

Prevalence of Diabetes Mellitus among Hepatitis B Infected Patients Attending Communicable Disease Research and Training Center, Suez City, Egypt

Fatma R. Moussa

Department of Endemic and Infectious Diseases, Faculty of Medicine, Suez Canal University, Egypt

Abstract

Background: HBV is a common major health problem in Egypt and world-wide with burden on national health care system. The association between HBV infection and type 2 diabetes mellitus (T2DM) has been reported over the past decade. However, the relationship between HBV infection and T2DM remains controversial. **Aim:** to study the prevalence of diabetes mellitus among hepatitis B patients in Suez, Egypt. **Patients and Methods:** the study included 216 HBV infected patients who attend for regular follow-up in the communicable disease research and training center-Suez city, Egypt. Medical information was collected from patients' medical record. **Results:** the prevalence of Diabetes among HBV patients was 20.4 %. About 29.6 % of HBV patients had liver cirrhosis, and 4.6% had HCC. The majority (54.54 %) of patients having both HBV and DM were males. **Conclusion:** DM is a common medical condition in patients with HBV.

Key words: T2DM, Cirrhosis, HCC

Introduction

Hepatitis B virus (HBV) infections are blood-borne viral infection that serious major public health threats worldwide. Regarding to the prevalence of chronic HBV infection, the World Health Organization (WHO) divided the world into three areas; areas with high prevalence (>8%), intermediate prevalence (2-8%), and low prevalence (<2%)⁽¹⁾. There are 350 million carriers of HBV worldwide^(2,5,6). Each year, about 877.000 people die due to the serious complications of HBV infection, including cirrhosis and hepatic neoplasm⁽³⁾. HBV remain a

major health problem in Egypt and Africa, which can lead to an acute or chronic courses of liver diseases, started from hepatic impairment to cirrhosis, hepatic cell failure or hepatocellular carcinoma (HCC) in a 20-30-years. Prevalence of HBV among the Egyptian population is about 1.4%⁽⁴⁾. DM is one of the most common systemic diseases worldwide. In 2002, the estimated numbers for patients with type II DM was 177 million, which is estimated to reach 300 million by 2025⁽⁷⁾. The prevalence of type II DM is expected to rise by 69% and 20% in developing and developed countries respectively by 2030, respectively; also, the number of di-

*Corresponding Author: frageh2002@hotmail.com

abetic patients will reach 24 million in Africa⁽⁸⁾. The association between HBV infection and type 2 diabetes mellitus (T2DM) has been studied during the last ten years. Patients with HBV-related cirrhosis have been found to have glucose intolerance attributable to insulin resistance (IR), which may disrupt glucose metabolism and ultimately augment the risk of T2DM. Meanwhile, advanced glucose metabolism disorders could have a role in liver deterioration and exacerbate liver damage⁽⁹⁾. However, the relationship between HBV infection and T2DM remains unclearly established. Cai et al. (2014) performed a meta-analysis that noticed that risk for developing DM in patients infected with HBV were higher compared to non-infected patients. However, they did not correctly differentiate between the HBV infection phases for many of the original articles⁽¹⁰⁾. Because whether hepatitis B virus infection increases the risk of type 2 diabetes mellitus (DM) has been a controversial topic all over the world and little is known about it is prevalence in Egypt, so this study is aimed to study the prevalence of diabetes mellitus among hepatitis B patients in Suez, Egypt.

Patients and Methods

Study design: the study was carried out as a cross sectional descriptive study, that conducted in the communicable disease research and training center in Suez city, Egypt. **Target population:** all patient attended to the center for follow up throughout the period from January 2017 to June 2019. Two-hundred & sixteen patients were participated in the study. **Sampling method:** all eligible patient attended to communicable disease research and training center Suez city; Egypt were included in the study. **Inclusion criteria:** HBV patients attended to

the center for follow-up and confirmed by PCR. **Exclusion criteria:** HCV infected patients or patients with co-infection with HBV & HCV. **Data collection:** Before starting the study, a detailed History taking regarding medical status. Medical data were collected from patients' medical record. **Laboratory Diagnosis of HBV infection:** All patients were subjected to the following tests; HBsAg, HBeAg, HbeAb and HBV-PCR. Patients were diagnosed as chronic hepatitis B if they had persistence of HBsAg for more than 6 months. **Diagnosis of DM:** DM was diagnosed according to the World Health Organization criteria (2006); fasting plasma glucose ≥ 126 mg% or postprandial plasma glucose ≥ 200 mg%.

