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Incidence of Hepatitis C Virus infection and the potential predictors among patients with diabetes mellitus in the Bamenda Regional Hospital in Cameroon

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ABSTRACT

Introduction: Diabetes mellitus (DM) and Hepatitis C Virus (HCV) infections are a global major public health threat. Their co-infections and associated risk factors have been postulated in many countries, unfortunately, no such data exist in Cameroon. This study aims to determine the prevalence and possible predictors of HCV among DM patients.

Methods: We conducted a cross-sectional study among DM patients at Regional Hospital Bamenda from February to June 2020. Blood samples were collected and tested for the presence of HCV. Data were analyzed using SPSS version 23.

Results: The study comprised 193 participants. The mean (Std. error) age and random blood sugar level of the participants were 46.12(0.9) years and 134.15(4.07) g/dl respectively. HCV prevalence was 3.11% (6). The distribution of HCV infection did not show any significant difference with social demographic factors ($p > 0.05$). Similarly, HCV was insignificantly ($p > 0.05$) higher in patients with T2DM 6(3.4%), those with disease duration >5 years 4(4.4%), and those receiving injectable drugs 2(9.1%). Possible predictors ($p<0.05$) of HCV identified in this study include; uncontrolled diabetes (7.4%), family history of diabetes (19.2%), hepatitis 2(15.4%), alcohol intake (7.6%), multiple sex partners (6.5%), sharing sharp objects (9.1%), those with Tattoos (9.4%), scarification marks (3.6%), as well as those who have been hospitalized (6.7%), or received blood transfusion (25.0%) at least once.

Conclusion: HCV testing and linkage to care among DM patients should be made imperative in order to design effective treatment and prevention programs that will reduce the morbidity and mortality rates.

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Introduction

Hepatitis C virus (HCV) infection and diabetes mellitus (DM) are two major public health problems that may coexist and cause increased morbidity and mortality rates worldwide [1–3]. HCV affects between 170-210 million people globally, of whom 80 million have chronic hepatitis infection with complications that can lead to cirrhosis, liver cancer, and chronic kidney disease [4–7].

Diabetes mellitus is one of the fastest-growing diseases around the world. It is characterized by chronic hyperglycemia occurring when the human system cannot produce enough insulin and/or cannot use it properly [8, 9]. Studies have shown that diabetic patients are susceptible to bacterial, viral, and fungal infections because of various deficiencies in the immune system, microvascular and macrovascular organs [6, 10]. Different types of diabetes include; Type 1 DM (T1DM), type 2 DM (T2DM), gestational DM, and those attributable to genetic disorders, endocrinopathies, drugs, etc [11, 12]. The International Diabetes Federation (IDF) in 2019 reported that close to 463 million adults' ≥20 years present with DM and of these, 79% are living in low- and middle-income countries where it poses health challenges. These health challenges include visual impairment (retinopathy), blindness, kidney disease (nephropathy), nerve damage, amputation, heart disease, and stroke that require constant medical care and can lead to disability [9,13].

It has been reported that HCV and DM coexist in patients such that the etiology of DM can quicken the development of cirrhosis, hepatocellular, and carcinoma [2, 14, 15]. In a review carried out in both developed and underdeveloped countries, HCV prevalence

among DM patients varies from 1.6 to 20.8% [1, 2, 5, 11, 14, 16]. Previous studies have reported different risk factors for acquiring HCV infections in the general population and specific groups to include medical practices (blood transfusion, dental procedure, etc), mother to child transmission, sexual transmission, sharing objects like razor blades or needles, toothbrushes, household articles (straws), tattooing and other forms of body piercing, unsterile equipment, malnutrition, physical and moral violence, and lack of knowledge about HCV transmission [15,17–20].

Considering that the liver is the principal site of hormone and glucose metabolism, adequate liver function is essential to maintain glucose homeostasis [14]. Thus, there is a need to evaluate the prevalence of HCV among DM patients. Although several studies have been carried out in other parts of the world, there exist no data on HCV prevalence and possible predictors to HCV among DM patients in Cameroon. Based on the previous studies, we assumed that DM patients are susceptible to HCV infection, thus the objectives of this study were to estimate the seroprevalence of HCV among DM patients and also to determine the possible predictors concomitant with HCV and DM co-infection. Data obtained from this study will increase awareness among the general population by providing important information necessary to undertake effective preventive measures, link HCV-positive patients to care to improve on disease management, and lastly to identify areas of knowledge gaps in other to drive new research areas.

