The Investigation on the Correlation between Obesity Indicator and Hepatitis B and C

Abstract

Background: Obesity is an important health issue worldwide, and hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are the two major causes of liver disease that lead to Taiwan's medical health and socio-economic problems. There are currently few studies in the nation on the correlation between obesity indicators and hepatitis B and C.

Purpose: This study uses adult health check data analysis to understand the correlation of obesity indicators and hepatitis B and C.

Methods: This study is a cross-sectional research. The study collected people who did health examinations of a regional hospital in Kaohsiung from 2011 to 2016. The waist
Add country name also
circumference (WC), body mass index (BMI), and waist-height ratio (WHR) are used as obesity indicators.

Results: A total of 16,459 cases were included in the analysis. The prevalence of abnormal WC is 20.5%, and the WHR abnormal prevalence rate is 32.1%. Underweight Body Mass Index (BMI) BMI $\leq$ 18.4kg/m^2 (3.8%), normal BMI ranging from 18.5-23.9kg/m^2 (48.1%), overweight BMI ranging from 24.0-26.9 kg/m^2 (26.7%), obesity BMI $\geq$ 27kg/m2 (21.4%). The abnormal rate of hepatitis B was 13.6%, and the abnormal rate of hepatitis C was 1.9%. Logistic regression analysis shows that WC is a risk factor for hepatitis B (OR=1.181，95%CI=1.014-1.377), and WHR is a protective factor (OR=0.771，95%CI=0.673-0.885). WHR is a risk factor for hepatitis C (OR=1.571，95%CI=1.246-1.981).

Conclusions: The WC and WHR are respectively the risk factors for hepatitis B and hepatitis C, and the WHR is the protective factor for hepatitis B.

Key words: Waist circumference (WC), Waist-height ratio (WHR), Body mass index (BMI)、Hepatitis B, Hepatitis C

Introduction

not standard abrv

In Mexico, the prevalence of chronic liver disease (CLD) is increasing (1,2) with obesity, diabetes, and metabolic syndrome (MS). Weight gain and diabetes or MS were significantly associated with the increased risk of alanine aminotransferase (ALT) (1). It is estimated that by 2050, 90% of CLD cases in Mexico are caused by obesity and alcohol consumption compared with other countries with higher rates of liver disease caused by hepatitis B virus (HBV) or hepatitis C virus (HCV) (3).

HBV or HCV infection and consuming alcohol are both confirmed risk factors for CLD (4,5). Other risk factors include obesity (6,7), MS (8,9) and diabetes (7,10,11); and the mechanism is developed through nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) (7,12,13). The ratio of CLD increases rapidly in Mexico with the prevalence of obesity, MS, and diabetes.

Studies have shown that overweight or obesity, weight gain over time that leads to changes in body mass index (BMI), and develops diabetes or MS are associated with a high risk of elevated ALT concentrations (1). This cross-sectional association between obesity and elevated ALT criteria was established in the literature (14-17).

A follow-up study shows that, patients with MS have a higher risk of ALT elevation than those without metabolic syndrome. Yvonne et al, study shows that a significant number of Mexicans are at risk of developing CLD due to high obesity rates, high diabetes rates, and high MS rates (1). In Western countries, 75 to 90% of primary hepatocellular carcinoma (HCC) are associated with CLD (18). The most common chronic liver disease that causes HCC is hepatitis B or C virus infection and excessive alcohol consumption. Whether the development of HCC is associated with obesity and diabetes or changes in NAFLD is still unclear (19). Obesity and diabetes have been found to increase the risk of uterine, breast, colon and pancreatic tumors (20-24).

There are currently few studies in Taiwan on the correlation between obesity indicator

(WC, WHR, BMI) and hepatitis B and C. Therefore, this study uses adult health examination data analysis to understand the correlation between obesity indicator and hepatitis B and C.

