Clinica Chimica Acta 474 (2017) 28–33

Contents lists available at ScienceDirect

Clinica Chimica Acta

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

Elevation of plateletcrit increasing the risk of non-alcoholic fatty liver disease development in female adults: A large population-based study

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ARTICLE INFO

Keywords:
Non-alcoholic fatty liver
Sex factors
Risk factor
Plateletcrit

ABSTRACT

Background: Non-alcoholic fatty liver disease (NAFLD) is the one of the most common form of chronic liver disease in China, so it is important to apply bio-marker in predict the development of NAFLD.
Aims: This study aims to evaluate association between plateletcrit (PCT) and non-alcoholic fatty liver disease (NAFLD) in Chinese female adults.
Methods: NAFLD was defined as per ultrasound in this study and 9737 NAFLD-free female subjects from Wenzhou People's Hospital were followed for five years in average in the study. The determination of NAFLD PCT quartiles (Q1 to Q4) were defined: 0–0.16, 0.17–0.18, 0.19–0.21, ≥ 0.22. With Q1 used as reference, 95% confidence intervals (CIs) and hazard ratios (HRs) in different models were computed across each quartile.
Results: From Q1 to Q4, the incidence ratios (95% CIs) were 8.30 (7.14–9.47), 11.51 (10.12–12.89), 12.68 (11.47–13.89) and 16.46 (15.03–17.88). Simply considering PCT, in the longitudinal population, values in Q2, Q3 and Q4 had HRs (95% CIs) are 1.51 (1.25–1.84), 1.72 (1.44–2.06) and 2.34 (1.96–2.79) versus Q1. After adjusting for all known confounding variables, values in Q2, Q3 and Q4 had HRs (95% CIs) of 1.31 (1.08–1.60), 1.30 (1.09–1.56) and 1.54 (1.29–1.84) in females compared with Q1.
Conclusions: We reported that elevated serum PCT levels are considered as an independently significant predictor for NAFLD development in females. The high PCT level contributes to the development of NAFLD.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is the one of the most common cause of chronic liver disease in China and the prevalence of this disease varies from 5% to 42% in numerous studies [1–4]. As a metabolic disease, NAFLD is associated with metabolic syndrome (MS) and likely develop into cirrhosis, diabetes, obesity, hyperlipidemia, hypertension and chronic kidney diseases, which has significantly jeopardized patients' lives [5–9]. Therefore, much attention should be attached to investigate appropriate risk factors associated with NAFLD and recent researches have made certain achievements [10–12]. In addition, a growing amount of literatures has investigated the gender differences of biomarkers in NAFLD patients and, interestingly, quite a few biomarkers in females manifest the more significant association with NAFLD [12,13].

Besides playing a part in NAFLD, MS is also related to inflammation and certain inflammatory marker such as C-reactive protein (CRP) provides prognostic information to the metabolic syndrome [14]. Similarly, platelet parameters including platelet count (PLT), mean platelet volume (MPV), and plateletcrit (PCT) have been found to be associated with certain inflammatory diseases and vascular diseases such as Crohn's disease, coronary artery disease, deep vein thrombosis and sepsis [15–17]. In addition, previous study suggested PLT and PCT were correlated with CRP [18]. Although, compared with PLT and MPV, PCT

Abbreviations: ALT, alanine aminotransferase; ANOVA, one-way analysis of variance; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; CIs, confidence intervals; Cr, creatinine; CRP, C-reactive protein; DBP, diastolic blood pressure; FPG, fasting plasma glucose; Hb, hemoglobin; HDL-C, high-density lipoprotein cholesterol; HRs, hazard ratios; LDL-C, low-density lipoprotein cholesterol; MPV, mean platelet volume; MS, metabolic syndrome; NAFL, Non-alcoholic fatty liver; NAFLD, Non-alcoholic fatty liver disease; PCT, plateletcrit; PLT, platelet count; SBP, systolic blood pressure; SD, mean ± standard derivations; TC, total cholesterol; TG, triglyceride; UA, uric acid

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http://dx.doi.org/10.1016/j.cca.2017.08.031
Received 27 April 2017; Received in revised form 17 July 2017; Accepted 28 August 2017
Available online 01 September 2017
0009-8981/

