

ORIGINAL ARTICLE

Diabetes Mellitus and chronic liver diseases: complications and management among Saudi Arabia Patients

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ABSTRACT

*Diabetes Mellitus (DM) is a major health problem because of its complications leading to severe pathological conditions such as nephropathy, retinopathy, vasculopathy, neuropathy and cardiovascular diseases, hepatopathy. Liver cirrhosis and diabetes influence each other while treatments, lifestyle interventions and effective control of cirrhosis might assist in good management of diabetes. Aim of this research is to study the association between DM type 2 & chronic liver diseases in Saudi Arabia and patient's management. Cross sectional descriptive study was carried out among diabetic patients with liver diseases who follow up at Hail University medical polyclinic, KSA and through questionnaire on google drive. The results showed that 185 patients (47 males and 138 females), 23.4% of males & 15.2% of females have diabetes type 1, while 55.3% males & 38.4% females have diabetes type 2. About 27% of patients said that DM is hereditary and became diabetes at age of 40-44 years. Most of patients treated with insulin (about 63%) and about 73% of patients was adherent to treatment. The level of glucose in female patients was more adjusted than males. About 22% of patients have diabetes first before having liver disease and 37% of patients measured their glucose level regularly. The level of HbA1c was higher >6.5% in about 30%, and 57.4% of patients visit the physician regularly. Obese people have high tendency to diabetes. We can conclude that health education seminars should be done among Saudi people about the usefulness of adherence to treatment, visiting physician and health life style is advised.*

**Key Words:** Diabetes Mellitus, Chronic Liver diseases, Complications, Managements.

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INTRODUCTION

It is estimated that 20.8 million people, 7.0% of the U.S. population, have diabetes. Type 2 diabetes, with its core defects of insulin resistance and relative insulin deficiency, accounts for 90–95% of those with the disease. Another 5.2 million people are estimated to have undiagnosed type 2 diabetes. It is the sixth leading cause of death in the U.S. and accounts for 17.2% of all deaths for those aged 25 years. The prevalence of diabetes in cirrhosis is 12.3–57% in the U.S [1]. In 2017, the mortality of DM was 1.37 million [2]. Liver cirrhosis and diabetes influence each other as pharmacological treatments and lifestyle interventions, effective control of cirrhosis might assist in a better management of diabetes. Different etiologies of liver cirrhosis, different therapeutic methods, such as antiviral treatment, may be more effective. Also, effective control of cirrhosis might be a strategy for better management of diabetes [3]. The prevalence of DM in cirrhotic subjects is higher than that in general population [1]. Liver plays a vital role in the maintenance of glucose level in the blood. Glycogen storage allows removal of glucose from blood and store it, and replenish it when the level falls below the normal. Thus, the liver buffers the blood glucose level. A person whose liver is not functioning in the right way may rise in blood glucose level after having a high-carb meal compared to a person whose liver is functioning optimally. Another way by which the liver maintains normal blood-glucose level is by gluconeogenesis [4]. There are many reports showing that hepatic disease plays a major role in morbidity and mortality of diabetic patients [5]. Also, there are many researches indicates that DM is associated with a number of liver abnormalities, such as abnormal glycogen deposition, non-alcoholic fatty liver disease, fibrosis, cirrhosis, hepatocellular

carcinomas, abnormal elevated hepatic enzymes, acute liver disease and viral hepatitis [6]. Additionally, an excessive accumulation of fat in the liver may worsen insulin resistance and lead to severe metabolic dysfunction [7]. Liver cirrhosis is an important cause of death in type 2 diabetes, About 30% of patients with liver cirrhosis have overt DM [8]. Chronic liver disease, including cirrhosis, is a major cause of death in the United States, especially among men [9]. Hepatic disease should be suspected in non-obese patients without family history of DM, hypertension, or hyperlipidemia [10]. The liver has a major role in the control of glucose homeostasis in the body [11]. The association between chronic liver disease and DM is known since long. Such association may be due to a common mechanism that leads to both diseases such as non-alcoholic fatty liver disease, hemochromatosis, autoimmune liver diseases, and chronic HCV [12]. Diabetes management in patients with liver disease is complicated by liver-related alterations in drug metabolism [3]. Also, long-term ACE or ARB use was not associated with a higher risk of end stage of renal disease in cirrhotic patients [13]. The main goal of this study is to establish the association between hepatic diseases, and DM type 2 in Saudi Arabia and patient's management among patients who follow up at Hail University medical polyclinic, Hail region, KSA and through questionnaire on google drive.

