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White blood cell subtypes and risk of type 2 diabetes

Hongmei Zhang [1], Zhen Yang [1], Weiwei Zhang, Yixin Niu, Xiaoyong Li, Li Qin *, Qing Su *

Department of Endocrinology, Xinhua Hospital affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China

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ABSTRACT

Objective: It is reported that total white blood cell is associated with risk of diabetes mellitus. The present study is to investigate the relationship of white blood cell subsets with incidence of type 2 diabetes at baseline and 3 year follow-up.

Methods: We chose individuals without diabetes history as our study population; 8991 individuals were included at baseline. All of the participants underwent a 75-g OGTT at baseline. White blood cell count including all the subsets were measured along with all the other laboratory indices. The participants who were not diagnosed with type 2 diabetes according to the WHO 1999 diagnostic criteria underwent another 75-g OGTT at 3 year follow-up.

Results: The total WBC count, neutrophil count, and lymphocyte count were significantly increased in subjects newly diagnosed with diabetes mellitus compared to non-DM subjects at baseline (all $p < 0.001$). The ORs for DM were increased from the 1st to the 4th quartiles at both baseline and follow-up (both $p < 0.001$ for trend). At baseline, in the highest WBC quartile, the adjusted OR of DM was 2.51 (95% confidence interval [CI] 2.09 to 3.02). In the highest neutrophils quartile, the adjusted OR of DM was 2.11 (95% confidence interval [CI] 1.78 to 2.51). In the highest lymphocytes quartile, the adjusted OR of DM was 1.85 (95% confidence interval [CI] 1.56 to 2.18). At follow-up, in the highest WBC quartile, the adjusted OR of DM was 1.79 (95% confidence interval [CI] 1.38 to 2.33). In the highest neutrophils quartile, the adjusted OR of DM was 1.58 (95% confidence interval [CI] 1.23 to 2.03). In the highest lymphocytes quartile, the adjusted OR of DM was 1.74 (95% confidence interval [CI] 1.37 to 2.22). HOMA-IR and HbA1c correlated to elevated levels of WBC count, neutrophils and lymphocytes significantly (all $p < 0.001$).

Conclusions: Increased levels of WBC count, neutrophils and lymphocytes are all predictors for incidence of type 2 diabetes.

1. Introduction

It is well accepted that type 2 diabetes is an inflammatory disease with a chronic low-grade activation of the immune system as a key component in the pathophysiology (Donath & Shoelson, 2011; Pickup & Crook, 1998). A number of inflammatory markers including white blood cell count (WBC) and cytokines are found to be elevated when the immune system is activated (Pratley, Wilson, & Bogardus, 1995; Schmidt et al., 1999). Total peripheral white blood cell count has been proved to be associated with diabetes risk in some epidemiological studies (Schmidt et al., 1999; Vozarova et al., 2002), but there was some inconsistency in these observations (Chao et al., 2010; Duncan et al., 2003). A concern of publication bias has been brought forward by Gkrania-Klotsas et al. in a systematic review and meta-analysis (Gkrania-Klotsas et al., 2010). Although WBC has been suggested to be able to predict incidence of type 2 diabetes, data on how WBC subtypes are associated to risk of type 2 diabetes are notably limited and conflict. Some studies reported that the levels of neutrophils, lymphocytes and the neutrophil:lymphocyte ratio (NLR) were all elevated in metabolic syndrome (Buyukkaya et al., 2014; Meng et al., 2012). Others studies suggested decreased lymphocyte levels and increased neutrophil counts (increased NLR) in uncontrolled diabetes (Khodabandehlou, Zhao, Vimeux, Aouane, & Le Devehat, 1998; Sefil et al., 2014). Another research showed no association between the NLR and development to diabetes (Lorenzo, Hanley, & Haffner, 2014) and the WBC count is independently related to race (Pratley et al., 1995). In China, very few large scale researches have been carried out to estimate the connection of WBC count to the risk of progressing diabetes. Even less studies have evaluated the association between different white cell count subsets and risk of type 2 diabetes.