Results

Mean age of the studied populations was 42.79 ± 11.44 years. About 58.8 % of studied population were males & 72.7 % were lived in urban area. More than half of the studied population had no work. More than three-fourth of patients were married (table 1). Diabetes Mellitus was present in about 20.6 % of the studied population with HBV. about 29.6 % had liver Cirrhosis and 4.6 % complicated with HCC. Most of patient were either Overweight (48.6 %) or Obese (49.5 %) (Table 2). Most of Diabetic patients were males (18.90 % of total cases) (table 3). Regarding the gender, hypertension was present in 17 male patients (13.39 %) versus 12 female patients (13.48%), 3.94 % of males had HCC vs. 5.62 % of females, while 29.92 % of males had liver Cirrhosis and near percentage (29.21 %) for females (table 3). This reflect that no deference in the percentage of liver cirrhosis between males and females, but the percentage of HCC were higher in females. On focusing in patients had diabetes mellitus in patients in-

fected with HBV, 14 patients had hypertension, 14 patients had liver cirrhosis, and 1 patient had HCC. For body weight, 2

patients were had normal weight 18 patients were overweight and 24 patients were obese.

Table 1: Socioeconomic data of the studied population

	Minimum	Maximum	Mean ±SD
Age	20	66	42.79±11.44
	Frequency		%
Gender	Male	127	58.8 %
	Female	89	41.2 %
Residence	Rural	59	27.3 %
	Urban	157	72.7 %
Occupation	Profession	56	25.9 %
	Employment	18	8.3 %
	Business	31	14.4 %
	Not Working	111	51.4 %
Education	Literate	94	43.5 %
	Illiterate	122	56.5 %
Marital status	Single	21	9.7 %
	Married	168	77.8 %
	Widow	14	6.5 %
	Divorced	13	6.0 %

Table 2: Medical status of the studied population

		Frequency	%
Diabetes	Yes	44	20.4 %
	No	172	79.6 %
Hypertension	Yes	29	13.4 %
	No	187	86.6 %
BMI	Normal	4	1.9 %
	Overweight	105	48.6 %
	Obese	107	49.5 %
HCC	Yes	10	4.6 %
	No	206	95.4 %
Cirrhosis	Yes	64	29.6 %
	No	152	70.4 %

Discussion

Chronic HBV infection is a serious public health medical problem globally. The association between HBV and T2DM has been reported over the last ten years. HBV infection is associated with significant health risks, with about 5% of adults with acute or non-symptomatic HBV infection chronically infected, and individuals infected with the virus are at risk to develop hepatic decompensation, cirrhosis and HCC^(11,12). Several studies have investigated the relationship between DM

and HBV infection, which suggested that chronic HBV infection had a strong association with DM. Moreover, these studies found that this association remained statistically significant even after adjusting the potential confounding variables such as age, sex, ethnicity, smoking, alcohol use and family history of DM⁽¹³⁻¹⁵⁾. However, some studies have found no association between T2DM and HBV infection⁽¹⁶⁻¹⁸⁾. Several hypotheses were settled for the co-factor of DM and HBV. DM leads to the disruption of multiple organ functions, including the suppression of

endocrine function, impaired cellular immunity, and hyper-humoral immunity⁽¹⁹⁾. A long-term continuous hyperglycemic state has been shown to accelerate the

occurrence and development of diabetic complications as retinopathy, neuropathy, and immune disorders⁽²⁰⁾.