## SUBJECTS AND METHODS

The Study will be conducted through cross-sectional descriptive study design. It will be carried out among diabetic patients with liver diseases who follow up at Hail University medical polyclinic in Hail region, KSA and through questionnaire on google drive among 3 months (November, 2019 to January 2020). The study excluded pregnant women, patients with a psychiatric illness or mental impairment, or patients unable to give informed consent. All participants were provided with clear and easy to understand information about the research paper in order to allow them to make an informed and voluntary decision about their participation. The data was collected through a well-structured questionnaire was used to address the study objective. The questionnaire consists of 22 questions, 5 about socio-demographic, 6 about diabetes and liver diseases, 5 about patients' adherence to treatment, to visiting physician, checking glucose level and finally 6 about patients' knowledge about medical analysis. Statistical analyses were performed using SPSS version 23 (SPSS, Chicago, IL, USA). Frequencies and percentages were calculated for categorical variables.

## RESULTS AND DISCUSSION

The number of diabetes patients around the world has increased. They predict by 2030, the global rate of morbidity for adult diabetes patients could increase from 6.4% to 7.7% [14]. DM and its associated complications decrease the quality of life of patients, shorten their life, increase the mortality, and promote the economic burden [15]. As the liver is the main organ for glucose metabolism [16], so, increase of glucose level in blood influences the clinical outcome of cirrhotic patients. Cirrhosis and diabetes interact and deteriorate each other. Table 1 showed that 185 patients (47 males and 138 females), 23.4% of males & 15.2% of females have diabetes type 1, while (55.3% males & 38.4% females) have diabetes type 2 and the rest of patients did not know their type of diabetes. Previous study found that Type I diabetic patients (10.9%) of participant, while the rest is type II diabetic patients [17].

Other survey showed that 20.8% of the people had DM. This is consistent with the other report about DM prevalence in North Sudan (18.7% and 19.1%) [18]. International Diabetes Federation report 2017, Sudan had DM prevalence of  $f \geq 12\%$  [19]. Lower DM prevalence (8.9%) was reported recently in Egypt [20], and also in Ethiopia (6.5%). Low prevalence of DM (8.0%) in Nigeria. [21]. The high prevalence of uncontrolled diabetes type 2 reported that 67.7% of T2DM patients had poor glycemic control in Riyadh, Saudi Arabia [22], 67.9%, was found in Al Hasa and 74% in Jazan [23]. Our study the age of patients that became diabetic starting from 40-50 years old (36.2% in males Vs 28.3% in females), followed by male at age of 20-29 years (27.7%), then females at age < 20 years and > 50 years (23.9%) (Table 1). Other study showed high prevalence of uncontrolled DM was reported with patient with diabetes in duration of < 7 years (62.8%) [24]. Higher percentage (33%) of patients below 45 years with DM might be due to early detection of DM, lifestyle changes and improve awareness [19]. Other study in Saudi Arabia reported that, an age-specific prevalence of 1 per 1000 for T2DM in children less than 18 years old was found [25], which was similar to the highest prevalence present in other country (American Indian and African American) in United States [26].

About 31.9% of males & 23.1% female patients said that diabetes Mellitus is hereditary (parents, 51.1% male Vs 45.7% female). According to the results of Hariri, a positive family history is a good indicator about the presence of DM more than obesity [27]. The four risk factors which raise the risk of the disease are patients' family history, duration of diabetes, exercise levels, and weight status. Family history and diabetes duration are non-modifiable risk factors [28,29].

About (21.3% in male Vs 13% female) patients had diabetes first before having liver disease. Many studies showed the relationship between DM and liver cirrhosis (Table 1). DM promotes hepatic fibrosis and inflammation, leading to liver failure. Also, DM may facilitate bacterial infections in cirrhosis, so increasing mortality [30]. Table 2 showed that only 31.9% patients that measure their glucose level once weekly, while in females measure once daily (38.4%) (Figure 1), and about 73% of patients was adherent to antidiabetic drugs (Figure 2). Metformin is used to treat prediabetes as first-line therapy of type 2 DM, and also, for DM of lesser severity or more recent onset. It improves insulin sensitivity, increased tissue utilization of glucose, reduced gluconeogenesis [31]. According to Doyle study, metformin treatment reduced mortality and improved outcomes in HCV-infected and in patients with coinfection of HCV and HIV [32]. About 57.4% of male patients Vs 47.8% females that visit the physician regularly (Figure 3), and only 19.1% male Vs 26.1% female patients who follows healthy diet. Fifty percentages of patients carried out medical analysis regularly and about 25% of them were careless (Figure 4).