Methods

Study Design

This was a cross-sectional study carried out in a diabetic unit at the Bamenda Regional Hospital (BRH) from February to June 2020. BRH is the largest hospital in the Northwest Region and is located in the chief town of the region, this hospital receives patients from all over the region and even beyond.

Ethical Considerations

Approval for the study was granted by the Northwest Regional delegation for Public Health, Department of Biological Sciences of the University of Bamenda, and from the BRH administration.

Study population

The least acceptable sample size for this study was premeditated using the formula $N=Z^2 * P(1-P)/i^2$ Where, Z^2 is the normal distribution value = 1.96 at 95% confidence interval, P =Relative prevalence of HCV in Cameroon = 6.5% [15] and í is precession (sampling error) = 0.05 at 95% confidence interval was calculated to be 94. All patients of both sexes, aged ≥18 years, with either type 1 or 2 DM who attended the medical consultation from February to June 2020, were eligible for the study. Participants who duly signed the informed consent form, answered the questionnaire, and accepted to give 3ml blood samples were recruited. Pregnant women with gestational diabetes were excluded from the study.

Data Collection

After explaining the purpose of the study, written informed consent was taken from all the participants before data collection and samples. The data collection instrument was pre-tested with twenty patients to identify possible adjustments in the close-ended questionnaire. The questionnaire was subdivided into five parts to include: identification and demographic variables, past medical history, relevant risk factors, and the result of serology tests for hepatitis C. Those who had difficulties in understanding or answering certain questions were assisted by the researcher.

Serological analysis

Diagnosis of HCV infection was performed using the Diaspot rapid diagnostic test (Diaspot, China). About three ml of venous blood was collected into sterile dry blood collection tubes and allowed to clot at room temperature. The samples were then centrifuged and the sera were used to detect the presence of anti-HCV antibodies following the manufacturer's procedures [21].

Random Blood Glucose Level: This was determined using the Accu-Chek glucometer machine (Corydon, IN, United States) as described in the manufacturer's procedure [22].

Statistical Analysis

The statistical analysis was performed using the program Statistical Package for Social Sciences Version 23.0 (SPSS Inc. Chicago, IL, USA). Socio-demographic and clinical data were analyzed using descriptive statistics and the results were presented as means and percentages. Possible associations between demographic characteristic and HCV seropositivity was determined by the Pearson-corrected chi-square test or two-tailed Fisher exact test at a 95% confidence level. Odds ratio (OR) and their respective 95% confidence intervals (CI) were determined. Pearson chi-square test was used to determine the difference among various categories concerning HCV.

Results

A total of 200 samples were collected and 7 had invalid results thus 193(96.5%) participants were included in this study. Description of the socio-demographic characteristics of the study participants is shown in Table 1. The mean age ± Std. error age of the participants was 46.11±12.79 years and ranged between 28-71 years. The majority of the population belong to the age group 40-60 years (85, 44.4%), came from an Urban area (115, 59.6%), males (101, 52.3%), married or in a cohabiting-marital relationship (111, 57.5%), and had attained the secondary level of education (99, 51.3%).

As concerns the DM disease profile (Table 1), the mean ± Std. error of the random blood level was 134.15±4.07g/dl and ranged between 78-315g/dl. Glycemic control was attained by 166 (86.0%) of the participants at the point of sample collection. Type 2 diabetes mellitus (T2DM) was the most common type of diabetes 177 (91.7%). Duration of the DM sickness ranged from 0.6year -26 years with mean ± Std. the error of 5.72 ±0.38 years. The majority of the patients were treated using oral drugs 161(83.4 %) and had no family history of DM 168(87.0 %).

