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Research article

Evaluating the Effects of the Components of Metabolic Syndrome, Fatty Liver and Liver Function on Chronic Hepatitis C: Data Analysis of Adult Health Examinations

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Abstract

Objective: The purpose of this study was to investigate the influential factors of chronic hepatitis C.

Methods: This was a cross-sectional study. Subjects aged 40 through 70, who received physical check-up from January 1, 2007 to December 31, 2011 in a hospital in central Taiwan, were included in this study. Among them, 200 cases had a diagnosis of chronic hepatitis C and 744 of them were free of hepatitis C. Physical data was obtained from health examinations and blood tests. Data were analyzed using SPSS for Windows, version 18.0.

Results: The prevalence rate of metabolic syndrome (MetS) in participants with chronic hepatitis C was 23.3%. The prevalence of chronic hepatitis C in women and participants aged 40–55 years was high (35.6% for women and 15.7% for men; 33.8% for participants aged 40–55 years and 16.9% for participants aged 56–70 years). Regarding composite factors for MetS, the prevalence of chronic hepatitis C in participants with a raised fasting plasma glucose (FPG) or hypertension was higher than that of participants without chronic hepatitis C (35.2% vs. 16.6% and 25.7% vs. 17.3% for hyperglycemia and hypertension, respectively); the results were all statistically significant. Logistic regression analysis was preformed to predict the influential factors of chronic hepatitis C. The results indicated that women and participants aged 40–55 years exhibited a relatively higher risk of chronic hepatitis C. In addition, participants with MetS, hyperglycemia, hypertension, or abnormal liver function exhibited a comparatively higher risk of chronic hepatitis C; the odds ratios for these participants were 1.72 (95% confidence interval [CI] = 1.10–2.70), 1.76 (95% CI = 1.08–2.89), 2.33 (95% CI = 1.61–3.37), and 2.40 (95% CI = 1.62–3.55), respectively.

Conclusion: This study indicated that abnormal liver function, MetS and its composite factors were correlated with chronic hepatitis C.

Keywords: metabolic syndrome, chronic hepatitis C, liver function, health examination

Introduction

According to a 2007 follow-up survey of patients with hypertension, hyperglycemia, and hyperlipidemia in Taiwan, the prevalence of metabolic syndrome (MetS) among Taiwanese people increases with age. In addition, cerebrovascular disease, heart disease, diabetes, and hypertension caused by MetS annually rank among the ten leading causes of death in Taiwan. These diseases have become critical public health issues [1]. Chronic hepatitis C occurs worldwide; 90% and 69% of posttransfusion hepatitis cases were hepatitis C in the United States and Taiwan, respectively. However, since the inclusion of the hepatitis C antibody test in the blood screening item in July 1992, almost no cases of posttransfusion hepatitis C have occurred [2]. Chronic hepatitis C can also cause liver disease; experts have stated that nonalcoholic fatty liver disease is a manifestation of MetS. The pathological spectrum of nonalcoholic fatty liver disease ranges from simple fatty infiltration to steatohepatitis, liver fibrosis, and liver cirrhosis. In recent years, nonalcoholic fatty liver disease has received increasing attention because of the increased prevalence, and multiple people with this problem have later experienced end-stage liver disease [3].

According to statistics from 2007, 4.4% of adults aged 20 years or above (approximately 400,000 people)

in Taiwan are chronic hepatitis C carriers. Chronic hepatitis C is a major cause of chronic liver disease with and approximately 170 million people worldwide have been diagnosed with chronic hepatitis C. The severity of chronic hepatitis C varies. Among the chronic hepatitis C patients discovered in clinic, few exhibit symptoms; however, the hepatitis C virus (HCV) can induce liver fibrosis, which can develop into fatty liver disease, liver cirrhosis, and liver cancer. Therefore, chronic hepatitis C treatment is extremely crucial for preventing liver cancer [4-7].

Previous epidemiology surveys have shown the incidence rate of MetS in patients with chronic hepatitis C is higher than that in healthy people. Regarding composite factors for MetS, the incidence of chronic hepatitis C in people with high waist circumference or hypertension is higher than that in healthy people. In addition, the incidence rate of MetS in patients with chronic hepatitis C was high [8]. The prevalence of MetS has increased annually and the probability of interaction between MetS and viral hepatitis has also increased. Previous studies have indicated that hepatic steatosis causes liver fibrosis in patients with chronic hepatitis C, and that the mortality rate of patients with chronic liver disease is related to composite factors for MetS [9]. Hepatitis B carriers and patients with hepatitis C who experience MetS may exhibit a high risk for liver cirrhosis or cancer. Therefore, in Taiwan, the incidence rate of liver cancer are the highest among all cancer types, but the mechanisms of these diseases are still unclear [10].