Table 3 showed that most of patients treated with insulin (about 63% either in male or female). Other study was agreed with our results, they said that non-glucometer users (60.6%), and insulin (62.1%) and tablet-only users (58.1%) [24]. On the other hand, the level of glucose in female patients was more adjusted than males (Figure 5). Only 27.7% male Vs 19.6% female patients walking regularly. Physical activity has a major role in the management of T2DM. It significantly improves glycemic control, by lowering HA1c by range of 0.6%–0.8% [33]. In 2015, the prevalence of physical inactivity in Saudi Arabia was found to be 60.1% among males and 72.9% among females [34]. Other study in Kuwait reported that the prevalence of type-2 DM among native Kuwait population was 25.4% [35]. The level of triglycerides was normal only in 12.8% male Vs 26.8% female patients. According to previous studies, the aberrant signal which promotes glucose production in the liver during DM suppose also to enhance oxidation of fatty acid for fuel demand. Other research suggest that the liver stops oxidation of fatty acids and uses them instead to synthesize triglycerides which then accumulate abnormally in the liver [36]. The level of HA1c was higher >6.5% in 34.0% males Vs 26.8% females (Figure 6), while the level of liver enzymes was normal only in (17% male Vs 35.5% females. Other authors showed a significant association between poor controlled T2DM (HbA1c ≥ 7) and elevated ALT and AST [37]. Elevation of serum alanine aminotransferase (ALT), while uncommon (0.5%) in apparently normal subjects [38], is common in patients with type 2 diabetes. Chronic mild elevation of transaminases (ALT and AST) are frequently found in type 2 diabetic patients. [39]. [The most common cause of a mild elevation of serum ALT is NAFLD [40]. The most prevalent liver disease in type 2 diabetes. Patients with Diabetes have an increased risk of decompensate complications of cirrhosis and liver diseases that influence patient's mortality rate [41]. Also, hepatic diseases increase the occurrence of DM with its complications, that affect conversely the prognosis of diabetes. Management of DM includes treatment with oral hypoglycemic agents or insulin and improvement of patients' lifestyle, such as appropriate physical exercise, ample sleep, and get rid of smoking. All these changes could control DM and reduce its complications [42]. Control of liver cirrhosis by antiviral treatments for virtual liver diseases lowers the severity of DM complications.

Table 1: Frequencies and percentages of Diabetic patients in Saudi Arabia who answering the following questions about Diabetes Mellitus. (n= 185)

Questions	Answers											
	Answer	Type 1				Type 2				Don't know		
What is the type of Diabetes?	Male	11	23.4%			26	55.3%			10	21.3%	
	Female	21	15.2%			64	46.4%			53	38.4%	
	Answer	<20 Years		20-29 Year		30-39 Year		40-50 Year		>50 Year		
What is the age of being Diabetic?	Male	5	10.6%	13	27.7%	8	17.1%	17	36.2%	6	12.8%	
	Female	33	23.9%	15	10.7%	18	13%	39	28.3%	33	23.9%	
	Answer	Parents		Brothers & Sisters		Grandfathers		Sons		None		
If any person in your family have DM?	Male	24	51.1%	11	23.4%	9	19.1%	1	2.1%	6	12.8%	
	Female	65	45.7%	25	18.1%	24	17.4%	5	2.9%	19	13.8%	
	Answer	YES			NO			I Don't Know				
If DM hereditary in your family?	Male	15	31.9%		10	21.3%		22		46.8%		
	Female	32	23.1%		30	22.7%		65		26.8%		
	Answer	YES			NO			I Don't Know				
Are you diabetic and have chronic liver diseases?	Male	7	14.9%		38	80.9%		2		4.3%		
	Female	6	4.3%		107	77.5%		24		17.4%		
	Answer	Diabetes is the first			Liver disease is the first		Not infected with liver disease		I Don't know			
Which is the first disease that get to the patients?	Male	10	21.3%		2	4.3%		27	57.4%		8	17.0%
	Female	18	13%		3	2.2%		117	84.8%		0	0