Methods

Study design

This study is designed as a cross-sectional study, collecting physical examination and blood test data as analytical data from people who had health examination from 2011 to 2016 in a regional hospital in Kaohsiung. All participants were above 20 years of age and met fasting for the examinations.

Inclusion criteria：Those who participated in adult health examination from 2011 to 2016 as subjects.

Exclusion criteria：Age <20 years old and those who had incomplete blood test data and repeated screening are deducted.

Definition of Variables：

Height and weight data were obtained using standardized techniques and equipment.

1. Definition of obesity indicator

(1) Waist circumference (WC) outlier: Male≧90 cm, female≧80 cm. WC was measured at the midpoint between the bottom of the rib cage and the top of the iliac crest.

(2) Waist-height ratio (WHR): Normal (＜0.5), abnormal (≧0.5).

WHR was calculated as WC divided by height.

(3) Body Mass Index (BMI): Taiwan Ministry of Health and Welfare's Standard Classification BMI for 2004

Underweight: BMI $\leq$ 18.4kg/m^2

Normal: BMI between 18.5-23.9kg/m^2

Overweight: BMI between 24.0-26.9kg/m^2

Obesity: BMI$\geq$27kg/m^2

2. Chronic hepatitis B, C:

After blood biochemical tests, the gastrointestinal specialist judged that it is the asymptomatic carrier of hepatitis B and C.

Ethical Considerations

Data collection of this study began after approval by the hospital's Institutional Review Board (IRB).

Data processing and statistical analysis

All statistical analyses were performed using SPSS software (IBM SPSS Statistics 20; Asia Analytics Taiwan Ltd., Taipei, Taiwan). Statistical methods include: Descriptive statistics (number of frequencies, percentage, mean, standard deviation), analytical statistics: logistic regression. The above are used to analyze the effects of obesity indicators on hepatitis B and C. Statistically significant level with $\alpha=0.05$, and with 95% confidence interval (CI)

Results

This study includes the analysis from year 2011 to 2016, with 16,459 cases included in the analysis. The result of table 1 shows that: obesity indicator defines (1) the prevalence of abnormal waist circumference (male: ≧ 90 cm, female: ≧ 80 cm) 20.5%. (2) Prevalence of abnormal waist-height ratio is 32.1%. (3) Body Mass Index: according to the Health and Welfare Department's standards for Body Mass Index (BMI) in 2004, underweight BMI ≤ 18.4kg/m^2 (3.8%), normal: BMI between 18.5-23.9kg/m^2 (48.1%), overweight: BMI between 24.0-26.9kg/m^2 (26.7%), obesity: BMI ≥ 27kg/m^2 (21.4%). The abnormal rate of hepatitis B was 13.6%, and the abnormal rate of hepatitis C was 1.9%.

Logistic regression analysis was performed respectively for the positive or negative of hepatitis B and hepatitis C. The variables included in regression analysis are: gender, age, BMI, waist circumference, waist-height ratio. Table 2 shows that waist circumference is a risk factor for hepatitis B (OR=1.181, 95%CI=1.014-1.377), and waist-height ratio is protective factor (OR=0.771, 95%CI=0.673-0.885). Table 3 shows that waist-height ratio is the risk factor of hepatitis C (OR=1.571，95%CI=1.246-1.981).

Discussions

Obesity is highly associated with many chronic diseases, including diabetes, metabolic syndrome, gallbladder disease, coronary heart disease, stroke, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, sleep apnea syndrome, degenerative arthritis, deep veins embolism, etc. Obesity is even one of the risk factors for some cancers, such as colorectal cancer, endometrial cancer, and breast cancer.