According to 2010 statistics provided by the Ministry of Health and Welfare of the Executive Yuan, malignancies were the leading cause of death in Central Taiwan (including Taichung, Changhua, Yunlin, and Nantou). In the category of malignancies, liver cancer and intrahepatic cholangiocarcinoma ranked among the three leading causes of death. MetS is a complex disease and is often complicated by numerous chronic diseases. Patients with chronic hepatitis C frequently exhibit MetS abnormalities and symptoms. However, few studies have investigated local epidemiology predicting the influential factors of chronic hepatitis C in Central Taiwan. Thus, the present study analyzed and evaluated the effects of the components of Mets, fatty liver and liver function on chronic hepatitis C.

Materials and Methods

Study design and data collection

We conducted a cross-sectional study on individuals that had undergone health examinations at a local teaching hospital in Chang-Hua County from January 1, 2007 to December 31, 2011. Data were collected from a medical institution in Central Taiwan after the institutional review board at the hospital approved this project. Participants were aged between 40 and 70 years who received adult health examinations. Serum test and physical examination results were collected from outpatient clinics and the health examination center's database. After excluding samples with incomplete biochemical blood tests, the valid sample size was 944 (comprising 200 cases with chronic hepatitis C and 744 cases without chronic hepatitis C).

Height was measured using a stadiometer to the nearest 0.1 cm, without shoes. Weight was measured using a beam balance scale to the nearest 0.1 kg, in light clothing and without shoes; BMI was calculated as the weight (kg) divided by height squared (m^2). In the current study, well-trained nurses measured the SBP and DBP two times in the right arm of seated participants according to a standardized protocol. A third blood pressure measurement was made if the first two blood pressure readings differed by more than 10 mm Hg. The average of the two closest readings was calculated to determine the reported blood pressure for each participant.

The biochemical blood examination included triglycerides, fasting plasma glucose (FPG), and HDL-C. Fasting venous blood samples were collected from each participant for a series of biochemistry analyses; the sample was venous blood drawn after 8 h of fasting.

Definition of terms:

Metabolic syndrome: We utilized previously established modifications for 2004 provided by the Health Promotion Administration, Ministry of Health and Welfare of the Executive Yuan. Any three of the following five criteria were grounds for identifying MetS: (1) abdominal obesity: BMI ≥27kg/m^2; (2) raised triglyceride (TG): ≥150 mg/dL; (3) reduced high-density lipoprotein cholesterol (HDL-C): HDL-C <40 mg/dL in men and <50 mg/dL in women; (4) hypertension: blood pressure of at least 130/85 mm Hg or taking antihypertensive medication; and (5) raised fasting plasma glucose (FPG) ≥100 mg/dL and/or taking anti-glycemic medication.

Chronic hepatitis C: Following a biochemical blood test, participants aged between 40 and 70 years were diagnosed as hepatitis C carriers or diagnosed with chronic hepatitis C.

Abnormal liver function: Irregular levels of serum glutamic oxaloacetic transaminase (SGOT) or serum glutamic pyruvic transaminase (SGPT) indicate abnormal liver function.

Fatty liver disease: Participants who received abdominal ultrasonography performed by a gastrointestinal specialist and were diagnosed with fatty liver disease (the information was recorded in a physical examination data file) were included in this study.

Statistical analysis:

Associations between chronic hepatitis C and demographic characteristics, fatty liver, live function, MetS, and composite factors were evaluated by $\chi 2$ tests. Multiple logistic regression was used to estimate the odds ratio (OR) and 95% confidence interval (CI) for predicted factors affecting chronic hepatitis C. All statistical tests were two-tailed, and values of $p<0.05$ were considered statistically significant. Data were analyzed using SPSS for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

