Correlation between Serum Alanine Aminotransferase Activity and Immunologic Response and Body Mass Index in Obese Patients with Chronic Hepatitis B Virus Infection

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Abstract

Background & Objective: Chronic B viral hepatitis is a common medical problem all over the world. However, obesity is important risk factors altered immune system response. This study was to examine the correlation between body mass index, serum alanine aminotransferase activity and immunologic response in obese hepatitis B Saudi patients.

Subjects and Methods: One hundred fifty Saudi male patients with hepatitis B viral infection (HBV); their age ranged from 30 to 45 (38.64±7.12) years. Patients were divided into two equal groups according to their body mass index:

Group (A): Included patients with HBV, their body mass index (BMI) was greater than 30kg/m2 (the obese group).

Group (B): Included patients with HBV, their BMI between 20 and 24kg/m2 (the normal-weight group).

Results: An elevation of serum alanine aminotransferase (ALT) activity was found to be associated with increased BMI, also we observed an elevation in white blood cells, neutrophils, monocytes, CD3, CD4 and CD8 for group A. CD3, CD4 and CD8 correlated with BMI only as a total amount, as well as with all measured parameters of blood count.

Conclusion: Obesity adversely affects the immunological response and rate of disease progression in HBeAg-negative chronic hepatitis B viral infection

Keywords: Immune system; Obesity; Body mass index; Chronic Hepatitis B virus Infection

Abbreviations: HBV: Hepatitis B Virus; HIV: Human Immuno-Deficiency Virus; ALT: Alanine Aminotransferase; BMI: Body Mass Index; HDL-C: High-Density Lipoprotein-Cholesterol.

Introduction

Hepatitis B virus (HBV) causes inflammation of the liver in humans and is a major public health problem worldwide. About a quarter of the world population (>2 billion) has been infected with HBV [1]. The risk of HBV is 50-100 times more than human immuno-deficiency virus (HIV) [2,3].

Obese subjects usually have abnormal results in liver function test than normal weight subjects [4-6] as obesity induce alterations in the hepatic histological structure as steatosis [7-9] associated with elevation of serum alanine aminotransferase (ALT) [8-9]. However, men with HBV infection have significantly high ALT level [10].

Hepatic cancer and cirrhosis that threaten life are commonly induced by HBV [11]. The Immune responses involved in viral clearance for HBV comprise both humoral and cellular immunity [12]. However, obesity, which is a risk factor in many chronic, disorders [13], there is a close relationship between the nutritional status and the immune system performance as some studies reported poor immune system efficiency among obese subjects [14-16]. Hepatic disorders are more common among obese subjects and their response to anti-viral medications are poor among obese subjects with chronic hepatic diseases [17-21].
The purpose of this study was to examine the relationship between body mass index, serum alanine aminotransferase activity and immunologic response in obese patients with HBV infection.

Subjects and Methods

One hundred fifty non-hypertensive, non-cirrhotic Saudi male patients with chronic HBV infection; their age ranged from 30 to 45 (38.6±4.7) years, were randomly selected from Gastroenterology and Hepatology Department, King Abdulaziz University Teaching Hospital, Saudi Arabia between the period of March 2014 and December 2015. Only patients diagnosed with chronic HBV mono-infection and undergo Real-Time polymerase chain reaction who were negative for HBeAg for at least six months ago according to the standards of the American Association for the study of Liver Disease [22]. However, patients with alcoholic liver disease, hepatitis C virus and hepatitis Cirrhosis were excluded. Participants were enrolled according to their body mass index into:

Group (A): Included HBV patients with a BMI more than 25 kg/m² (the obese group).

Group (B): Included HBV patients with a BMI between 18.5 and 23 kg/m² (the normal-weight group).

Methods

Evaluated Parameters

Flow cytometry analysis: Flow cytometry using Cytomics FC500 and CXP software (Beckman Coulter) was used to measure the leukocyte differentiation antigens CD3, CD4 and CD8 (Beckman Coulter, Marseille, France).

Analysis of peripheral blood cells: Beckman Coulter AcT 5diff hematology analyzer was used in analysis of peripheral blood cells.

Serum alanine aminotransferase and viral serology tests: Automatic spectrophotometer (Bioclin, Quibasa, Belo Horizonte, MG, Brazil) was used to measure serum alanine aminotransferase.

Body mass index (BMI): Weight and height scale (Metrotype - England) was used to measure weight and height to calculate the body mass index (BMI). Body mass index was calculated by dividing the weight in kilograms by the square of the height in meters (Kg/m²) [23].

Statistical analysis

Independent t-test was used to compare differences between both groups. Statistical analysis of data was performed using SPSS (Chicago, IL, USA) version 17. Pearson or Spearman rank correlation was used to detect the relationship between continuous variables and BMI (P<0.05).