According to the nation's Nutrition and Health Survey in Taiwan (NAHSIT) 2013-2014, the prevalence of overweight and obesity in adults was 43%, with 48.9% for male and 38.3% for female. (Note: Adult BMI has a cut-off weight with overweight 24≦BMI<27kg/m^2, and with obesity BMI≧27kg/m^2). This study includes 16,459 cases from 2011 to 2016 in the analysis. The results show that the prevalence of abnormal WC is (male: ≧90 cm, female ≧80 cm) 20.5%. The prevalence of abnormal WHR (≧0.5) is 32.1%. Underweight BMI≤18.4kg/m^2 (3.8%), normal BMI between 18.5-23.9kg/m^2 (48.1%), overweight BMI between 24.0-26.9kg/m^2 (26.7%), obesity BMI≥27kg/m^2 (21.4%). Among them, subjects with overweight BMI and obesity were lower than domestic surveys. It may be due to regional differences that the study subjects are from a single hospital.

Hepatitis virus infection is a progressive disease that leads to the development of cirrhosis and even hepatocellular carcinoma (HCC); there are about 20 ± 30% of patients worldwide (25,26). HBV and HCV infection are the two major causes of liver disease that leads to health and socio-economic problems in Taiwan (27,28). Seventy-five percent of all chronic HBV infections occur in Asia. The prevalence in Taiwan is 15%-20%, and >90% of adults have been infected with hepatitis B virus in the past. It is estimated that there are two million to three million HBV carriers in Taiwan today (29).

According to data from the Liver Disease Prevention and Treatment Research Foundation, among adults over the age of 20, the prevalence of HCV in Taiwan is estimated at 4.4% (or 423,283 anti-HCV positive carriers) (30). The study analyzed 157,720 patients between 1996 and 2005, the infection rates were similar between males and females, with significant increases in age and geographic differences. Although the prevalence in most countries is between 1% and 2%, the prevalence in some countries is relatively high, including Egypt (15%), Pakistan (4.7%) and Taiwan (4.4%). The global prevalence of hepatitis C virus (HCV) is about 2% -3%. Between 1990 and 2005, the prevalence of positive anti-HCV antibodies increased from 2.3% to 2.8%. (31) HCV infection causes 60%-80% of those who were infected to develop chronic hepatitis. (32) and it is associated with liver steatosis, fibrosis, cirrhosis and hepatocellular carcinoma. (33) The abnormal rate of hepatitis B in the study was 13.6%, and the abnormal rate of hepatitis C was 1.9%, both are lower than the average domestic populace. It may be different because this is a non-national sample survey that it only shows the results of health examination data in a regional hospital.

Previous studies have highlighted the important role of hepatitis virus infection in interacting with obesity. Hepatitis virus infections such as HCV, HBV and HCV/HBV co-infection are positively correlated with the increase in percent body fat (PBF), especially for male (34). Logistic regression analysis was performed in this study, on whether or not patients have hepatitis B and whether or not they have hepatitis C. The variables included in the regression analysis model are: gender, age, BMI, WC, WHR. It shows that WC is a risk factor for hepatitis B (OR=1.181, 95%CI=1.014-1.377), and WHR is protective factor (OR=0.771, 95%CI=0.673-0.885). The WHR is a risk factor for hepatitis C (OR=1.571, 95% CI=1.246-1.981). Previous studies show that elevated BMI was an independent risk factor associated with possible liver cirrhosis (LC) across the three different etiologies of CLD. Therefore, weight loss can be beneficial for the patients (35). Another study points out that WHR may be a better obesity indicator on identifying the individual risk for non-alcoholic fatty liver disease in Korean women (36). Since previous studies used less of the three obesity indicators: WC, WHR, and BMI respectively on the effects on hepatitis B and C, therefore, it is difficult to compare directly in the literature comparison. However, some studies have shown that obesity is indeed associated with chronic hepatitis B and C and is associated with nonalcoholic fatty liver disease and metabolic diseases. As previous literature has shown, obesity is significantly associated with NAFLD, and visceral fat is more directly related to the onset of NAFLD. (37) Compared with BMI, abdominal obesity is considered a better predictor of CVD and metabolic diseases. WC has become a widely used measurement method for quantifying abdominal fat accumulation. Epidemiological studies have shown that WHR appears to be more strongly associated with obesity-related diseases and metabolic risk factors than other obesity indicators. (38,39)

This study had several limitations. First, the study was cross-sectional in design, and hence causal relationships cannot be inferred. Second, this study can only present demographic characteristics, obesity indicators, biochemical blood tests and the correlation between hepatitis B and C. Due to the use of health examination data to perform analysis, the potential impact factors affecting the above results cannot be fully collected, so it is also necessary to be conservative in inference.