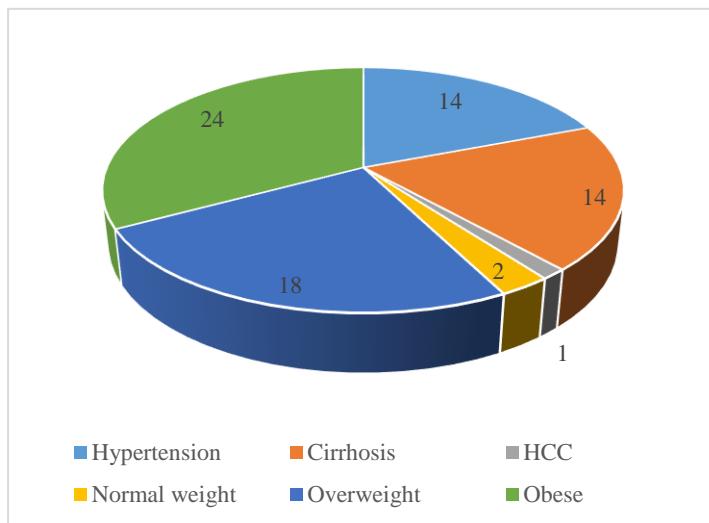


Figure 1: Medical status regarding the diabetes status

Table 3: Distribution of medical condition regarding the gender

		Male (n=127)		Female (n=89)		P value
		n.	%	n.	%	
Diabetes	Yes	24	18.90 %	20	22.47 %	0.023
	No	103	81.10 %	69	77.53 %	
Hypertension	Yes	17	13.39 %	12	13.48 %	0.022
	No	110	86.61 %	77	86.52 %	
HCC	Yes	5	3.94 %	5	5.62 %	0.047
	No	122	96.06 %	84	94.38 %	
Cirrhosis	Yes	38	29.92 %	26	29.21 %	0.031
	No	89	70.08 %	63	70.79 %	
BMI	Normal	1	0.79 %	3	3.37 %	0.124
	Overweight	67	52.76 %	38	42.70 %	
	Obese	59	46.46 %	48	53.93 %	

In addition, immunocompromised patients are at higher risk of HBV infection than individuals with normal immune systems⁽²¹⁾. Diabetic group was diagnosed based on the criteria of the WHO (2006) as; fasting plasma glucose ≥ 126 mg% or postprandial plasma glucose ≥ 200 mg%. One abnormal laboratory value was diagnostic in a patient with typical hyperglycemic symptoms; two values were needed in asymptomatic patients⁽²²⁾. The percentage of diabetic patients among

HBV patients in our study was 20.4 %, and this percentage was higher than the results of Assis et al (2015) which was 11.2%⁽²³⁾. The age ranged between 20 – 66 years old with a mean age of 42.79 ± 11.44 years, agreeing with a large study conducted by Hassan et al⁽²⁴⁾ with the same mean age of 39. However mean age reported by Assis, et al (2015) was 42 years that was higher⁽²³⁾. A study on Chinese population infected with HBV reported that DM increase the risk of liver cancer,

as occurred with cigarette smoking and high levels of HBV DNA. Examination of patients with known risk factors for liver cancer may improve early detection rates and treatment to prevent tumor progression⁽²⁵⁾. In the study of Wai et al., the overall DM prevalence was 31%. The prevalence of DM was higher in patients having non-alcoholic fatty liver disease (56%), cryptogenic (51%), hepatitis C (32%), or alcoholic (27%) cirrhosis. To assess the prevalence of DM as a function of liver disease severity, the assessable data was only available for hepatitis C and hepatitis B cirrhosis. DM may be more prevalent in cirrhosis than previously thought⁽²⁶⁾. Infection with HBV is associated with significant risks for health. About 5% of adults with acute or non-symptomatic HBV infection are chronically infected, and individuals infected with the virus are at increased risk of cirrhosis, damaging the liver and liver tumors⁽²⁷⁾. Previous reports founds that hepatitis B prevalence among diabetics in long-term care facilities, indicating that the risk of hepatitis B virus (HBV) is higher in this population⁽²⁸⁾. There was a conflicting result regarding the relationship between severity of liver disease and prevalence of DM. Large cross-sectional studies have highlighted an association between Child-Pugh score and the prevalence of DM, predominantly in viral cirrhosis⁽²⁹⁾. Diabetes may complicate the medical management of patients with liver disease as it may be worsening the prognosis, partly due to the increased risk of developing HCC. However, the association between liver cirrhosis and diabetes is not well measured with wide variation in the reported estimates of the prevalence of diabetes in cirrhotic patients⁽³⁰⁾. Many studies have reported that DM increase the risk of HCC in patients with cirrhosis⁽³¹⁾. A national representative survey showed that

