Original Article

Association between White Blood Cells Count and Diabetes Mellitus in Tabari Cohort Study: A Case-Control Study

Abstract

Background: White Blood Cells (WBC) can be a useful marker to predict diabetes. In this study, we aimed to investigate the association between WBC count with type 2 diabetes in a large-scaled population-based cohort study. **Methods:** In the present study we used a subset of data collected in enrolment phase of Tabari cohort study**.** Participants with fasting blood glucose ≥126 or those who report as having diabetes or taking glucose-lowering medications were selected as case group (1765 participants) and control group included participants who did not report as having diabetes (1765 participants) and they randomly selected from the baseline population. Hematology indices were measured for all participants using Celltac Alpha MEK-6510 K. Chi-squared and independent t-test were used to compare categorical and continuous variables, respectively. **Results:** The mean of WBC in diabetic patients and control group was 6.89 ± 1.67 and 6.37 ± 1.49 respectively ($P \leq 0.001$). The odds of diabetes based on WBC count in crud model was 1.23 [CI 95% 1.181.28] and after adjustment for all possible confounding factor was 1.17 [CI 95% 1.111.23]. **Conclusions:** Results of the present study showed a significant association between WBC count and diabetes. This association remained significant after adjustment for all possible confounders.

Keywords: *Cohort study, diabetes mellitus, leukocyte count*

Motahareh Kheradmand, Hossein Ranjbaran[1], Reza Alizadeh-Navaei[2], Reza Yakhkeshi[3], Mahmood Moosazadeh

Health Sciences Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran, [1]Immunogenetic Research Center, Mazandaran University of Medical Sciences, Sari, Iran, [2]Gastrointestinal Cancer Research Center, Mazandaran University of Medical Sciences, Sari, Iran, [3]Gastrointestinal Cancer Research Center, Non-communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran

Address for correspondence:
Dr. Mahmood Moosazadeh, Gastrointestinal Cancer Research Center, Non-communicable Diseases Institute, Mazandaran University of Medical Sciences, Sari, Iran. E-mail: mmoosazadeh1351@gmail.com

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Introduction

The prevalence of type 2 diabetes is increasing substantially all over the world and it has become one of the greatest public health concerns. Considering the huge burden of diabetes including therapy, patient's survival and quality of life, and diseases complication, prevention of diabetes and early diagnosis should be given high priority.[1,2]

It has been suggested that inflammatory pathways are the underlying pathogenic mediators for diabetes mellitus, and cardiovascular diseases.[3,4] Along with some lifestyle-related factors,[5] association of several inflammatory biomarkers with various none communicable diseases (NCDs) such as type 2 diabetes,[6] and coronary artery disease[7] has been reported although this relationship is not consistent.[8]

Various inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) are linked with glucose disorders and diabetes.[9,10] In several studies association of White Blood Cells (WBC), as a marker of subclinical inflammation, with insulin resistance and type 2 diabetes, has been reported but controversy exists.[10,11] A U-shape relationship between WBC count and risk of diabetes in young Chinese workers has been reported,[11] whereas there was no association between WBC count and incidence of diabetes in a Japanese healthy population.[10] On the other hand, Kashima *et al*. reported WBC count as independent risk factor for type 2 diabetes in Japan.[12]

Regarding increasing incidence of diabetes globally, due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity,[13] identification of a person in risk especially in a prediabetic state which is a state between a normal value of glucose and diabetes[14] is an important public health issue. In the present study, we aimed to investigate the association between WBC counts with type 2 diabetes in a large-scale population-based cohort study.

Methods

Population and study design

In this case-control study, we used a subset of data collected in enrolment phase of

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Tabari cohort study (TCS)[15] which is part of mega cohort named as Prospective Epidemiological Research Studies in IrAN (PERSIAN).[16,17] In enrolment phase of TCS, 10255 participants aged 35-70 were recruited from the urban and mountainous areas in Sari, Mazandaran, Iran (7012 urban and 3243 mountainous populations).

Among all population, participants with FBS ≥126 or those who report as having diabetes in baseline or taking glucose-lowering medications were selected as case group (1765 participants) and control group includes participants with FBS <126 and who did not report as having diabetes (1765 participants). Control group was selected randomly from the baseline population from TCS.

TCS was approved by Mazandaran University of Medical science ethical committee (IR.MAZUMS. REC.1395.2524). The survey includes of questionnaire survey and blood collection.

Questionnaire

A structured questionnaire that was standardized by PERSIAN cohort team was utilized in this study. The collected data were related to participants' demographic information, socioeconomic status, type of home fuel used, lifestyle, reproductive history, occupational history, history of chronic diseases, familial history, oral health, sleep status, physical activity, smoking and drinking habits, food frequency, use of food supplements, dietary habits, and exposure to pesticides.