Conclusion

The obesity indicators have different effects on whether or not patients have hepatitis B, and whether they have hepatitis C. Waist circumference is a risk factor for hepatitis B, while waist-height ratio is a protective factor. The waist-height ratio is a risk factor for hepatitis C.

Table 1 Descriptive statistics of demographic characteristics, obesity indicators and Hepatitis B ,C (n=16459)

Variables	Number of people	Percentage	Mean ± standard deviation
Gender			
Male	8987	54.6	
Female	7472	45.4	
Age			45.4±11.4
＜40 years old	5735	34.8	
40 years old and above	10724	65.2	
Waist circumference			77.7±10.9
Male<90 cm, female<80 cm	13092	79.5	
Male≧90 cm, female≧80 cm	3367	20.5	
BMI			24.3±3.9
$< 27kg/m^2$	12940	78.6	
$\geq 27kg/m^2$	3519	21.4	
BMI			
$\leq 18.4kg/m^2$	627	3.8	
$18.5\text{-}23.9kg/m^2$	7918	48.1	
$24.0\text{-}26.9kg/m^2$	4395	26.7	
$\geq 27kg/m^2$	3519	21.4	
Waist-height ratio			
Normal＜0.5	11170	67.9	
Abnormal≥0.5	5289	32.1	
Hepatitis B			
Negative	14220	86.4	
Positive	2239	13.6	
Hepatitis C			
Negative	16140	98.1	
Positive	319	1.9	

Table 2 Regression analysis of obesity indicators on hepatitis B (n=16459)

Variables#	β	wald	OR(95%CI)	*P* value
Gender(female)	0.193	16.363	1.213(1.105-1.332)	<.001
Age(＜40 years old)	0.096	3.872	1.101(1.000-1.211)	0.049
WC(normal)	0.167	4.548	1.181(1.014-1.377)	0.033
WHR(normal)	-0.260	13.795	0.771(0.673-0.885)	<.001

Note 1: Stepwise regression method, the variables included in the regression analysis are: gender, age, BMI, WC, WHR.

Note 2: Dependent variable (1) with hepatitis B, (0) without hepatitis B.

#( ) is indicated as the reference group.

Table 3 Regression analysis of obesity indicators on hepatitis C (n=16459)

Variables#	β	wald	OR(95%CI)	*P* value
Gender(female)	-0.254	4.765	0.776(0.618-0.974)	0.029
Age(＜40 years old)	0.568	17.336	1.766(1.351-2.307)	<.001
WHR(normal)	0.452	14.567	1.571(1.246-1.981)	<.001

Note 1: Stepwise regression method, the variables included in the regression analysis are: gender, age, BMI, WC, WHR.

Note 2: Dependent variable (1) with hepatitis C, (0) without hepatitis C.

#( ) is indicated as the reference group.