HBV infection was 60% more prevalent amongst people with diagnosed diabetes than amongst people without diagnosed diabetes throughout the period between 1999 to 2010⁽³²⁾. In another study in the United States, a comparison of 865 patients with acute HBV and 90,941 controls found that adults who did not have the risk of hepatitis B and with reported diabetes, the incidence of acute hepatitis B comparison among adults with or without diabetes is 1.9; the odds risks for both age groups 23–59 and ≥60 years were 2.1 and 1.5 respectively⁽³³⁾. In Turkey, comparison of 630 people with diabetes and 314 without diabetes found significantly positive associations of HBsAg-positive serology with history of previous admission to hospital, increased duration of diabetes, and use of insulin⁽³⁴⁾. In our study, 72.7 % of the studied population were belong urban area, and this parallel to the study of Hassan et al⁽²⁴⁾ which was 64.4%. In our study 51.4 % were not working, and near similar (49.2%) result were reported by Hassan et al⁽²⁴⁾ & he reported that 76.4% of the patients were married which is slightly lower than our result (77.8 %).

Conclusion

DM is a common medical condition in patients with HBV. Further reposed studies is needed to define the relation between DM & HBV.

References

1. El-Zayadi, A. Editorial Hepatitis B Virus Infection: The Egyptian Situation. Arab J Gastroenterol. 2006. https://www.researchgate.net/publication/228902727_Editorial_Hepatitis_B_Virus_Infection_The_Egyptian_Situation
2. World Health Organization. Immunization, Vaccines and Biologicals.

- Last update: 3 December 2013. Retrieved from: https://www.who.int/immunization/diseases/hepatitisB/new_vaccine/en/index3.html
3. Chen HF, Li CY, Chen P, See TT, Lee HY. Seroprevalence of hepatitis B and C in type 2 diabetic patients. *J Chin Med Assoc.* 2006; 69(4):146-52.
 4. Ismail SA, Cuadros DF, Benova L. Hepatitis B in Egypt: A cross-sectional analysis of prevalence and risk factors for active infection from a nationwide survey. *Liver Int.* 2017; 37(12):1814-1822.
 5. World Health Organization. Hepatitis B. [updated 18 July 2018]. Retrieved from: <http://www.who.int/media-centre/factsheets/fs204/en/>
 6. World Health Organization. Hepatitis C. [updated 2017 October; cited 2017 Dec 28]. Available from: <https://www.who.int/news-room/fact-sheets/detail/hepatitis-c>
 7. Ephraim R, Nsiah P, Osakunor D, Adoba P, Sakyi S, Anto E. Seroprevalence of Hepatitis B and C Viral Infections among Type 2 Diabetics: A Cross-sectional Study in the Cape Coast Metropolis. *Ann Med Health Sci Res.* 2014; 4(5): 719-22.
 8. Deshpande G, Klink AJ, Shenolikar R, Singer J, Eisenberg Lawrence DF, Krishnarajah G. Economic burden of hepatitis B infection among patients with diabetes. *Hum Vaccin Immunother.* 2016; 12(5):1132-40.
 9. Li Q, Li WW, Yang X. et al. Type 2 diabetes and hepatocellular carcinoma: a case-control study in patients with chronic hepatitis B. *Int J Cancer.* 2012; 131: 1197–1202.
 10. Cai C, Zeng J, Wu H, Shi R, Wei M, Gao Y, and Ma W. Association between hepatitis B virus infection and diabetes mellitus: a meta-analysis. *Exp Ther Med.* 2015; 10:693–698
 11. Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. *Clin. Infect. Dis* 1995; 20: 992–1000
 12. Weinbaum CM, Mast EE, and Ward, JW. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm. Rep* 2008; 57:1–20
 13. Li-Ng M, Tropp S, Danoff A, Bini EJ. Association between chronic hepatitis B virus infection and diabetes among Asian Americans and Pacific Islanders. *Dig Liver Dis.* 2007; 39:549–556
 14. Hsu CS, Liu CH, Wang CC, et al. Impact of hepatitis B virus infection on metabolic profiles and modifying factors. *J Viral Hepatitis.* 2012; 19: e48–e57.
 15. Mavrogiannaki A, Karamanos B, Manesis EK, Papatheodoridis GV, Koskinas J, Archimandritis AJ. Prevalence of glucose intolerance in patients with chronic hepatitis B or C: a prospective case-control study. *J Viral Hepatitis.* 2009; 16: 430–436.
 16. Spradling PR, Simons B, Narayanan M, et al. Incidence of diabetes mellitus in a population-based cohort of persons with chronic hepatitis B virus infection. *J Viral Hepatitis.* 2013; 20: 510–513.
 17. Wang CS, Yao WJ, Chang TT, Wang ST, Chou P. The impact of type 2 diabetes on the development of hepatocellular carcinoma in different viral hepatitis statuses. *Cancer Epidemiol Biomarkers Prev.* 2009; 18: 2054–2060.
 18. Knobler H, Schihmanter R, Zifroni A, Fenakel G, Schattner A. Increased risk of type 2 diabetes in noncirrhotic patients with chronic hepatitis C virus infection. *Mayo Clin Proc.* 2000; 75: 355–359
 19. Gong J. and Wang J. Relationship between type 2 diabetes mellitus and neuroendocrine immune network. *Guide China Med* 2016; 14: 54–55
 20. Shan S, Gu L, Lou Q, et al. Evaluation of glycemic control in patients with type 2 diabetes mellitus in Chinese. *Clin Exp Med.* 2017 Feb;17(1):79-84.
 21. Song L, Ma C, Li Q, Fan A, Wang K.