Blood collection

Blood samples were collected after 12 h of fasting from all participants during the survey. Triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and fasting blood glucose (FBG) levels were measured using the BT 1500 (Biotecnica, Italy). Hematology indices were measured for all participants using Celltac Alpha MEK-6510 K (Tokyo, Japan).

Anthropometric indices

Qualified and trained persons were in charge of measuring anthropometric indices. They followed standardized methodology. Weight was measured using a calibrated balance scale SECA 755 (SECA, Hamburg, Germany). For measuring height, we utilized SECA 226 (SECA, Hamburg, Germany) and we asked participants to face ahead with arms by the side and take off shoes and put feet together. Waist and hip circumference were measured based on national health and nutrition definition.[18]

Statistical analysis

Diabetes was defined as fasting blood sugar ≥126 mg/dL or a history of diagnosis or taking glucose-lowering medications.[15] All statistical analysis was performed in SPSS software ver. 16 (SPSS Inc., Chicago, Illinois, USA). Data were described as percentage (frequency), mean, and standard deviation (SD). We used Chi-squared test and independent t-test to compare categorical and continuous variables in the case and control group, respectively. The relationship between WBC count and diabetes analyzed using logistic regression and the effect size of its association was assessed using odds ratios (ORs) and 95% confidential intervals (95% CIs). An OR of <1 represents a protective effect. While an OR of >1 indicates a risk factor. A P value less than 0.05 was considered statistically significant.

Results

The mean age of participants in case and control group was 55.08 ± 8.12 and 49.19 ± 9.13, respectively ($P < 0.001$). In case group 63.4% of subjects and in control group 59.3% were female ($P = 0.012$). Frequency of urban residence in case and control group was 68.2% and 68.3%, respectively ($P = 0.942$). In case group 24.2% were illiterate versus 14.3% in control group ($P < 0.001$). Among diabetic participants 6.3% were smoker and 9.2% of non-diabetic subjects were smoker ($P < 0.001$). Frequency of positive family history in case and control group was 61.66% and 38.31%, respectively ($P < 0.001$) [Table 1].

The mean of body mass index (BMI) in case and control group was 29.28 and 28.28, respectively, ($P < 0.001$). In case group the mean of waist circumference (WC) was 98.41 and in control group it was 92.83, ($P < 0.001$). The mean of LDL-C level in case group was higher than control (176.89 versus 170.10). On the other hand, the mean of HDL-C level in case group was lower than control (49.76 versus 50.35). The mean of systolic and diastolic blood pressure in case group was higher than control (120/13 versus 113/88 and 75/19 versus 72/53 respectively) [Table 1].

The mean of WBC in diabetic patients and control group was 6.89 ± 1.67 and 6.37 ± 1.49 respectively ($P \leq 0.001$) [Table 1]. The odds of diabetes based on WBC count in crud and adjusted models are shown in Table 2. The crude odds of diabetes increase by 23% with each unit increase of WBC, ($P < 0.001$). After adjustment for age and BMI, the odds increase by 26% and 20% respectively. The odds of diabetes after adjustment for age, BMI, WC, waist-hip ratio, family history of diabetes, systolic and diastolic blood pressure, smoking, gender, HDL-C, LDL-C, TG, and cholesterol level increase by 17% [Table 2].

Discussion

Results of the present study showed a significant association between WBC count and diabetes. This association remained significant after adjustment for all possible confounder variables.

Considering the correlation between inflammation and diabetes, detecting the inflammatory markers in order to

Table 1: Comparing of clinical and demographic variables between case and control group (Univariate analysis with Chi square or *t*-test independent)

Variables		Mean±SD		*P*
		Case	Control	
WBC		6.89±1.67	6.37±1.49	<0.001
Age		55.08±8.12	49.19±9.13	<0.001
BMI		29.98±5.01	28.28±4.88	<0.001
WC		98.41±11.10	92.83±11.47	<0.001
WHR		0.94±0.07	0.90±0.07	<0.001
LDL-C		176.89±55.40	170.10±47.93	<0.001
TG		186.28±126.85	152.01±102.79	<0.001
TC		189.39±43.44	190.05±39.17	0.636
HDL-C		49.76±10.79	50.35±10.54	0.098
BP systolic		120.13±14.99	113.88±13.74	<0.001
BP diastolic		75.19±7.93	72.53±7.80	<0.001
		n (%)	n (%)	
Gender	Male	646 (36.6)	719 (40.7)	0.012
	Female	1119 (63.4)	1046 (59.3)	
Family history of diabetes	Yes	1058 (61.66)	658 (38.34)	<0.001
	No	707 (38.97)	1107 (61.03)	
Area residence	Urban	1203 (68.2)	1205 (68.3)	0.942
	Rural	562 (31.8)	560 (31.7)	
Smoking	Yes	112 (6.3)	163 (9.2)	0.001
	No	1653 (93.7)	1602 (90.8)	
Social economic level	1 (lowest)	383 (21.7)	335 (19.0)	0.011
	2	393 (22.3)	338 (19.2)	
	3	351 (19.9)	369 (20.9)	
	4	308 (17.5)	349 (19.8)	
	5 (highest)	330 (18.7)	374 (21.2)	
Education	University	289 (16.4)	449 (25.4)	<0.001
	9-12 years in school	422 (23.9)	491 (27.8)	
	6-8 years in school	193 (10.9)	205 (11.6)	
	1-5 years in school	433 (24.5)	368 (20.8)	
	No schooling	428 (24.2)	252 (14.3)	