In the present study, we are going to examine the relationship of WBC and newly diagnosed type 2 diabetes in a population without previous diabetes history and further explore the association between white cell count subsets and risk of diabetes. We not only conducted this study cross-sectionally, but also assessed the ability of WBC and differential WBC types to predict the risk of progressing diabetes after

Conflict of interest: None.

* Corresponding authors at: Department of Endocrinology, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, 1665 Kongjiang Road, Shanghai, 200092, China.
E-mail addresses: qinli@medmail.com.cn (L. Qin), suqingxinhua@163.com (Q. Su).

[1] These authors contributed equally to this work.

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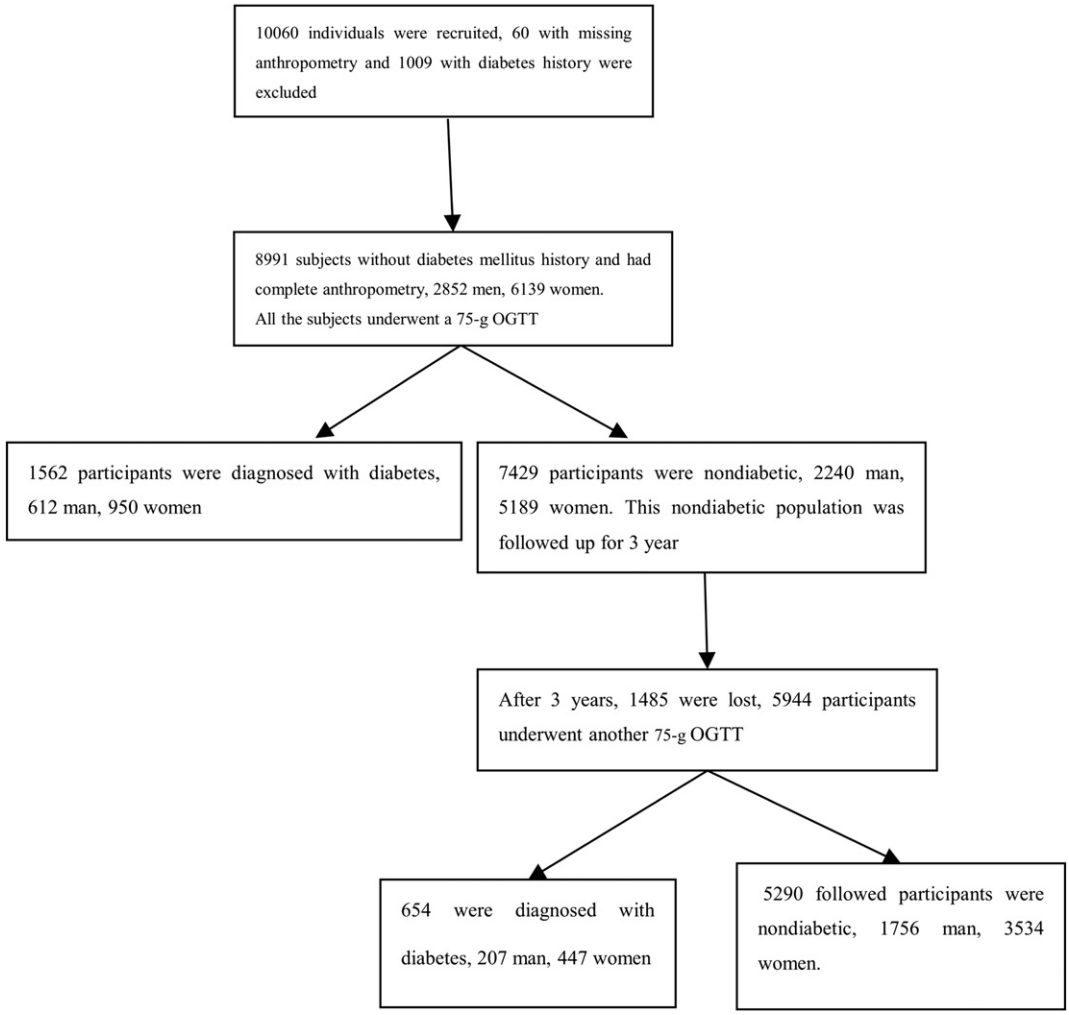

Fig. 1. Study design flow diagram.