- Global dynamics of an HBV model with two immune response sources. *J. Southwest University (Natural Science Edition)*, 2018, vol. 32, pp. 5–10.
22. World Health Organization 2006. Retrieved from https://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf
23. Assis DR, Tenore Sde B, Pinho JR, Lewi DS, Ferreira PR. Characteristics of an Outpatient Chronic Hepatitis B Virus Infection Cohort. *Einstein (Sao Paulo)*. 2015 Apr-Jun; 13(2): 189–195.
24. Hassan AA, Shedeed MM, Salem AG, Shalapy AS, Faisal A, Mosaad M. Natural history and responses to antiviral therapies for chronic hepatitis B patients in Suez city, Egypt. *WJPR* 2017;6(17):60-71
25. Li X, Xu H, Gao P. Diabetes Mellitus is a Risk Factor for Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Virus Infection in China. *Med Sci Monit*. 2018; 24: 6729–6734.
26. Lee WG, Wells CI, McCall JL, Murphy R, Plank LD. Prevalence of diabetes in liver cirrhosis: A systematic review and meta-analysis. *Diabetes Metab Res Rev*. 2019; e3157. <https://doi.org/10.1002/dmrr.3157>
27. Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep*. 2008; 57(RR-8):1–20.6.
28. Zhang X, Zhu X, Ji Y, Li H, Hou F, Xiao C, Yuan P. Increased risk of hepatitis B virus infection amongst individuals with diabetes mellitus. *Biosci Rep*. 2019 Mar 28;39(3). pii: BSR20181715. doi: 10.1042/BSR20181715. Print 2019 Mar 29.
29. Alavian SM, Hajarizadeh B, Nematizadeh F, Larijini B. Prevalence and determinants of diabetes mellitus among Iranian patients with chronic liver disease. *BMC Endocr Disord*. 2004; 4(1):4.
30. Takai S, Inoue J, Kogure T. et al. Acute-onset autoimmune hepatitis in a young woman with Type 1 diabetes mellitus. *Intern Med*. 2018; 57(11):1591–1596.
31. Donadon V, Balbi M, Ghersetti M. et al. Antidiabetic therapy and increased risk of hepatocellular carcinoma in chronic liver disease. *World J Gastroenterol*. 2009 May 28; 15(20): 2506–2511.
32. Schillie SF, Xing J, Murphy TV, Hu DJ. Prevalence of hepatitis B virus infection among people with diagnosed diabetes mellitus in the United States, 1999–2010. *J Viral Hepat*. 2012; 19 (9):674-6.
33. Reilly ML, Schillie SF, Smith E. et al. Increased risk of acute hepatitis B among adults with diagnosed diabetes mellitus. *J. Diabetes Sci. Technol* 2012; 6: 858–866
34. Gulcan A, Gulcan E, Toker A, Bulut I. and Akcan Y. Evaluation of risk factors and seroprevalence of hepatitis B and C in diabetic patients in Kutahya, Turkey. *J. Invest. Med*. 2008; 56(6):858-6

