.73	0.29	1.17	0.001	0.77 (0.32 to 1.21)	0.001
Sex	1.13	-13.06	15.33	0.87		
Sleep quality score	0.32	-0.13	0.77	0.15		
Nap Duration on weekdays, Minutes	-0.03	-0.34	0.27	0.8		

Nap Duration on weekends, Minutes	-0.1	-0.27	0.06	0.2
Night sleep duration on weekdays	-0.87	-4.64	2.89	0.65
Night sleep duration on Weekends	-0.92	-4.07	2.21	0.55
Time to fall asleep, Minutes	-0.05	-0.31	0.2	0.65
Time to go to bed on weekdays	-2.78	-8.46	2.9	0.35
Wake-up time on weekdays	-3.84	-8.28	0.6	0.09
Time to go to bed on weekends	-1.89	-7.38	3.59	0.5
Snoring	0.76	-0.93	2.46	0.35
Mood status score	0.3	-0.27	0.89	0.3
Physical activity	-1.99	-6.35	2.37	0.35
Diet score	-0.76	-1.61	0.07	0.075
Smoking, Pack-years	-0.03	-0.74	0.67	0.95
Social activity	-2.37	-6.41	1.66	0.25
Disease duration, years	0.11	-0.51	0.73	0.7
Number of tender joints	0.55	-0.65	1.76	0.35
Number of swollen joints	0.14	-1.15	1.43	0.85
Extra-articular manifestations	-12.54	-28.19	3.1	0.1
Hemoglobin level	-1.17	-3.76	1.41	0.35
C-reactive protein	-0.009	-0.37	0.36	0.95
Prednisolone use	3.7	-23.59	30.99	0.8
Methotrexate use	2.31	-12.33	16.96	0.75
Leflunomide use	11.79	-0.92	24.51	0.06
Sulfasalazine use	-3.03	-15.23	9.16	0.6

Table 4: Association of FBG and independent variables measured by the multivariable linear regression model (R_2=0.23).

In multivariable GAM regression along with backward elimination built for BMI, only two variables left in the final model: sleep duration during the weekdays and smoking (β estimate=-0.17, P=0.04). No other variable showed significant association with BMI. Figure 1 shows the association of BMI and sleep duration during the weekdays in females (EDF=1.50, P=0.04) and males (EDF=1, P=0.7). The gender difference in the pattern and the strength of association between BMI and sleep duration shows the relevant modification effect of sex. Females sleeping less than 7 hours during the weekdays demonstrated significantly higher BMI (mean BMI = 32.8 kg/m^2) than females sleeping more than 7 hours (mean BMI=28.9 kg/m^2, p=0.02, Figure 1) whereas for males, no significant difference in BMI was observed between those sleeping less than 7 hours (mean BMI=27.5 kg/m^2) and those sleeping more than 7 hours (mean BMI=25.5 kg/m^2, p=0.5, Figure 1).

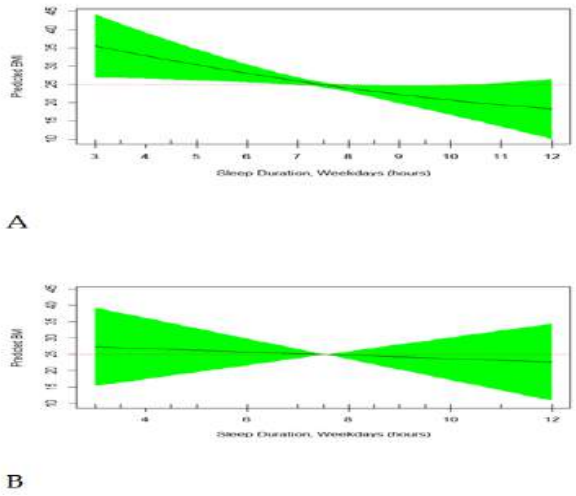

Figure 1: Effect modification of gender on the relationship of BMI and sleep duration drawn by generalized additive model. The relationship was significant in females (A) whereas it was non-significant in males (B). (EDF=1.50, P<0.04 and EDF=1, P=0.7, respectively).

Application of backward elimination on multivariable GAM regression for WC showed only one significant variable in the final model: sleep duration during the weekdays (EDF=2.00, P<0.005) (Figure 2). No other variable showed significant association with WC. Figure 2 shows the association of BMI and sleep duration during the weekdays in females (EDF=2.60, P<0.005) and males (EDF=1, P=0.3). The gender difference in the pattern and the strength of association between WC and sleep duration shows the relevant modification effect of sex. Females sleeping less than 7 hours during the weekdays demonstrated significantly higher WC (mean WC=102.2 cm) than females sleeping more than 7 hours (mean WC=89.6 cm, P=0.01, Figure 2A) whereas for males, no significant difference in WC was observed between those sleeping less than 7 hours (mean WC=93.7 cm) and those sleeping more than 7 hours (mean BMI=85.9 cm, P=0.4, Figure 2B).