Table 1: Distribution of Patients with DM According to Demographic and Clinical Variables (n = 193)

Variable	Categories	Frequency	Percentage
Locality	Rural	78	40.4
	Urban	115	59.6
Age (year)	<40	77	39.9
	40-60	85	44.0
	>60	31	16.1
Gender	Female	92	47.7
	Male	101	52.3
Marital Status	Married, Cohabiting, Divorced, Widow/er	148	76.7
	Single	45	23.3
Educational level	None	9	4.7
	Primary	60	31.1
	Secondary	99	51.3
	Tertiary	25	13.0
Glycemic Control	Normal	166	86.0
	High	27	14.0
Type of diabetes	1	16	8.3
	2	177	91.7
Use diabetic drug	No	9	4.7
	Yes	184	95.3
Type of drugs	Injectable	22	11.4
	Oral	145	75.1
	Both injectable and oral	18	9.3
	Diet control	8	4.1
Duration of Diabetes (years)	<5	103	53.4
	≥5	90	46.6
Family history of diabetes	No	167	86.5
	Yes	26	13.5

Prevalence Study by Socio-Demographic, Clinical, Biological, and Social Lifestyle

Of the 193 patients, 4.7 % (9) had multiple sex partners. Sharing objects such as sewing needles, shaving devices, toothbrushes, blades were reported by 5.7 % (11) of the patients. A total of 38.9 %(75) have been hospitalized, 7.8% (15) have undergone surgery and 4.1% (8) had received transfused blood at least once in their lifetime. The majority of patients 86.0% (166) have scarification (tribal or traditional treatment marks) while 17.1% had tattoos on their bodies. All the participants 100% (21) that were on an injectable drug (Insulin) often reuse their syringe.

This data revealed that the seroprevalence of HCV was 3.11% (6). The prevalence of HCV did not differ significantly with locality (p=0.71) although the occurrence was 1.4 times higher in patients from the rural area. Furthermore, no significant difference was recorded in the occurrence of HCV concerning age, gender, marital status, and level of education P>0.05. However, the prevalence was higher in the age group >60 years (2, 6.5%), female (5, 5.4%), married participants (5, 3.4%), and those who were educated (4%). T2DM patients had a higher 6(3.4%) positivity rate with a risk of 1 fold compared to T1DM. Similarly, those who use the injectable drug (9.1%) had a 0.24 risk of being positive for HCV. Interestingly, none of the diabetic patients on diet control had HCV. Patients whose diabetes has progressed for ≥5 years had higher seropositivity 2(3.3%) than those whose disease had been for <5 years. This difference was still not significant (p=0.544). Furthermore, our data revealed that patients with uncontrolled diabetes had a significantly ($p = 0.022$) higher prevalence of HCV infection compared to the controlled group (OR = 3.24, 95%CI = 5.56-18.62). Moreover, subjects with a family history of diabetes 5(19.2%) and hepatitis 2(15.4%) had a higher positivity rate with a risk fold of 39.52 and 8.0 respectively. These differences were found to be significant ($P < 0.05$). Assessing social lifestyles, higher positivity rates to HCV infection were registered in participants with a history of alcohol consumption 5 (7.6%), multiple sex partners 5(6.5%), sharing sharp object 1(9.1%), have scarification 6 (3.6%.1%), and tattoos 3(9.4%). The risk was significant with respect to alcohol consumption (OR 10.33; $p = 0.012$), multiple sex partners (OR 8.00; $p = 0.026$), tribal/ traditional treatment marks ($p = 0.006$) and those with tattoos (OR 5.45; $p = 0.025$). Significantly ($p<0.05$), higher HCV prevalence rates were associated among subjects with past history of hospitalization 6.7% (OR 0.86; 95% CI 0.81-0.91), blood transfusion 25% (OR 15.08; 95% CI 2.30-99.06) and without any surgery 13.3 % (OR 6.69; 95% CI 1.19-40.02).