Results

Regarding the demographic variables, the two groups were considered homogeneous (Table 1). The mean age of the obese group was 39.16±7.33 years, and was 37.64±6.98 years in the normal weight group. There was no significant differences in fasting glucose, triglyceride, total cholesterol, high-density lipoprotein-cholesterol, systolic blood pressure and diastolic blood pressure between the obese and normal-weight groups. However, body weight, body mass index (BMI), alanine aminotransferase (ALT) and HBV viral load were significantly different between the obese and normal-weight groups.

Table 1: Comparison of clinical data between HBV patients in both groups.

|                  | Group (A)       | Group (B)       |
|------------------|-----------------|-----------------|
| Age (year)       | 39.16±7.33      | 37.64±6.98      |
| BMI (kg/m²)      | 31.15±4.32*     | 20.36±4.67      |
| ALT activity (IU/L) | 80.78±6.84*    | 23.31±4.92      |
| Fasting glucose (mg/dL) | 103.23±15.63  | 98.43±16.54     |
| Triglyceride (mg/dL) | 132.62±17.54  | 129.37±12.38    |
| Total cholesterol (mg/dL) | 195.21±25.42 | 192.84±17.52  |
| HDL-C (mg/dL)    | 50.44±12.60     | 47.11±14.28     |
| Systolic blood pressure (mm Hg) | 120.68±17.73 | 116.62±13.36    |
| Diastolic blood pressure (mm Hg) | 80.23±7.41 | 77.52±6.93      |
| HBV DNA (IU/mL)  | 3.57±0.85×10^6* | 5.14±0.64×10^5* |

BMI: Body Mass Index; ALT: Alanine aminotransferase; HDL-C: High-density lipoprotein-cholesterol

(*) indicates a significant difference between the two groups, P<0.05.

Table 2: Mean value and significance of white blood cells, total neutrophil, monocytes, CD3, CD4 and CD8 count of group (A).

|                  | Group (A)       | Group (B)       |
|------------------|-----------------|-----------------|
| White blood cells count (10^9/µL) | 9.31±3.41*     | 5.87±3.11      |
| Total neutrophil count (10^9/µL) | 6.12±2.38*    | 4.15±2.16      |
| Monocytes (10^9/µL) | 0.58±0.16*   | 0.37±0.11      |
| CD3 count (10^9/µL) | 1.86±0.93*    | 1.39±0.78      |
| CD4 count (10^9/µL) | 1.41±0.85*   | 1.12±0.76      |
| CD8 count (10^9/µL) | 0.82±0.34*    | 0.51±0.25      |

(*) indicates a significant difference between the two groups, P<0.05.

The number of white blood cells, total neutrophil count, monocytes, CD3, CD4 and CD8 were significantly elevated in obese individuals when compared with normal controls (Table
2. The Pearson's correlation coefficients test for the relationship between body mass index & ALT activity, white blood cells, total neutrophil count, monocytes, CD3, CD4 and CD8 in both groups showed a strong direct relationship in both groups (Table 3 & 4).

Table 3: Shows the Pearson’s correlation coefficients test value and the relationship between the BMI & ALT activity, white blood cells, total neutrophil, monocytes, CD3, CD4 and CD8 count of group (A).

| Pearson’s value (r)          |         |
|-----------------------------|---------|
| ALT activity (IU/L)         | 0.42*   |
| White blood cells (10^9/µL) | 0.46*   |
| Total neutrophil (10^9/µL)  | 0.35*   |
| Monocytes (10^9/µL)         | 0.32*   |
| CD3 count(10^9/µL)          | 0.41*   |
| CD4 count(10^9/µL)          | 0.33*   |
| CD8 count(10^9/µL)          | 0.34*   |

ALT: Alanine aminotransferase; Significance was calculated by Spearman or Pearson correlation (2-tailed)
*p<0.05; r, correlation coefficient.

Table 4: Shows the Pearson’s correlation coefficients test value and the relationship between the BMI & ALT activity, white blood cells, total neutrophil, monocytes, CD3, CD4 and CD8 count of group (B).

| Pearson’s Value (r)          |         |
|-----------------------------|---------|
| ALT activity (IU/L)         | 0.41*   |
| White blood cells (10^9/µL) | 0.42*   |
| Total neutrophil (10^9/µL)  | 0.41*   |
| Monocytes (10^9/µL)         | 0.35*   |
| CD3 count(10^9/µL)          | 0.34*   |
| CD4 count(10^9/µL)          | 0.31*   |
| CD8 count(10^9/µL)          | 0.32*   |

ALT: Alanine aminotransferase; Significance was calculated by Spearman or Pearson correlation (2-tailed), *p<0.05; r, correlation coefficient.