References

1. Yvonne N. FLORES, Allyn AUSLANDER, Catherine M. CRESPI, Michael RODRIGUEZ, Zuo-Feng ZHANG, Francisco DURAZO & Jorge SALMERÓN. Longitudinal association of obesity, metabolic syndrome and diabetes with risk of elevated aminotransferase levels in a cohort of Mexican health workers. Journal of Digestive Diseases 2016; 17; 304–312doi: 10.1111/1751-2980.12341
2. Rivera JA, Barquera S, González-Cossío T, Olaiz G, Sepúlveda J. Nutrition transition in Mexico and in other Latin American countries. Nutr Rev 2004; 62: S149–57.
3. Méndez-Sánchez N, Villa AR, Chávez-Tapia NC et al. Trends in liver disease prevalence in Mexico from 2005 to 2050 through mortality data. Ann Hepatol 2005; 4: 52–5.
4. World Health Organization. Hepatitis. (2013). Cited: 22 March 2016. Available from URL: http://www.who.int/immunization/topics/hepatitis/en/
5. Rehm J, Samokhvalov AV, Shield KD. Global burden of alcoholic liver diseases. J Hepatol 2013; 59: 160–8.
6. Zheng RD, Chen ZR, Chen JN, Lu YH, Chen J. Role of body mass index, waist-to-height and waist-to-hip ratio in prediction of nonalcoholic fatty liver disease. Gastroenterol Res Pract 2012; 2012: 362147.
7. Regimbeau JM, Colombat M, Mognol P et al. Obesity and diabetes as a risk factor for hepatocellular carcinoma. Liver Transpl 2004; 10 (2 Suppl 1): S69–73.
8. Watanabe S, Yaginuma R, Ikejima K, Miyazaki A. Liver diseases and metabolic syndrome. J Gastroenterol 2008; 43: 509–18.
9. Smits MM, Ioannou GN, Boyko EJ, Utzschneider KM. Nonalcoholic fatty liver disease as an independent manifestation of the metabolic syndrome: Results of a US national survey in three ethnic groups. J Gastroenterol Hepatol 2013; 28: 664–70.
10. Firneisz G. Non-alcoholic fatty liver disease and type 2 diabetes mellitus: the liver disease of our age? World J Gastroenterol 2014; 20: 9072–89.

11. Davila JA, Morgan RO, Shaib Y, McGlynn KA, El-Serag HB. Diabetes increases the risk of hepatocellular carcinoma in the United States: a population based case control study. Gut 2005; 54: 533–9.

12. Ascha MS, Hanouneh IA, Lopez R, Tamini TA, Feldstein AF, Zein NN. The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. Hepatology 2010; 51: 1972–8.

13. Clark JM. The epidemiology of nonalcoholic fatty liver disease in adults. J Clin Gastroenterol 2006; 40 Suppl 1: S5–10.

14. Pendino GM, Mariano A, Surace P et al. Prevalence and etiology of altered liver tests: a population-based survey in a Mediterranean town. Hepatology 2005; 41: 1151–9.

15. Ruhl CE, Everhart JE. Determinants of the association of overweight with elevated serum alanine aminotransferase activity in the United States. Gastroenterology 2003; 124: 71–9.

16. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol 2003; 98: 960–7.

17. Pan JJ, Qu HQ, Rentfro A, McCormick JB, Fisher-Hoch SP, Fallon MB. Prevalence of metabolic syndrome and risks of abnormal serum alanine aminotransferase in Hispanics: a population-based study. PLoS One 2011; 6: e21515.

18. Colombo M. The natural history of hepatocellular carcinoma in Western countries. Hepatogastroenterology 1998;45:1221–1225.

19. Yang S, Lin HZ, Hwang H, Chacko VP, Diel AM. Hepatic hyperplasia in noncirrhotic fatty livers: obesity steatosis, a premalignant condition? Cancer Res 2001; 61: 5016–5023.

20. Lawson DH, Gray JM, McKillop C, Clarke J, Lee FD, Patrick RS. Diabetes mellitus and primary hepatocellular carcinoma. Q J Med 1986; 61:945–955.

21. Lagiou P, Kuper H, Stuver SO, Tzonou A, Trichopoulos D, Adami HO. Role of diabetes mellitus in the cause of hepatocellular carcinoma. J Natl Cancer Inst 2000;

92:1096 –1099.