Table 2: Bivariate Analysis for Significant Risk Factors for Hepatitis C Based on Social Demographic Parameters, Clinical Risk Factor, Lifestyle-Risk Factors

Variable	Categories	HCV Negative (%)	HCV positive (%)	Chi-square	OR(CI at 95%CI)	P-value
Locality	Urban*	111 (96.5)	4 (3.5)			
	Rural	76 (97.4)	2 (2.6)	0.132	1.40(0.25-7.67)	0.717
Age (year)	<40*	75(98.7)	1(1.3)	1.754		0.416
	40-60	83(96.5)	3(3.5)	1.745	0.19(0.02-2.22)	0.187
	>60	29(93.5)	2(6.5)	0.470	0.52(0.08-3.30)	0.491
Gender	Male*	100 (99.0)	1 (1.0)			
	Female	87(94.6)	5(5.4)	3.160	0.17(0.02-1.52)	0.076
Marital Status	Single	44 (97.8)	1(2.2)			
	Married	143 (96.6)	5(3.4)	0.150	0.65(0.07-5.71)	0.696
Educational level	None*	9(100.0)	0(0.0)			
	Primary	59(98.3)	0(0.0)	0.000	**	0.999
	Secondary	95 (96.0)	4(4.0)	0.502	0.351(0.02-6.47)	0.479
	Tertiary	24(96.0)	1(4.0)	0.006	0.91(0.92-9.07)	0.948
Type of diabetes	2*	171 (96.6)	6(3.4)			
	1	16(100.0)	0(0.0)	1.056	0.91(0.86-0.96)	0.304
Type of drugs	Injectable	20(90.9)	2(9.1)	2.950	0.24(0.41-1.39)	0.086
	Oral*		167(97.7)	4(2.3)		
Treatment duration in years	<5	101(98.1)	2(1.9)	0.349	1.74(0.28-0.66)	0.599
	≥5*	87(96.17)	4(4.4)			
Glycemic control	Uncontrolled	25(92.6)	2(7.4)	5.495	3.24(5.56-18.6)	0.022
	Controlled *	162(97.6)	4(2.4)			
Family history of diabetes	No	166(99.4)	1(0.6)	25.930	39.5(4.40-35.74)	0.001
	Yes*	21(80.8)	5(19.2)			
Family history of hepatitis	No	176(97.8)	4(2.2)	6.973	8.0(1.32-48.56)	0.008
	Yes*	11(84.6)	2(15.4)			
Alcohol	No	126(99.2)	1(0.8)	6.369	10.33(1.18-90.3)	0.012
	Yes*	61(92.4)	5(7.6)			
Smoke	No	172(97.2)	5(2.8)	0.457	2.29(0.25-20.92)	0.490
	Yes*	15(93.8)	1(6.2)			
Multiple sex partners	Yes	72(93.5)	5(6.5)	4. 87	8.00 (0.91-69.75)	0.026
	No*	114(99.1)	1(0.9)			
Sharing sharp objects	No	177(97.3)	5(2.7)	3.38	4.54(0.98-17.24)	0.044
	Yes*	10(90.9)	1(9.1)			
Tattoos	No	158 (98.1)	3(1.9)	5.60	5.45(1.05-28.32)	0.025
	Yes*	29(90.6)	3(9.4)			
Scarification	No	27 (100)	0(100)	7.58	**	0.006
	Yes*	160(96.4)	6(3.6)	1.84		
History of Hospitalization	No	154(96.9)	1(0.8)	5.16	8.36(0.96-73.01)	0.023
	Yes*	70(93.3)	5(6.7)			
History of previous surgery	No	13(86.7)	2(13.3)	5.65	6.69(1.19-40.02)	0.018
	Yes*	174(97.8)	4(2.2)			
History of blood transfusion	No	181(97.8)	4(2.2)	5.88	15.08(2.30-99.06)	0.015
	Yes*	6(75.0)	2(25.0)			

Discussion

The relationship between diabetes and the liver has been shown to cause a huge health care burden [6, 15, 23]. However, there is a scarcity of such information in most developing countries especially in Cameroon due to the high cost of the test.

In this study, the prevalence of HCV was 3.11%. Lower prevalence (1.8%) of HCV has been reported among blood donors [24] and 0.2-2.6% range reported in different age groups in the general public [25,26]. The result from this study is consistent with findings from different studies that reported a higher prevalence of the range 3.3%-24.8% [1, 3, 7, 14, 17, 20, 27]. The high prevalence in this small population can be attributed to the fact that diabetic patients are immune-compromised and secondly these individuals are exposed to HCV infection since they undergo frequent exposure to medical interventions and instrumentation. On the other hand, lower HCV prevalence in the range 0.02%-2.7% has also been reported among DM patients in other countries [2, 6, 15, 23, 28]. These differences in the epidemiology of diabetes and HCV between countries can be due to the differences in the study design.