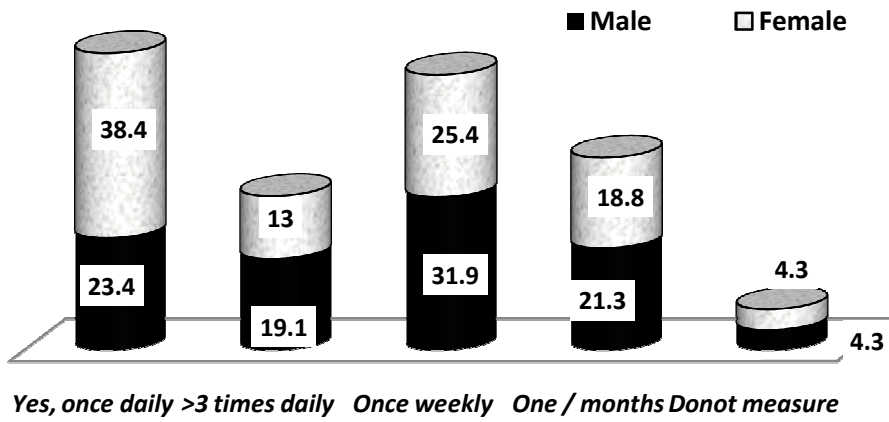
Table 2: Frequencies and percentages of Diabetic patients in Saudi Arabia who are being adherent to antidiabetic drugs treatment. (n= 185)

Questions	Answers										
	Do you take the antidiabetic drug regularly?	Answer	YES				NO				Sometimes
Male		35	74.5%	6	12.8%	6	12.7%				
Female		101	73.1%	4	2.9%	32	23.2%				
How many times you visit your physician?	Answer	YES				NO				Sometimes	
	Male	27	57.4%	9	19.1%	11	23.4%				
	Female	66	47.8%	25	18.1%	46	33.3%				
Are you follow healthy diet?	Answer	YES				NO				Sometimes	
	Male	9	19.1%	26	55.3%	12	25.5%				
	Female	36	26.1%	52	37.7%	48	34.8%				
Do you carry out medical analysis regularly?	Answer	YES				NO				Sometimes	
	Male	23	48.9%	13	27.7%	11	23.4%				
	Female	65	47.1%	27	19.6%	45	32.6%				
How many times you measure your glucose level?	Answer	Once daily		>3 times daily		Once weekly		One / month		I Don't measure	
	Male	11	23.4%	9	19.1%	15	31.9%	10	21.3%	2	4.3%
	Female	53	38.4%	18	13%	35	25.4%	26	18.8%	6	4.3%

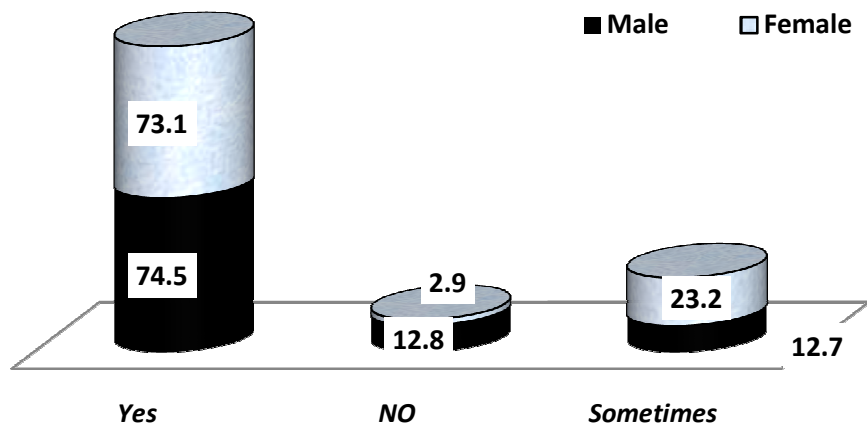
Table 3: Frequencies and percentages of Diabetic patients in Saudi Arabia who answering the following questions about some medical analysis. (n= 185)

