

Original Article



Longitudinal Changes in Liver Aminotransferases Predict Metabolic Syndrome in Chinese Patients with Nonviral Hepatitis

CHEN Qi Cai^{1,¶}, XIAO Juan^{2,¶}, ZHANG Peng Peng^{2,3}, CHEN Li Li^{2,4},
CHEN Xiao Xiao², and WANG Shu Mei^{2,¶}

1. Department of Prevention and Health Care, DongyingShengli Oilfield Central Hospital, Dongying 257000, Shandong, China; 2. Department of Epidemiology, School of Public Health, Shandong University, Jinan 250012, Shandong, China; 3. Tianjin Entry-Exit Inspection and Quarantine Bureau, Tianjin 300000, China; 4. Department of Nutrition and Food Safety, Zhejiang Center for Disease Control and Prevention, Hangzhou 310051, Zhejiang, China

Abstract

Objective This study explored the correlation of longitudinal changes in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels with the incidence of metabolic syndrome (Mets) based on a dynamic health examination cohort.

Methods A Mets-free dynamic cohort involving 4541 participants who underwent at least three health examinations from 2006 to 2011 was included in the study. Mets was defined according to the Chinese Medical Association Diabetes Branch definition that included hypertension, obesity, hyperlipidemia, and hyperglycemia. Generalized estimating equation (GEE) model was used to analyze multivariate relative risk (RR) of repeated observations of ALT and AST in quartiles for Mets or its components according to gender.

Results In all, 826 Mets cases were reported. Adjustment of relevant parameters indicated that time-varying changes in ALT and AST levels were positively associated with the incidence of Mets in a dose-response manner. Positive association between high ALT levels and fatty liver was much stronger than that between high AST levels and fatty liver, particularly in male participants. These associations were consistently observed in the following subgroups: participants with ALT and AST levels of <40 U/L, participants with BMI of <25 kg/m², and participants with non-fatty liver. Furthermore, participants with 2 Mets components at baseline showed lower multivariate adjusted RRs of ALT and AST for Mets than participants with 0-1 Mets component.

Conclusion These results suggested that elevated serum ALT and AST levels were early biomarkers of Mets or its components.

Key words: Alanine aminotransferase; Aspartate aminotransferase; Metabolic syndrome; Dynamic cohort study; Generalized estimating equation model

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INTRODUCTION

Metabolic syndrome (Mets), which is characterized by various metabolic disorders (hypertension,

hyperlipidemia, obesity, and hyperglycemia), is an important risk factor for cardiovascular diseases and all-cause mortality^[1-2]. The prevalence of Mets is increasing in China in recent decades because of the spread of the western lifestyle and increase in life

[¶]These authors contributed equally to this work.

[#]Correspondence should be addressed to WANG Shu Mei, Professor, PhD, Tel: 86-13156443025, E-mail: wshm@sdu.edu.cn

Biographical notes of the first authors: CHEN Qi Cai, male, born in 1962, Chief Physician, majoring in preventive medicine; XIAO Juan, female, 1989, Master, majoring in epidemiology.

expectancy^[3]. It is very important to prevent and control Mets in its early stage in different patient groups in China through targeted measures.

Some epidemiological studies^[4] have used increasing levels of serum liver aminotransferases, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as surrogate markers of nonalcoholic fatty liver disease (NAFLD). Recent studies suggest that NAFLD is a hepatic expression of Mets at an early stage^[5-6]. Increased levels of liver aminotransferases are associated with vascular endothelial disorders and body insulin sensitivity, which is independent of obesity^[7-8]. Moreover, association between elevated ALT and AST levels and Mets has been reported^[9-12].

Till date, the association of serum ALT and AST levels with the incidence of Mets has not been confirmed in cross-sectional studies^[10,13]. Furthermore, although AST and ALT levels may vary over time, existing cohort studies have ignored the changes in serum ALT and AST levels during follow-up and have only analyzed the association between baseline ALT and AST levels and incidence of Mets^[14]. Therefore, it is unclear whether high serum ALT and AST levels are associated with the incidence of Mets.

Moreover, various metabolic conditions may affect the association between ALT and AST levels and incidence of Mets. In addition, there is no consensus on whether sequential changes in ALT and AST levels within the reference range can predict Mets.

To clarify the relationship between ALT and AST and the incidence of Mets, the study used a dynamic health examination cohort study in Dongying City, China, which included repeated observations on the same sample. Data were analyzed using the generalized estimating equation (GEE) model that helps in analyzing inherent correlations in data, in handling unbalanced and incomplete data, and in characterizing changes in variables overtime in longitudinal data; moreover, the GEE model is free of distributional assumption^[15]. Thus, in this dynamic longitudinal study, we investigated the association of time-varying changes in serum ALT and AST levels with Mets in different subgroups to determine whether serum liver aminotransferases were biomarkers of Mets.

MATERIALS AND METHODS

Study Population

This study was performed at a general hospital

in Dongying City, China, from January 2006 to December 2011. Annual health examination including analysis of physical characteristics and comorbidities, assessment of previous surgeries, analysis of biochemical characteristics, and color Doppler ultrasonography, was performed in a unified manner. In all, 5856 participants who underwent at least three intact health examinations during January 2006 to December 2011 and who agreed to provide their data for analysis were recruited. Data of each participant's first health examination was used as baseline data. In total, 226 participants who did not have data on aminotransferase tests at baseline, 803 participants who had Mets at baseline according to the Chinese Medical Association Diabetes Branch (CDS) definition, 29 participants who had (at baseline) or developed (during follow-up) severe systemic diseases such as congestive heart failure and renal failure, 244 participants who showed positivity for hepatitis B virus surface antigen, 8 participants who showed positivity for hepatitis C virus antibody, and 5 participants with hepatitis A infection during follow-up were excluded from the study. Thus, 4541 participants aged 24-75 years were included in the study.

General Examination

Standardized Interviews During each health examination, medical examiners performed standardized interviews to obtain the following information: age (in years); behavior, including smoking and drinking; medical history (cardiovascular diseases, metabolic diseases, kidney diseases, liver diseases, and so on); and prescription medication use (excluding medication such as antihypertensives, antihyperlipidemic and antihyperglycemic drugs, and hepatotoxicity medication on the day of the health examination; $n=5$). Participants were asked to report current smoking behavior and alcohol intake over the month before the study. Smoking was defined as smoking any tobacco product continuously or accumulatively for >6 months and at least once a day in the previous 30 days^[16]. Drinking was defined as consumption of any type of alcoholic beverage once a week, excluding occasionally drinking during festivals^[17].

Anthropometric Variables Anthropometric variables, including weight, height, and blood pressure, were analyzed. Weight and height were measured by asking the participants to wear light clothes and no shoes. Body mass index (BMI) was calculated by dividing the weight (in kilograms) by

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