22. Gerber M, Corpet D. Energy balance and cancers. Eur J Cancer Prev 1999;8:77– 89.
23. Stoll BA. Breast cancer: the obesity connection. Br J Cancer 1994;69:799–801.
24. Terry PD, Miller AB, Rohan TE. Obesity and colorectal cancer risk in women. Gut 2002;51:191–194.
25. Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The OBSVIRC, METAVIR, CLINIVIR, and DOSVIRC groups. Lancet (London, England).1997; 349(9055):825±32.
26. Fattovich G, Brollo L, Giustina G, Noventa F, Pontisso P, Alberti A, et al. Natural history and prognostic factors for chronic hepatitis type B. Gut. 1991; 32(3):294±8. PMID: 2013423.
27. Chen CJ, Yu MW, Liaw YF. Epidemiological characteristics and risk factors of hepatocellular carcinoma. Journal of gastroenterology and hepatology. 1997; 12(9±10): S294±308. PMID: 9407350.
28. Chen CH, Yang PM, Huang GT, Lee HS, Sung JL, Sheu JC. Estimation of seroprevalence of hepatitis B virus and hepatitis C virus in Taiwan from a large-scale survey of free hepatitis screening participants. Journal of the Formosan Medical Association = Taiwan yi zhi. 2007; 106(2):148±55. https://doi.org/10. 1016/S0929-6646(09)60231-X PMID: 17339159.
29. Department of Health, Executive Yuan, Taiwan, ROC. Public health report. Available from: http://www.doh.gov.tw/ufile/doc/Taiwan_Public_Health_Report2008.pdf; 2008.
30. Chen CH, Yang PM, Huang GT, *et al*. Estimation of sero prevalence of hepatitis B virus and hepatitis C virus in Taiwan from a large-scale survey of free hepatitis screening participants. *J Formos Med Assoc* 2007;106:148–55.
31. Mohd Hanafiah K, Groeger J, Flaxman AD, *et al*. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence.

Hepatology 2013;57:1333–42.

32. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;5:558–67.
33. Negro F, Sanyal AJ. Hepatitis C virus, steatosis and lipid abnormalities: clinical and pathogenic data. *Liver Int* 2009;29(Suppl 2):26–37.
34. Yuan-Yuei Chen, Wen-Hui Fang, Chung-Ching Wang, Tung-Wei Kao, Yaw-Wen Chang, Hui-Fang Yang, Chen-Jung Wu, Yu-Shan Sun, Wei-Liang Chen. Increased body fat percentage in patients with hepatitis B and C virus infection. *PLOS ONE | https://doi.org/10.1371/journal.pone.0200164 July 2, 2018
35. Yi-Hao Yen, Kuo-Chin Chang, Ming-Chao Tsai, Po-Lin Tseng, Ming-Tsung Lin, Cheng-Kun Wu, Jung-Ting Lin, Tsung-Hui Hu, Jing-Houng Wang, Chien-Hung Chen. Elevated body mass index is a risk factor associated with possible liver cirrhosis across different etiologies of chronic liver disease. Journal of the Formosan Medical Association (2018) 117, 268e275
36. Hyun-Jae Lim, Min-Seok Seo, Hye-Ree Lee, Jae-Yong Shim, Hee-Taik Kang, Yong-Jae Lee. Waist-to-Height Ratio as a Simple and Useful Indicator for Non-alcoholic Fatty Liver Disease in Korean Women. Korean J Obes 2016 March;25(1):19-23. http://dx.doi.org/10.7570/kjo.2016.25.1.19
37. van der Poorten D, Milner KL, Hui J, Hodge A, Trenell MI, Kench JG, et al. Visceral fat: a key mediator of steatohepatitis in metabolic liver disease. Hepatology 2008;48:449-57.
38. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev 2012;13:275-86.
39. Hsieh SD, Yoshinaga H, Muto T. Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. Int J Obes Relat Metab Disord 2003;27:610-6.