Questions	Answers											
	What is the rout of DM treatment?	Answer	Oral hypoglycemic				Insulin				Diet	
Male		16	34%	30	63.8%	9	19.1%					
Female		52	37.7%	85	61.6%	20	14.5%					
Do your glucose level is adjusted?	Answer	YES				NO				Sometimes		
	Male	12	25.5%	18	38.3%	17	36.2%					
	Female	23	36.2%	20	14.5%	68	49.3%					
If the patients walking regularly	Answer	YES				NO				Sometimes		
	Male	13	27.7%	17	36.2%	17	36.2%					
	Female	27	19.6%	52	37.7%	57	41.3%					
What is your HA1c level?	Answer	3.7-5.1%				5.2-6.5%				>6.5		Don't know
	Male	4	8.5	6	12.8	16	34%	21	44.7%			
	Female	10	7.2%	20	14.4%	37	26.8%	65	47.1%			
What is your triglyceride level?	Answer	Normal				High				I Don't know		
	Male	6	12.8%	14	29.8%	27	57.4%					
	Female	37	26.8%	37	26.8%	64	46.4%					
What is your liver enzymes level?	Answer	Normal				High				I Don't know		
	Male	8	17%	1	2.1%	38	80.9%					
	Female	49	35.5%	13	9.4%	81	55.1%					

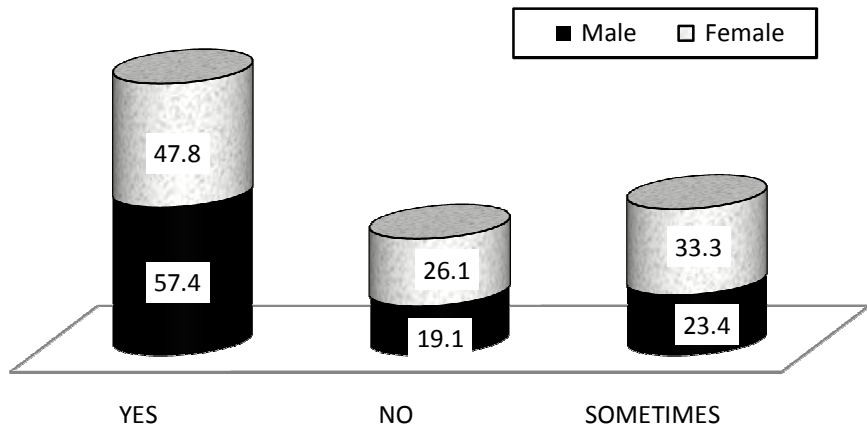
**Figure 1: Answers of patients (%) about how many times do you measure your glucose level?**



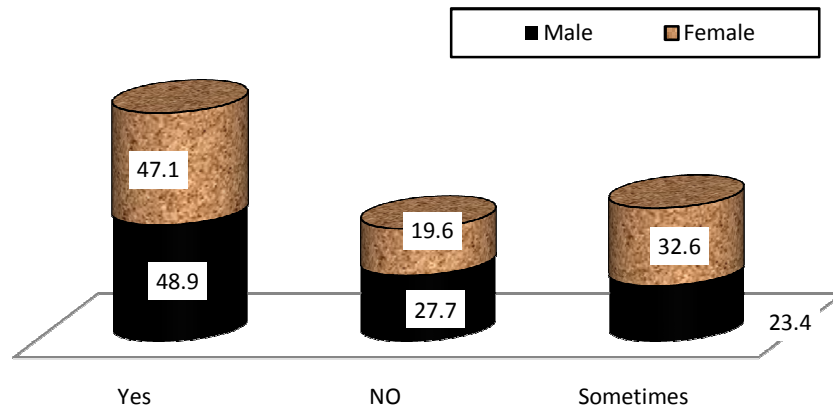
**Figure 2: Answers of patients (%) about Do you take the antidiabetic drug regularly?**



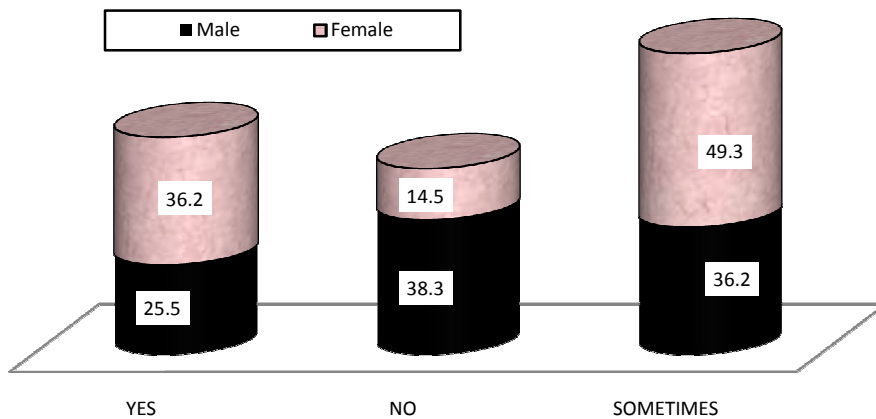
**Figure 3: Answers of patients (%) about how many times you visit your physician?**