BMI=body mass index; WC=Waist Circumference; WHR=Waist Hip Ratio; TC=total cholesterol; LDL-C=low density lipoprotein cholesterol; HDL-C=high density lipoprotein cholesterol; TG=triglyceride; BP=blood pressure

identify diabetic patients might be a cost-effective approach. Among different inflammatory markers, measuring WBC is simple and can be done in any clinical setting. Finding of our study showed that WBC count is significantly higher in case group compared to control. Results of previous studies are not consistent.[10,11,19,20] Reviewing pervious articles revealed that BMI play a role in the relationship between WBC and diabetes. In study by Oda *et al*.[10] after six-year follow-up, no association between WBC count and diabetes was reported in healthy Japanese population where obesity was not prevalent. In our study after adjustment for BMI, the odds increase by 20%. Interestingly another study conducted by Kashima *et al*. in Japanese population reported that after 5.5 years of follow-up among 9,706 participants, crude and adjusted HRs for diabetes incidence were significantly increased among participants with a high level of WBC count compared to participants with a low level of WBC.[12] Different sample size and data analysis might be the reason of inconsistent results. In another study conducted by Ford, association between leukocyte count and incident of diabetes among US adults after 20 years follow-up was analyzed. They adjusted all potential confounder variables such as age, smoking status, systolic blood pressure, and cholesterol concentration, use of antihypertensive medication, physical activity, alcohol use, and BMI. Results revealed doseresponse relationship between WBC count and diabetes.[21] Unlike our study, design of both mentioned studies was prospective yet there was consistent result. In another cross-sectional study conducted in Iranian population there was no association between WBC count and insulin resistance in type 2 diabetic patients.[22]

Our study results are consistent with the important role of inflammation in etiology of diabetes, although the exact mechanism of harming the β cells of the pancreas remain to be elucidated.

The main limitation of this study is, we used the enrolment data of TCS, therefore interpreting the causality relationship

Table 2: Relationship between white blood cell and diabetes using multivariate regression logistic

Model	Variables adjusted	OR	CI 95%	*P*
1	Crud	1.23	1.181.28	<0.001
2	Age	1.26	1.201.32	<0.001
3	BMI	1.20	1.141.25	<0.001
4	BMI, WC, WHR	1.17	1.111.22	<0.001
5	BMI, WC, WHR, Age	1.20	1.141.26	<0.001
6	Family history of diabetes	1.21	1.161.27	<0.001
7	BP systolic, BP diastolic	1.19	1.141.24	<0.001
8	Gender	1.23	1.181.28	<0.001
9	HDL-C	1.23	1.181.28	<0.001
10	LDL-C	1.22	1.171.28	<0.001
11	HDL-C, LDL-C,	1.22	1.171.28	<0.001
12	TG, TC	1.21	1.151.25	<0.001
13	HDL-C, LDL-C, TG, TC	1.20	1.151.26	<0.001
14	Smoking	1.25	1.191.30	<0.001
15	Social economic level, Area residence, Education	1.24	1.181.29	<0.001
16	Age, BMI, WC, WHR, Family history of diabetes, BP systolic, BP diastolic, Smoking, Gender, HDL-C, LDL-C, TG, TC	1.17	1.111.23	<0.001

ORs=odds ratios; CIs=confidential intervals; BMI=Body Mass Index; WC=Waist Circumference; WHR=Waist Hip Ratio; TC=total cholesterol; LDL-C=low density lipoprotein cholesterol; HDL-C=high density lipoprotein cholesterol; TG=triglyceride; FBG=fasting blood glucose

should be done with caution. In the follow-up phase of our cohort study this relationship might be confirmed. Another limitation of the present study is we did not identify the dose-response relationship between WBC with diabetes, which can be assess in the future studies.

Conclusions

Results of our study showed there is a significant association between WBC count and diabetes. This association remained significant after adjustment for all possible confounder variables.

Abbreviations

BMI = body mass index; WC = Waist Circumference; WHR = Waist Hip Ratio; TC = total cholesterol; LDL-C = low density lipoprotein cholesterol; HDL-C = high density lipoprotein cholesterol; TG = triglyceride; BP = blood pressure.

Availability of data and materials

Supporting data are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

TCS was approved by Mazandaran University of Medical science ethical committee (IR.MAZUMS. REC.1395.2524).

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Conflicts of interest

There are no conflicts of interest.

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