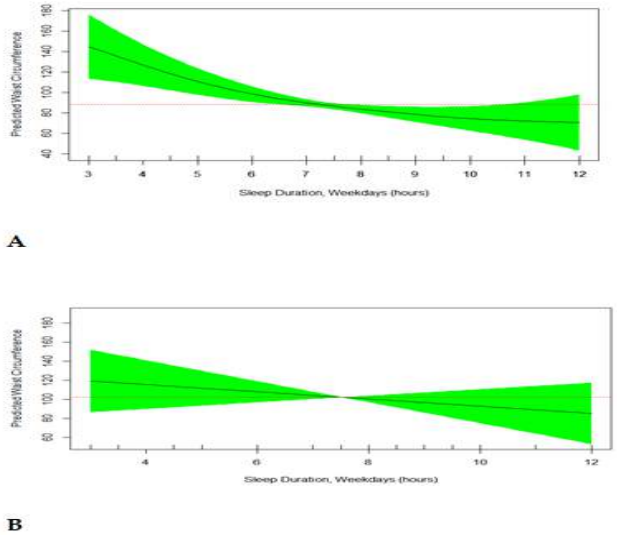

Figure 2: Effect modification of gender on the relationship of WC and sleep duration drawn by generalized additive model. The relationship was significant and non-linear in females (A) whereas it was non-significant and linear in males (B). (EDF=2.60, P<0.005 and EDF=1, P=0.3, respectively).

Discussion

The current research assessed the patterns of FBG, BMI and WC and their associated risk factors in patients with rheumatoid arthritis. The prevalence of prediabetic FBG and diabetic FBG were 27% and 19%, respectively. The prevalence of overweight and obesity were 32% and 39%, respectively. The prevalence of abdominal obesity was 48%. In addition, the significant associated factors revealed in the current study June indicate the need for further education of patients with rheumatoid arthritis on the importance of sleep hygiene.

The relationship between a healthy sleep schedule and FBG, BMI, and WC are well documented [23]. Many of the mechanisms at play in are inflammatory in nature. In summary, stage 3 is an essential stage of sleep since Growth Hormone (GH) and GH Releasing Hormone (GHRH) are released at this time. They induce fat burning, bone building, and general repair and regeneration [23]. The longest part of stage 3 in sleep takes place before midnight and therefore, delayed sleep onset until midnight or later, would suppress the largest GH pulse limiting its fat burning potential [23]. Additionally, sleep restriction induces high levels of ghrelin and low levels of leptin, a combination that together promotes appetite stimulation and increased caloric intake [23]. Advanced Glycation End Products (AGEs) are significantly increased in chronic sleep insufficiency and are also associated with insulin resistance in males with chronic sleep insufficiency [23].

Sleep insufficiency is also known to increase sympathetic activity and pro-inflammatory cytokines, both of which contribute to insulin resistance, increasing the risk of DM. Accumulations of extracellular β amyloid protein plaques and intracellular tau neurofibrillary tangles in brain tissues start immediately after one night of sleep insufficiency. These plaques and tangles are neurotoxins that potentiate each other's destructive effects on the structures and functions of brain cells and cause neuronal death. The consequence is a global decrease in cognition and decision making, manifested in increased consumption of fatty foods and unhealthy snacks in late sleepers. This further perpetuates weight gain and poor insulin responsiveness, indicating that poor sleep is impacting FBG/WC/BMI through a number of direct and indirect mechanisms.

In addition to our findings on sleep as a predictor of FBG/BMI/WC, our results indicate that prescription of adalimumab might be associated with increased risks of diabetes mellitus in vulnerable patients. Adalimumab is a TNF-α inhibitor used in RA to reduce inflammation. Interestingly, research has demonstrated that TNF-α inhibitors have been connected to cases of glycemic disturbances. One study demonstrated that RA patients without diabetes experienced an increase in HbA1C levels 12 months after a baseline measurement [24]. This supports our findings that adalimumab use is associated with adverse FBG affects. This indicates that further research on the glycemic effects of adalimumab use, especially in patients with higher risk of diabetes.

On the other hand, our results indicate a protective effect of hydroxychloroquine use on FBG. Hydroxychloroquine has been shown to have beneficial effects in terms of increasing serum insulin levels and reducing glucose levels in pre-diabetic patients [25]. These findings agree with our data, indicating a beneficial effect of hydroxychloroquine on glycemic metabolism. These findings June help physicians in decision making on what pharmacotherapies to use for RA patients depending on their risk of diabetes.

Conclusion

In patients with rheumatoid arthritis, adalimumab, hydroxychloroquine and wake-up time on weekends were the most significant factors associated with FBG. Sleep duration and smoking were significantly associated with BMI in female patients. Additionally, sleep duration was significantly associated with WC in female patients.

Strengths and Limitations

The main strengths of the current study included multilateral and unilateral review of the studied indicators and their relationship with existing risk factors and some regimens and methods in treatment.

The first limitation of the current study is the cross-sectional design which prohibits inferring the causal association outcomes and sleep characteristics. Seasonal variations in duration of sleep and recall bias might induce information bias. Finally, having the detail of dietary intake related to obesity and diabetes mellitus June improve the evaluation of outcomes and sleep association.

Given the current prevalence of sleep insufficiency and the growing prevalence and incidence of obesity and diabetes mellitus, finding the significant relationship of sleep characteristics and high FBG, BMI and WC in patients with rheumatoid arthritis target sleep as a serious risk factor for cardiovascular outcomes. Longitudinal studies June improve the reliability and the generalizability of findings.

Conflict of Interest

The authors declared that they have no conflict of interest.

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