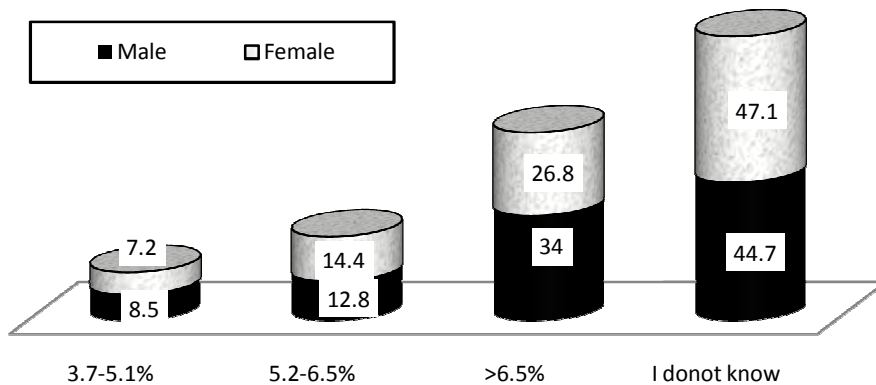
**Figure 4: Answers of patients (%) about Do you carry out medical analysis regularly?**



**Figure 5 : Answers of patients (%) about Do your glucose level is adjusted?**



**Figure 6 : Answers of patients (%) about What is your HA1c level?**



**CONCLUSION**

We can conclude that health education seminars should be done among Saudi people about the usefulness of adherence to treatment either diabetes or chronic liver diseases, basic information about their disease, also health life style is advised. Proper management of diabetes and DM-related complications is of utmost importance in patients with DM and liver diseases.