The research participants in this study comprised 683 men (72.4%) and 261 women (27.6%), including 180 participants with MetS (19.4%), 448 participants with fatty liver disease (49.4%), and 206 participants with abnormal liver function (21.9%). Table 1 shows the correlations between chronic hepatitis C and demographic characteristics, MetS, and composite factors. Sex and age were significantly correlated with the chronic hepatitis C ($P < 0.001$). The prevalence rates of chronic hepatitis C in women and participants aged between 40 and 55 years were higher than among other participants. In addition, triglyceride level was significantly correlated with the chronic hepatitis C ($P < 0.001$). Participants with a high FPG level or hypertension more frequently experienced chronic hepatitis C ($P < 0.001$ and $P = 0.002$). Fatty liver disease and abnormal liver function were significantly correlated with the chronic hepatitis C ($P < 0.001$). Body mass index (BMI), HDL-C, and MetS were not significantly correlated with the chronic hepatitis C. However, compared with other participants, the prevalence rate of chronic hepatitis C in participants with a high BMI or MetS was higher (23.0% vs. 20.8% and 23.3% vs. 20.1% for BMI and MetS, respectively).

In this study, multiple logistic regression models (I and II) were used to estimate the OR and 95% CI for predicted factors affecting chronic hepatitis C. The results (Table 2) show that sex, age, MetS, fatty liver, liver function, FPG and hypertension were significant contributing factor to chronic hepatitis C in multiple logistic regression model I and II. However, age (56-77 years) and fatty liver disease indicated a protective effect

(OR<1).

The OR of chronic hepatitis C in women were respectively 3.10 and 3.18 times those in men, and the OR in participants with abnormal liver function were 2.40 and 2.37 times those in participants with normal liver function. The risk of chronic hepatitis C in participants with MetS was 1.72 times that in participants without MetS. Participants with abnormal MetS components (hyperglycemia, hypertension) exhibited a higher OR (1.76, 2.33) of chronic hepatitis C. The results for triglycerides, HDL-C, and BMI were not statistically significant.

Discussion

This study determined that women were more frequently diagnosed with chronic hepatitis C than were men. According to logistic regression models (I and II), the OR of chronic hepatitis C in women were respectively 3.10 and 3.18 times those in men; the results were significant. Previous studies have indicated similar results [11-13]. This study found that participants aged 40–55 years more frequently experienced chronic hepatitis C than did participants aged 56–70 years; the ORs for participants aged 40–55 years and those aged 56–70 years were 0.38 and 0.31 ($P < 0.001$), respectively. However, previous studies have showed that participants aged 56-70 more frequently experience chronic hepatitis C than do others [14-16]; these results were inconsistent with the results of this study. The reason for the inconsistency between previous studies and this study may be that data sources varied, causing the age levels of people who experienced chronic hepatitis C to vary.

According to Models I and II, fatty liver disease indicated a protective effect with chronic hepatitis C. Other studies indicated that when chronic hepatitis C develops into liver cirrhosis, hepatic steatosis can decrease. The mechanism by which liver cirrhosis reduces hepatic steatosis is still unclear. Researchers have stipulated that reduced hepatic steatosis likely occurs because liver cirrhosis causes portosystemic shunt, inhibiting contact between the liver and blood insulin [17,18]. This study showed that the OR of chronic hepatitis C in participants with abnormal liver function were 2.40 and 2.37 times those in participants with normal liver function ($P < 0.001$); the results were consistent with previous studies [17,19,20]. According to univariate analysis, participants with normal triglyceride level exhibited a higher prevalence of chronic hepatitis C. The logistic regression analysis yielded insignificant but similar results. Previous studies have indicated that patients infected with hepatitis C typically exhibit low triglyceride levels. This study determined that triglyceride level was correlated with chronic hepatitis C infection, which corresponded with the study by Jan et al. (2006) [21]. According to the present study, participants with hyperglycemia or hypertension more frequently experienced chronic hepatitis C. Previous studies have obtained similar results. Furthermore, patients with chronic hepatitis C were more frequently diagnosed with type-2 diabetes, insulin resistance, and hypertension [14,15].

The OR of chronic hepatitis C in participants with MetS was 1.72 times that in participants without MetS (95% confidence interval (CI) = 1.10–2.70). In this study, hyperglycemia and hypertension, which are composite factors for MetS, were influential factors that predicted chronic hepatitis C. Epidemiological research indicated that diabetic patients showed a high risk of nonalcoholic fatty liver disease and hepatocellular carcinoma [17]. Insulin resistance has emerged as an important prognostic factor for the clinical course of hepatitis C virus (HCV) infection, due to its association with resistance to antiviral therapy [23-27], progression of hepatic fibrosis [28-32], development of hepatocellular carcinoma (HCC) [33], and poor quality of life [34].