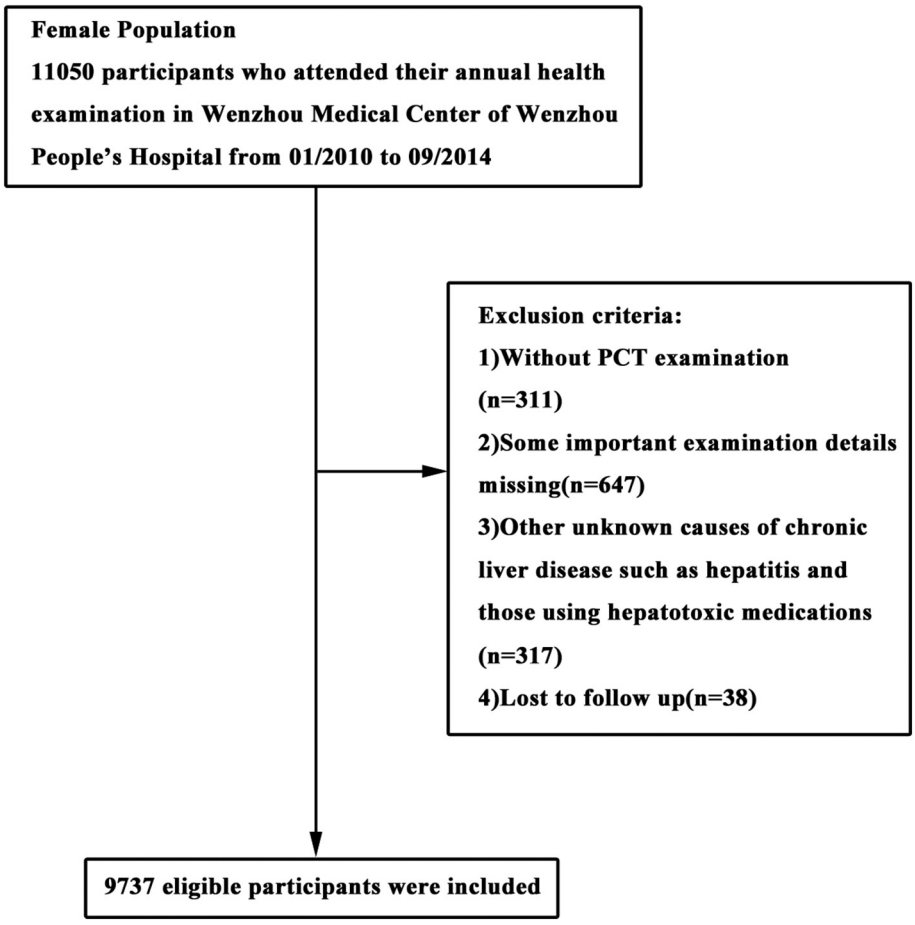

Fig. 1. Study flow diagram.
A total of 11,050 female participants were enrolled initially, whereas 1313 participants who did not meet the inclusion criteria were excluded. Finally, 9737 individuals were included.

is a relatively neglected biomarker, some studies demonstrate the specific value of PCT in Crohn's disease, cardiac syndrome X, coronary slow flow phenomenon, gestational diabetes and saphenous vein graft disease, which indicates the potential application of this parameter [15,19–22]. Among the diseases associating with PCT, it is remarkable that some diseases, namely coronary slow flow phenomenon and gestational diabetes, are metabolic syndrome related diseases. Considering the close relation between NAFLD and MS, there probably exists a connection of NAFLD and PCT. Due to the formula (PCT = PLT × MPV / 107), PCT can provide more comprehensive information about total platelet mass and be more sensitive than other platelet parameters [19]. Accordingly, it is promising to extend the application of PCT. Moreover, platelet parameters exist gender-dependent difference, which probably results from menstrual blood loss and hormone difference [23]. However, to the best of our knowledge, the association between sex-specific PLT and NAFLD has not been reported.

In this study, we investigate the relationship between the gender-specific PLT and NAFLD in southeastern China.

2. Materials and methods

2.1. Study design

This is a prospective cohort study aimed to investigate the underlying association between sex-specific PCT levels and NAFLD. The study population is made up of 9737 initially NAFLD–free subjects who underwent an annual health check-up in the Wenzhou People's Hospital. The ethical committee of Wenzhou People's Hospital approved our study. Each subject gave verbal informed consent.

2.2. Diagnosis of NAFL

According to guidelines for the assessment and management of NAFLD in the Asia-Pacific region, diagnosis of NAFLD can be made based on the following factors: the imaging findings are consistent with diagnostic criteria of fatty liver disease; no history of alcohol consumption habit or weekly alcohol intake < 70 g; certain diseases that can lead to steatosis (hepatobiliary infections, celiac disease, Wilson's disease, and alpha-1-antitrypsin deficiency) have been excluded [24]. Fatty liver is defined by the occurrence of at least two of three abnormal findings by abdominal ultrasonography in our study: diffusely enhanced echogenicity of the liver with the liver echogenicity greater than kidney or spleen, deep attenuation of ultrasound signal, and vascular blurring. The ultrasound was examined by two experienced imaging doctors who were unaware of the study. A third doctor with expertise in medical imaging was invited if the diagnoses previously made by the two doctors contradicted each other.

Clinical and laboratory examinations were reported in our previous studies at length [13,25–27].

2.3. Exclusion criteria

Subjects meeting any of the following criteria were excluded: without PCT examination; important check-up detail(s) missing; subjects developing viral hepatitis, hepatocellular carcinoma or autoimmune liver diseases (autoimmune hepatitis, primary sclerosing cholangitis, and primary biliary cirrhosis) or taking hepatotoxic medications; subjects lost to follow-up.