Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Platelet count and 8-year incidence of diabetes: The Korean Genome and Epidemiology Study

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ARTICLE INFO

Article history:
Received 12 March 2018
Received in revised form
2 July 2018
Accepted 30 July 2018
Available online 1 August 2018

Keywords:
Platelet count
Type 2 DM
KOGES
Cohort study

ABSTRACT

Aims: The aim of this study is to investigate the effect of platelet count on the incidence of type 2 diabetes mellitus (DM) in the overall Korean adults and in participants with impaired glucose tolerance (IGT) at baseline.

Methods: A total of 7502 participants (3528 men and 3974 women) aged 40–69 years were enrolled in this study. The study population was divided into tertiles (T) of serum platelet counts. We used Cox regression to analyse the relationship between baseline platelet count and new-onset type 2 DM.

Results: A total of 602 (8.0%) subjects developed type 2 DM during a mean follow-up of 8.4 years. Compared to the lowest tertile, the hazard ratio (95% confidence interval [CI]) for the incidence of type 2 DM was 1.28 (1.04–1.57) for T3 after adjusting for possible confounding factors. In subjects with IGT at baseline, the hazard ratio (95% CI) for the incidence of type 2 DM in T3 compared with T1 was 1.45 (1.05–2.00) after adjusting for the same confounders.

Conclusion: This prospective longitudinal study demonstrated that the incidence of type 2 DM increased as the serum platelet count at baseline increased within the normal range. This positive association was more prominent in subjects with IGT.

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder that is known as a "prothrombotic state" related to atherosclerosis and inflammation [1]. It is also characterised by hyperglycaemia associated with both microvascular and macrovascular complications that cause organ and tissue damage [2]. It is well established that platelet reactivity is increased in patients with diabetes, especially those with type 2 DM [3]. Increased platelet activity plays an important role in the development of macrovascular (cardiovascular disease [CVD], stroke, and peripheral arterial disease) and microvascular (nephropathy, neuropathy, and retinopathy) complications of type 2 DM [4].

In clinical practice, platelet count is a simple and economical indicator of haemostasis. Recent studies suggest that platelet count is a useful biomarker for diseases such as diabetes, CVD, and metabolic syndrome as well as haemostasis [5–7]. Platelet indices such as platelet count and mean platelet volume (MPV) might be affected by established cardiovascular risk factors such as smoking, hypertension, and diabetes, in

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https://doi.org/10.1016/j.diabres.2018.07.033
0168-8227/

addition to age and sex [8–10]. Even within the normal range, a higher platelet count is related with insulin resistance and CVD [11,12].

Emerging evidence has suggested that platelet count and MPV are associated with prognosis of metabolic syndrome and diabetes [13]. Furthermore, in a large series of case-control and cohort studies, platelet activation in diabetes has been linked to the production of large platelets, altered platelet shape, and enlargement of circulating platelets [14]. Platelet life is shorter in subjects with insulin resistance, which may cause an increase in platelet counts [15]. In addition, the interaction between inflammation and thrombosis provides a potential mechanism linking platelet count to type 2 DM. In this regard, platelet count is a meaningful marker that reflects chronic inflammation and pro-thrombotic status as well as insulin resistance. Furthermore, the platelet count is highly correlated with reactive oxygen stress, which is also linked to insulin resistance [16].

However, to the best of our knowledge there has been no prospective community-based cohort study assessing the relationship between platelet count and development of type 2 DM. Therefore, the aim of this study was to investigate the effect of platelet count on the incidence of type 2 DM in a Korean adult population and in participants with impaired glucose tolerance (IGT) at baseline.

2. Methods

2.1. Study population

This study is based on a population-based prospective cohort study of all participants in the Korean Genome and Epidemiology Study in the Korean General Population (KoGES). Aims and detailed information of KoGES were described in a previous study. In the KoGES study, adults aged 40–69 in rural and urban areas of Ansung and Ansan were enrolled to analyse the causes of diseases by collecting information on genes involved in the occurrence of specific diseases in Korea and the lifestyle and health status of Koreans. A total of 10,038 adults (5018 participants from the Ansung area and 5020 participants from the Ansan area) aged 40–69 years were included in the baseline study conducted from 2001 to 2002. Study participants were invited biennially for a follow-up visit. All study participants were enrolled in the follow-up survey. We used data from the baseline study to the 6th survey, from 2013 to 2014. To investigate the development of type 2 DM, we excluded 1508 subjects with type 2 DM at baseline. In addition, we excluded 17 subjects with hepatitis, which might affect the platelet count. We also exclude 174 subjects with hs-CRP levels greater than 1 mg/dL reflecting inflammatory status. Furthermore, 690 subjects with missing data of confounding factors are excluded. Participants with platelet counts within an a priori defined range of 100,000–450,000/μL were included. We therefore excluded subjects with thrombocytopenia (platelet count <100,000/μL) or thrombocytosis (platelet count 450,000/μL). Finally, 7502 subjects were eligible for analysis (Fig. 1).

The study protocol was approved by the Institutional Review Board of College of Medicine. Participants' data were provided anonymously after they had signed the informed consent form.

2.2. Anthropometric measurements and general data

At baseline and the follow-up examination, participants completed questionnaires regarding demographic information (age, sex, residential area, marital status, and education), medical history (T2D, coronary artery disease [CAD], stroke, and cancer), lifestyle (smoking, alcohol drinking, and exercise) and underwent physical examinations and laboratory tests by standard procedures. Weight was measured in kg to

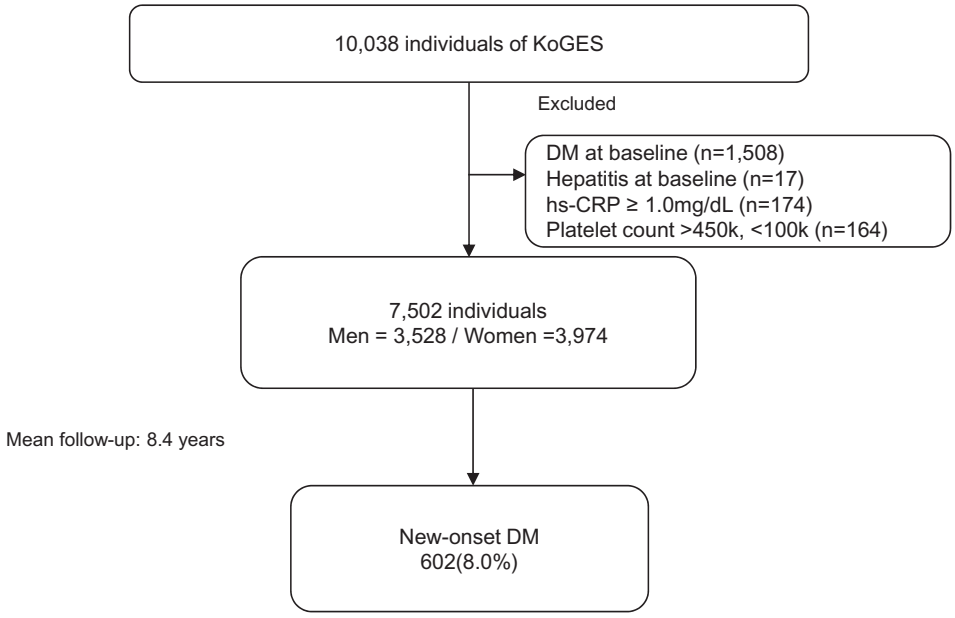

Fig. 1 – Study population.