**REFERENCES**

1. Kaveeshwar, S.A., Cornwall, J.(2014).The current state of diabetes mellitus in India. *AMJ*. 2014; 1:45–8. [PMC free article] [PubMed] [Google Scholar]
2. GBD.(2018). Causes of Death Collaborators, “Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017,” *The Lancet*, vol. 392, no. 10159, pp. 1736–1788.
3. Zhao, y., Xing, H., Wang, X., Ou, W., Zhao, H., Li, B., Li, Y., Duan, Y., Zhuang, L., Li, W., Cheng, D., Quan, M., Zhang, Y., Ji, S.(2019).Management of Diabetes Mellitus in Patients with Chronic Liver Diseases. *Journal of Diabetes Research*, Article ID 6430486, 9 pages <https://doi.org/10.1155/2019/6430486>
4. Kumar, V., Abbas, A.K., Fausto, N., Aster, J.C. (2014). *Robbins and Cotran Pathologic Basis of Disease*. Elsevier health sciences professional edition 2014.e-book.
5. Forouhi, N.G., Merrick, D., Goyder, E., Ferguson, B.A., Abbas, J., Lachowycz, K., Wild, S.H. (2006). Diabetes prevalence in England, 2001—estimates from an epidemiological model. *Diabet. Med.* 23 (2), 189–197. <https://doi.org/10.1111/j.1464-5491>.
6. Guven,A., Yavuz, O., Cam, M., Ercan,F., Bukan, N., Comunoglu,C., et al. (2006).Effects of melatonin on streptozotocin-induced diabetic liver injury in rats. *ActaHistochem* 108:85–93. doi: 10.1016/j.acthis.2006.03.005.
7. Levinthal,G.N.& Tavill, A.S. (1999).Liver disease and diabetes mellitus. *Clin Diabetes*. 17:73.
8. Garcia-Compean, D., Jaquez-Quintana, J.O., Gonzalez-Gonzalez, J.A., Maldonado-Garza, H. (2009). Liver cirrhosis and diabetes: risk factors, pathophysiology, clinical implications and management. *World J Gastroenterol*. 15(3):280-8.
9. Hyattsville, MD.(2016).Health, United States.: Health, United States, 2015: With Special Feature on Racial and Ethnic Health Disparities. National Center for Health Statistics (US). National Center for Health Statistics (US); May. Report No.: 2016-1232.
10. Orsi, E., Grancini, V., Menini, S., Aghemo, A., Pugliese, G. (2017). Hepatogenous diabetes: Is it time to separate it from type 2 diabetes? *Liver Int*. 37:950–62.
11. Han, H.S., Kang, G., Kim, J.S., Choi, B.H., Koo, S.H. (2016). Regulation of glucose metabolism from a liver-centric perspective. *Exp Mol Med*. 48: e218.
12. Williams, K.H., Shackel, N.A., Gorrell, M.D., McLennan, S.V., Twigg, S.M. (2013). Diabetes and nonalcoholic fatty liver disease: A pathogenic duo. *Endocr Rev*. 2013; 34:84–129.
13. Hsu, W-F., Yu, S-H., Lin, J-T., Wu, J-C., Hou, M-C., Yi-Hsiang Huang, Y-H., Wu, C-Y., Peng, C-Y. (2019).Renal Effects of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Patients with Liver Cirrhosis: A Nationwide Cohort Study. *Gastroenterology Research and Practice*, Volume 2019, Article ID 1743290, 8 pages, <https://doi.org/10.1155/2019/1743290>
14. Shaw, J.E., Sicree, R.A., & Zimmet P.Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030, *Diabetes Research and Clinical Practice*, 87(1): 4–14.
15. Silva, T.E., Ronsoni M.F., & Schiavon L.L. (2018). Challenges in diagnosing and monitoring diabetes in patients with chronic liver diseases. *Diabetes and Metabolic Syndrome: Clinical Research and Reviews*.12 (3):431–440.
16. Nishida, T. (2017). Diagnosis and clinical implications of diabetes in liver cirrhosis: a focus on the oral glucose tolerance test. *Journal of the Endocrine Society*.1(7):886–896.
17. Alshareef, S.M., Adayel, A.Y., AlKhathlan, M.A., Alduaij, K.O., Alshareef, F.G., et al. (2019). The evaluation of glycemic control measures based on emergency department utilization and the percentages of adherence to the recommended follow-ups for microvascular complications. *Saudi medical journal*, 40(3): 271.
18. Eltom, M.A., Babiker Mohamed, A.H., Elrayah-Eliadarous, H., et al. (2017).Increasing prevalence of type 2 diabetes mellitus and impact of ethnicity in North Sudan. *Diabetes Res Clin Pract*. 136: 93–99.
19. International Diabetes Federation. (2017). *IDF diabetes atlas*. 8th ed. Brussels: International Diabetes Federation, 2017.
20. Khedr, E.M., Fawi, G., Allah Abbas, M.A., El-Fetoh, N.A., Al Attar G., Zaki AF, Gamea A. (2016).Prevalence of diabetes and diabetic neuropathy in Qena Governorate: population-based survey. *Neuroepidemiology*. 46: 173–181.
21. Arugu, G.M., Maduka, O. (2017).Risk factors for diabetes mellitus among adult residents of a rural district in Southern Nigeria: implications for prevention and control. *Niger J Clin Pract*. 20: 1544–1549.
22. Al-Rasheedi,A.A. (2014).The role of educational level in glycemic control among patients with type II diabetes mellitus. *Int J Health Sci (Qassim)*. 8(2):177–187.
23. Badedi, M., Solan, Y., Darraj, H., et al. (2016).Factors associated with long-term control of type 2 diabetes mellitus. *J Diabetes Res*. 2109542.