In this study, glycemic control, family history of diabetes, family history of hepatitis, multiple sex partners, tattoos, scarification, hospitalization, blood transfusion were identified as possible risk factors for HCV infection in patients with DM. Data from this study identified that HCV is common in individuals with a family history of hepatitis (9.1%) compare to their counterparts (2.3%) ascertaining the fact that there is possible viral transmission among family members. This can be supported by the fact that HCV can survive on surfaces such as needles, lancet pens, lancets, and glucometers on average for five to seven days [14]. As such, there is a high possibility of being infected when there is inadequate sterilization of medical equipment and sharp objects such as needles, razor blades, toothbrushes, or other household articles like shaving machines, tattooing, and body piercing [5,17,18], this advocates the significantly high prevalence seen among DM patients sharing sharp objects (9.1%), those with Tattoos (9.4%), scarification (3.6%), participants who have been hospitalized (6.7%) and had a blood transfusion (25.0%) at least once. To further attest to this, our data showed that the higher occurrence of HCV was seen in those with a family history of HCV (19.2%) compared to their counterpart (0.6%), suggesting that there is likely intra-household viral transmission. On the contrary, other studies showed that previous history of blood transfusion, as well as sharing razor blades were non-predictors of HCV [2, 3].

Higher prevalence of HCV seen in those with uncontrolled DM (7.4%) is because the presence of HCV in the hepatocyte up-regulates tumor necrosis factor which leads to the phosphorylation of insulin receptor 1 or 2. Thus preventing it from associating with the insulin receptor leading to an increased risk of hyperglycemia [14,16]. Similar findings of high glucose intolerance among patients with HCV infection have been reported in another study [19]. However, another study carried out elsewhere had dissimilar results in which persons with HCV infection have good glycemic control [1, 5]. This, therefore, calls for further research to ascertain the facts.

The majority of the participants (86.5%) did not have a family history of diabetes. Comparable to findings in a study by Ndako et al. [17], our data showed that HCV was higher (15.4%) in those with a family history of diabetes. The possible justification could be because persons with a family history of DM are prone to HCV infection and this HCV infection can easily be transmitted among family members. Secondly, it might be attributed to other related risky behaviors due to their social lifestyles like having multiple sexual partners and high alcohol intake similar to what has been reported in Nigeria [19].

A significant (p=0.018) high prevalence of HCV (13.3%) among those without previous history of surgery suggests that infection with HCV in this group might be a result of another predisposing factor like having multiple sex partners, or the use of sharp objects. Additionally, the difference may be explained by the difference in the proportion of patients with surgery.

Although blood and blood products are being screened before transfusion in this setting, the use of poor sensitivity and specificity methods in detecting viral infections during their long window period remains a major hindrance [24]. This accounts for the high prevalence among those who have received a blood transfusion.

We did not observe any significant difference in HCV distribution with respect to socio-demographic variables and history of the disease. However, the prevalence of HCV is higher in individuals from urban towns (3.5%) compare to rural areas (2.6%). The variance could be attributed to differences between urban and rural prevalence probably as a result of a different lifestyle. People from Urban areas are more exposed to risky activities such as alcohol intake, tattooing, frequent hospital checkups that have been identified in this study as predictors of HCV.

Age was not a predictor of HCV in our study even though the prevalence of HCV increases with age. This could be explained by the fact that older people have had more exposure to risk factors with the increased duration of DM illness. These findings are concurrent with previous studies elsewhere [1, 2, 5, 16, 17, 25]. However, other studies have reported that age was a predictor of HCV among DM patients [3, 14, 16]. The distribution of HCV infection was the same in both sexes (P>0.05). A higher prevalence in women (5.4%) compared to men (1.0%) has been described in other studies [3, 5, 19]. This could be because females are more prone to predictors of HCV transmission. HCV prevalence on the contrary was sex-dependent with the male gender experiencing a higher occurrence [1]. Our findings suggest that HCV was higher among those that were married (3.4%) compare to the singles (2.2%). There is a high probability of parenteral transmission among people sharing the same room as reported by [29].