Discussion

As the influence of obesity on the immune system in the HBV Saudi patients is not well known, our study was conducted to explore the relationship between the obesity and immune system in obese HBVSaudi patients. In our study, obese HBVSaudi patients showed elevated ALT activity than HBV patients with normal body weight; our findings are in line with the results of many previous studies as Moulin et al. [33] who showed in his study that obesity is associated with the altered parameters of immune system as there was elevation in the number of total WBC, monocyte, neutrophil and leucocyte associated with elevated inflammatory cytokines among obese subjects [34-39]. In addition, Kintscher et al [40] reported that there was an association between BMI and number of CD3 and CD4 lymphocytes among obese women. Moreover, Antuna-Puente et al. [41] found a positive correlation between the number of macrophages and BMI in adipose tissue.

Conclusions

Obesity adversely affects the immunological response and rate of HBV progression, therefore control of body weight is important in the management of among patients with HBV.

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References

1. WHO Media Center (2008) Hepatitis B factsheet. WHO Media Center, Geneva, Switzerland.
2. Franco E, Bagnato B, Marino MG, Mieleko C, Serino L, et al. (2012) Hepatitis B: Epidemiology and prevention in developing countries. World J Hepatol 4(3):74-80.
3. Busca A, Kumar A (2014) Inmate immune responses in hepatitis B virus (HBV) infection. Virol J 11:22.
4. Tanaka S, Inoue S, Isoda F, Waseda M, Iishihara M, et al. (1993) Impaired immunity in obesity: suppressed but reversible lymphocyte responsiveness. Int J Obes Relat Metab Disord 17(11):631-636.
5. Friedman LS, Dienstag JL, Watkins E, Hinkle CA, Spiers JA, et al. (1987) Evaluation of blood donors with elevated serum alanine aminotransferase levels. Ann Intern Med 107(2):137-144.
6. Nomura F, Ohnishi K, Satomura Y, Ohtsuki Y, Fukunaga K, et al. (1986) Liver function in moderate obesity-study in 534 moderately obese subjects among 4613 male company employees. Int J Obes 10(5):349-354.
7. Guzzaloni G, Grugni G, Minocci A, Moro D, Marabito F (2000) Liver steatosis in juvenile obesity: correlations with lipid profile, hepatic biochemical parameters and glycemic and insulinemic responses to an oral glucose tolerance test. Int J Obes 24(6):772-776.
8. Tazawa Y, Noguchi H, Nishinomiya F, Takada G (1997) Serum alanine aminotransferase activity in obese children. Acta Pediatr 86(3):238-241.
9. Anderson T, Chrisoffersen P, Glaud C (1984) The liver in consecutive patients with morbid obesity: a clinical, morphological, and biochemical study. Int J Obes 8(2):107-115.
10. Hisen-Feng Lin, Shih-Wei Lai, Wen-Yuan Lin, Chiu-Shong Liu, Cheng-Chieh Lin, et al. (2016) Prevalence and factors of elevated alanine aminotransferase in central Taiwan – a retrospective study. Biomedicine (Taipei) 6(2):11-19.
11. Pramoolsinsup C (2002) Management of viral hepatitis B. J Gastroenterol Hepatol 17(Suppl): S125-S145.

12. Chisari FV, Isogawa M, Wieland SF (2010) Pathogenesis of hepatitis B virus infection. Pathobiol (Paris) 58(4): 258-266.

13. WHO (2011) Obesity and overweight fact sheet, 2011. World Health Organization, Geneva, Switzerland.

14. Cyril O (2006) Complex interactions between malnutrition, infection and immunity: relevance to HIV/AIDS infection. Nigerian Journal of Clinical & Biomedical Research 1: 6-14.

15. Nieman D, Henson D, Nehlsen-Camarell S, Ekiens M, Utter A (1999) Influence of obesity on immune function. J Am Diet Assoc 99(3): 294-299.

16. O'Rourke R, Kay T, Scholz M, Digs B, Jobe B (2005) Alterations in T-cell subset frequency in peripheral blood in obesity. Obes Surg 15(10): 1463-1468.

17. Lo Iacono O, Venezia G, Peta S, Mineo C, De Lisi S, et al. (2007) The impact of insulin resistance, serum adipokytokines and visceral obesity on steatosis and fibrosis in patients with chronic hepatitis C. Aliment Pharmacol Ther 25(10): 1181-1191.

18. Delgado-Borrego A, Healey D, Negre B, Christofi M, Sabharwal S, et al. (2010) Influence of body mass index on outcome of pediatric chronic hepatitis C virus infection. J Pediatr Gastroenterol Nutr 51(2): 191-197.