24. Alebachew, F., Belete, B., Molla, A. (2019). Glycemic control and diabetes complications among diabetes mellitus patients attending at University of Gondar Hospital, Northwest Ethiopia. *Diabetes, metabolic syndrome and obesity: targets and therapy*, 12: 75.
25. Al-Rubeaan, K. (2015). National surveillance for type 1, type 2 diabetes and prediabetes among children and adolescents: a population-based study (SAUDI-DM) *J Epidemiol Community Health*. 69:1045–1051.
26. Zeitler, P., Fu, J., Tandon, N., Nadeau, K., Urakami, T., Barrett, T., Maahs, D. (2014). ISPAD Clinical Practice Consensus Guidelines 2014. Type 2 diabetes in the child and adolescent. *Pediatr Diabetes*. 15 Suppl 20:26–46.
27. Hariri, S., Yoon, P.W., Qureshi, N., Valdez, R., Scheuner, M.T., Khoury, M.J. (2006). Family history of type 2 diabetes: a population-based screening tool for prevention? [Internet]. *Genetics in medicine: official journal of the American College of Medical Genetics*. U.S. National Library of Medicine. <https://www.ncbi.nlm.nih.gov/pubmed/16481893>
28. Mansour, A.M., Al Shalahi, M.H., Al Johani, A., Rami, M. (2017). Forward and backward logistic regression analysis to give the estimation of tight diabetes control: review. *Int J Diabetes Endocrinol*. 2(1):1–4.
29. Adeniyi, O.V., Yogeswaran, P., Longo-Mbenza, B., Ter Goon, D., Ajayi Al. (2016). Cross-sectional study of patients with type 2 diabetes in OR Tambo district, South Africa. *BMJ Open*. 6(7):e010875
30. Garcia-Tsao, G. (2005). Bacterial infections in cirrhosis: Treatment and prophylaxis," *Journal of Hepatology*, 42(1): S85–S92.
31. Nathan, D.M., Buse, J.B., Davidson, M.B. et al. (2009). Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes, *Diabetologia*, 2009, vol. 52, no. 1, pp. 17–30.
32. Doyle M.-A., Singer J., Lee T., Muir M., and Cooper C. (2016). Improving treatment and liver fibrosis outcomes with metformin in HCV-HIV co-infected and HCV mono-infected patients with insulin resistance: Study protocol for a randomized controlled trial. *Trials*, 17(1): 331,
33. Lanhers, C., Duclos, M., Guttmann, A., Coudeyre, E., Pereira, B., Ouchchane, L. (2015). General practitioners' barriers to prescribe physical activity: the dark side of the cluster effects on the physical activity of their type 2 diabetes patients. *PLoS One*. 10: e0140429.
34. Al-Zalabani, A.H., Al-Hamdan, N.A., Saeed, A.A. (2015). The prevalence of physical activity and its socioeconomic correlates in Kingdom of Saudi Arabia: A cross-sectional population-based national survey. *J Taibah Univ Med Sci*. 10:208–15.
35. IDF-Diabetes Atlas (2016) 7th Edition, available at: <http://www.idf.org/diabetesatlas/data-visualisations>, Nov 20, 2016.
36. Reid, AE. (2006). Non-alcoholic fatty liver disease. In: Feldman M, Friedman LS, Brandt LJ, Eds. *Sleisenger and Fordtran's Gastro-intestinal and Liver Disease: Pathophysiology/diagnosis/ management*, 8th ed. St. Louis, Missouri, USA: Saunders, 1772–99.
37. Kunutsor, S.K., Apekey, T.A., Walley, J. (2013). Liver aminotransferases and risk of incident type 2 diabetes: a systematic review and meta-analysis. *Am. J. Epidemiol*. 178 (2), 159–171. <https://doi.org/10.1093/aje/kws469>
38. Trombetta, M., Spiazzi, G., Zoppini, G., Muggeo, M. (2005). Type 2 diabetes and chronic liver disease in the Verona diabetes study. *Aliment Pharmacol Ther* 2005, 22 (Suppl. 2):24–27.
39. Harris, E.H. (2005). Elevated Liver Function Tests in Type 2 Diabetes. *Clinical Diabetes*. 23(3): 115–119. <https://doi.org/10.2337/diaclin.23.3.115>
40. Mandal, A., Bhattarai, B., Kafle, P., Khalid, M., Jonnadula, S.K., Lamicchane, J., Rajan Kanth, R., & Gayam V. (2018). Elevated Liver Enzymes in Patients with Type 2 Diabetes Mellitus and Non-alcoholic Fatty Liver Disease. *Cureus*. 10(11): e3626. doi: 10.7759/cureus.3626 PMID: PMC6347442
41. Wild, S.H., Walker, J.R. Morling et al. (2018). Cardiovascular disease, cancer, and mortality among people with type 2 diabetes and alcoholic or nonalcoholic fatty liver disease hospital admission," *Diabetes Care*. 41(2):341–347.
42. Zheng, Y., Ley, S.H., & Hu, F.B. (2018). Global etiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews. Endocrinology*, 14(2): 88–98.

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