MetS involves numerous risk factors for cardiovascular disease. In addition to affecting the human cardiovascular system, MetS affects the respiratory, urinary, reproductive, and digestive systems, and causes

obstructive sleep apnea and nonalcoholic fatty liver disease. Therefore, the impact of MetS on various systems and functions in the human body has received substantial attention from researchers. Because of the prevalence of metabolic diseases worldwide, the probability of the joint occurrence of nonalcoholic fatty liver disease caused by metabolic syndrome and viral hepatitis will increase substantially, indicating that active treatment of liver diseases related to MetS is necessary.

Conclusion

This study determined that sex and age were correlated with the risk of chronic hepatitis C; in addition, MetS and the composite factors (hyperglycemia and hypertension) were correlated with chronic hepatitis C. Sex and age are unmodifiable factors. If MetS and the composite factors are effectively controlled, the probability of cardiovascular disease can be reduced, and the deterioration of liver diseases related to hepatitis C prevented; the costs of the medical system can also be reduced.

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Competing interests

The authors declare no conflict of interest.

Table1: The correlations between chronic hepatitis C and demographic characteristics, fatty liver, live function, MetS, and composite factors (N=944)

Variables	**Chronic hepatitis C**		
	Absent (%)	**Present (%)**	***P value***
Sex			<0.001
Man	576(84.3)	107(15.7)	
Woman	168(64.4)	93(35.6)	
Age			<0.001
40~55y	159(66.3)	81(33.8)	
56~70y	585(83.1)	119(16.9)	
BMI(kg/m^2)			0.508
BMI<27.0	587(79.2)	154(20.8)	
BMI≧27.0	151(77.0)	45(23.0)	
Triglyceride(mg/dL)			<0.001
Normal	463(75.8)	148(24.2)	
Abnormal(≧150)	281(85.2)	49(14.8)	
FPG(mg/dL)			<0.001
Normal	604(83.4)	120(16.6)	
Abnormal(≧100)	140(64.8)	76(35.2)	
Hypertension(mm Hg)			0.002
Normal	415(82.7)	87(17.3)	
Abnormal(≧130/85)	323(74.3)	112(25.7)	
HDL-C(mg/dL)			0.198
Normal	602(78.3)	167(21.7)	
Abnormal (Man：＜40；Woman：＜50)	139(82.7)	29(17.3)	
Metabolic syndrome			0.329
Normal	598(79.9)	150(20.1)	
Abnormal	138(76.7)	42(23.3)	
Fatty liver			<0.001
Normal	334(72.9)	124(27.1)	
Abnormal	372(83.0)	76(17.0)	
Live function			<0.001
Normal	601(81.7)	135(18.3)	
Abnormal	143(69.4)	63(30.6)	

*The lack of sample size represents the missing data.
* Using chi-squared statistical analysis and two-tailed test; significant level of α=0.05.

Table 2: Multiple logistic regression analysis of the predicted factors affecting chronic hepatitis C (N=944)

	Model Ⅰ OR (95% CI) [a]	***P value***	**Model Ⅱ OR (95% CI)** [a]	***P value***
Sex				
Man	1		1	
Woman	3.10(2.15-4.47)	<0.001	3.18(2.16-4.69)	<0.001
Age				
40~55y	1		1	
56~70y	0.38(0.27-0.55)	<0.001	0.31(0.21-0.46)	<0.001
Fatty liver				
Normal	1		1	
Abnormal	0.56(0.39-0.81)	0.002	0.67(0.44-1.00)	0.049
Live function				
Normal	1		1	
Abnormal	2.40(1.62-3.55)	<0.001	2.37(1.58-3.57)	<0.001
Metabolic syndrome				
Normal	1			
Abnormal	1.72(1.10-2.70)	0.018		
Triglyceride(mg/dL)				
Norma;			1	
Abnormal(≧150)			0.67(0.44-1.03)	0.068
FPG(mg/dL)				
Normal			1	
Abnormal(≧100)			1.76(1.08-2.89)	0.024
Hypertension(mm Hg)				
Normal			1	
Abnormal(≧130/85)			2.33(1.61-3.37)	<0.001
HDL-C(mg/dL)				
Normal			1	
Abnormal(男：＜40；女：＜50)			1.03(0.62-1.70)	0.914
BMI(kg/m^2)				
BMI<27.0			1	
BMI≧27.0			0.99(0.62-1.58)	0.958

[a]OR=odds ratio, 95% CI=(95% confidence interval)

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