A higher prevalence of the occurrence of T2DM compared to T1DM in a general population has been reported in other countries [2, 6, 11, 16]. The occurrence of HCV was higher in T2DM (3.4%) compare to T1DM (0.0%) though there was no significant difference similar findings have been reported in other countries [5, 6, 17]. However, a significantly higher prevalence among T2DM patients was reported in a similar study carried out in Congo [3]. It has been reported that T2DM patients have a higher risk to be infected with HCV since HCV replication is favored by hyperinsulinemia [27]. This will increase the likelihood of further complications (impaired insulin signaling, insulin resistance, disturbed glucose, protein, and lipid metabolism) that will further lead to the progression of liver disease complications such as steatosis, steatohepatitis, liver fibrosis cirrhosis, and hepatocellular carcinoma [1, 5, 6, 14].

The high prevalence of HCV in patients who use injectable drugs (9.1%) compared to those with oral drugs (3.3%) can be explained by the fact that HCV is transmitted parenterally since these individuals are subjected to daily treatment and control procedures that require the use of sharp objects [2]. This is comparable to

reports elsewhere [5, 14] and opposes another study by Jadoon et al., [1]. Such daily procedures are usually performed with the aid of untrained family members. In addition, this study also showed that HCV was high among people with a family history of hepatitis, therefore, supporting the fact that, HCV is transmitted parenterally.

The association of exposure to HCV and a longer time of DM showed no association of infection although it was higher in those with longer duration (3.3% vs 1.9%). Diabetes duration of ≥5 years showed that a person with longer DM has a 1.7% fold of being infected with HCV. Similar findings have been demonstrated in other countries [2, 6]. However, this result is conflicting with those of Ndako et al., [17] who reported higher prevalence in those with shorter duration. Longer duration with diabetes illness indicate increased risk with longer duration of medical interventions.

Limitations and Strengths

The limitation in this study includes the fact that the study did not use a control group as such patients were studied in comparison to similar studies carried out elsewhere. Secondly, we could not carry out the confirmation screening method for HCV due to financial and technical constraints. Nevertheless, despite these limitations, our findings are promising compared to other epidemiologic data. This study being a pioneer study in Cameroon has generated an avenue for new research areas that might be useful in improving the quality of health in persons with DM. Secondly, HCV-positive patients were linked to care. Lastly, this data adds to the growing number of literature on the relationship between HCV and DM.

Conclusions

Our data reported a 3.11% prevalence of HCV infection among patients with DM. It is also evident that certain factors including glycemic control, family history of diabetes, family history of hepatitis, multiple sex partners, tattoos, scarification, hospitalization, blood transfusion are predictors of beginning infected with HCV. This warrants special attention to patients with these risk factors. Thus this calls for an urgent need to educate the populace on the dangers of HCV and DM co-infection to improve the management of HCV and DM co-infection patients.

Recommendations

There is an urgent need to educate the public on the dangers of HCV and diabetes. Screening for HCV among all DM patients should be made mandatory and at an affordable price. Consequently, measures of glycemic control should be enhanced in this population to reduce the HCV positivity rate. Similar studies are carried out at the national level to elucidate the relationship between HCV infection and DM to implement pertinent strategies to address the related burden and thus improve management strategies.

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Abbreviations

Diabetes mellitus: (DM), Hepatitis C Virus: (HCV), Type 1 DM: (T1DM), Type 2 DM: (T2DM)

Authors' contributions

Authors' contributions LEA and NBK conceptualized the work and designed the study. NBK, NMN, KRN. collected and curated the data, LEA and NMN performed the formal statistical analysis, LEA and NNM drafted the manuscript, LEA, NBK, and NMN critically reviewed and edited the manuscript, LEA, NBK, and NNM oversaw resources acquisition. All authors have read and agreed to the published version of the manuscript.

Competing interests: The authors declare that they have no competing interests.

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