19. Weber DJ, Rutała WA, Samsa GP, Santimaw JE, Lemon SM (1985) Obesity as a predictor of poor antibody response to hepatitis B plasma vaccine. JAMA 254(22): 3187-3189.

20. Simó-Miñana J, Gaztambide Ganuza M, Fernández Millán P, Peña Fernández M (1996) Hepatitis B vaccine immunoresponsiveness in adolescents: a revaccination proposal after primary vaccination. Vaccine 14(2): 103-106.

21. Young MD, Gooch WM, Zuckerman AJ, Du W, Dickson B, Maddrey MC (2001) Comparison of a triple antigen and a single antigen recombinant vaccine for adult hepatitis B vaccination. J Med Virol 64(3): 290-298.

22. Lok A, McMahon B (2009) Chronic hepatitis B: update 2009. Hepatology 50(3): 661-672.

23. Han S, Jeon K, Kim M, Kim H, Lee A (2011) Obesity with a body mass index under 30 does not significantly impair the immune response in young adults. Nutri Res 31(5): 362-369.

24. Wang Y, Lin S, Sheu W, Liu P, Tung K (2010) Obesity and diabetic hyperglycemia were associated with serum alanine aminotransferase activity in patients with hepatitis B infection. Metabolism 59(4): 486-491.

25. Pratt D, Kaplan M (2000) Evaluation of abnormal liver-enzyme results in asymptomatic patients. N Engl J Med 109(17): 588-590.

26. Clark J, Brancati F, Diehl A (2003) The prevalence and etiology of elevated aminotransferase levels in the United States. Am J Gastroenterol 98(5): 960-967.

27. Erbey J, Silberman C, Lydiick E (2000) The prevalence of abnormal serum alanine aminotransferase levels in obese patients and patients with type 2 diabetes. Am J Med. 2000;109(7): 588-590.

28. Ioannou G, Weiss N, Boyko E, Kahn S, Lee S (2005) Contribution of metabolic factors to alanine aminotransferase activity in persons with other causes of liver disease. Gastroenterology 129(3): 627-635.

29. Prati D, Taioli E, Zanella A, Della Torre E, Butei S, et al. (2002) Updated definitions of healthy ranges for serum alanine aminotransferase levels. Ann Intern Med 137(1): 1-10.

30. Piton A, Pouyrad T, Imbert-Bismut F, Khalil L, Delattrel, et al. (1998) Factors associated with serum alanine transaminase activity in healthy subjects: consequences for the definition of normal values, for selection of blood donors, and for patients with chronic hepatitis C. Hepatology 27(5): 1213-1219.

31. Kim H, Nam C, Lee S, Han K, Oh D, et al. (2004) Normal serum aminotransferase concentration and risk of mortality from liver diseases: prospective cohort study. BMJ 328(7446): 983-986.

32. Yuen M, Yuan H, Wong D, Yuen J, Wong W, et al. (2005) Prognostic determinants for chronic hepatitis B in Asians: therapeutic implications. Gut 54(11): 1610-1614.

33. Moulin C, Margutti I, Peron J, Rizzo L, Halpern A (2009) Impact of adiposity on immunological parameters. Arq Bras Endocrinol Metab 53(2): 183-189.

34. Nieman D, Nehlsen-Camarell S, Henson D, Butterworth D, Fagoaga O (1996) Immune response to obesity and moderate weight loss. Int J Obes Relat Metab Disord 20: 353-360.

35. Womack J, Tien P, Feldman J (2007) Obesity and immune cell counts in women. Metabolism 56(7): 998-1004.

36. Iyer A, Fairlie D, Prins J, Hammock B, Brown L (2010) Inflammatory lipid mediators in adipocyte function and obesity. Nat Rev Endocrinol 6(2): 71-82.

37. Stošić A (2009) Leptine and adiponectin: from energy and metabolic dysbalance to inflammation and autoimmunity. EndocrRegul 43(4): 157-168.

38. Karalis K, Giannoponas P, Kodela E, Zoumakis M, et al. (2009) Mechanisms of obesity and related pathology: linking immune responses to metabolic stress. FEBSJ 276(20): 5747-5754.

39. Ilyavska S, Horváthova M, Szabova M, Nemessnyi T, Jahnova R, et al. (2012) Association between the human immune response and body mass index. Hum Immunol 73(5): 480-485.

40. Kintschera U, Hartge M, Hess K, Forst-Ludwig A, Clemenz M, et al. (2008) T-lymphocyte infiltration in visceral adipose tissue: a primary event in adipose tissue inflammation and the development of obesity-mediated insulin resistance. Arterioscler Thromb VascBiol 28(7): 1304-1310.

41. Antuna-Puente B, Feve B, Fellah S, Bastard J (2008) Adipokines: the missing link between insulin resistance and obesity. Diabetes Metab 34(1): 2-11.