3-year follow-up. And we also examined the impact of different levels of WBC and WBC subsets on blood glucose (HbA1c) and HOMA-IR.

2. Materials and methods

2.1. Study design

This study is a part of a national survey of Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal (REACTION) study (Ning, 2012), which was conducted among adults aged 40 years and older. The data presented here are from the survey of subsamples from Shanghai in eastern China. The participants were from the Chongming District in Shanghai, China. We recruited 10,060 individuals in total and they were all approved to take part in the first step of our survey. We set missing anthropometry as an exclusion criteria. Other exclusion criteria included acute or chronic inflammatory diseases obtained from medical history. In order to avoid the influence of antidiabetic medication on white blood cell count, participants with diagnosed diabetes history were also excluded. At last, 8991 individuals (2852 men and 6139 women) were included for the study population. All the 8991 individuals underwent a 75-g oral glucose tolerance test (OGTT) at baseline. After 3 year follow-up, the participants who were not diagnosed with diabetes at baseline according to WHO 1999 diagnostic criteria underwent another 75-g OGTT (5944 subjects approved to continue the survey, 1963 men and 3981 women). For the whole study design flow diagram, see Fig. 1. Comparison between the individuals lost to follow-up and the individuals stayed showed no statistical difference in the clinical parameters at baseline. The research protocol was approved by the ethics committee of Xinhua Hospital Affiliated to Shanghai Jiaotong

Table 1
Clinical and laboratory characteristics of study subjects at baseline.

Characteristics[a]	Diabetes group	Non-diabetes group	*P* value
N	1562	7429	
Age (yr)[b]	58.51 ± 7.33	55.11 ± 7.95	<0.001
Sex (male/female)[b]	612/950	2240/5189	0.789
BMI (kg/m^2)	25.68 ± 3.53	24.37 ± 5.29	<0.001
SBP (mmHg)	137.65 ± 18.41	127.91 ± 18.65	<0.001
DBP (mmHg)	82.85 ± 10.12	79.62 ± 10.31	<0.001
FBG (mmol/l)	7.64 ± 2.27	5.68 ± 0.52	<0.001
2 h OGTT (mmol/l)	13.40 ± 4.55	7.09 ± 1.71	<0.001
HbA1C (%)	6.60 ± 1.34	5.69 ± 0.42	<0.001
Insulin (pmol/l)	9.20 ± 9.15	7.01 ± 3.51	<0.001
HOMA-IR	3.14 ± 1.37	1.84 ± 0.94	<0.001
WBC (10^9/l)	6.34 ± 1.59	5.78 ± 1.46	<0.001
Neutrophil (10^9/l)	3.73 ± 1.22	3.39 ± 1.12	<0.001
Lymphocyte (10^9/l)	2.14 ± 0.67	1.97 ± 0.77	<0.001
Monocyte (10^9/l)	0.33 ± 0.10	0.31 ± 0.14	0.373
Eosinophil (10^9/l)	0.14 ± 0.11	0.13 ± 0.10	0.001
Basophil (10^9/l)	0.02 ± 0.01	0.02 ± 0.01	0.525
NLR	1.87 ± 0.81	1.87 ± 2.29	>0.05
Drink (yes/no)	419/1143	1760/5569	>0.05
Smoke (yes/no)	299/1263	1224/6205	>0.05

[a] Data are means ± SD or number (percent); *P* value was calculated after adjustment for age and gender.
[b] Not adjusted for itself.

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