

Unstimulated Salivary Flow Rates in Patients with Hepatitis B Virus Infection: A Case-Control Study

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ABSTRACT

Objective: Salivary dysfunction is one of the extrahepatic manifestations of hepatitis B virus infection. Although the pathophysiology is not fully understood, it has been linked with immune complex sequelae and liver dysfunction. Unstimulated salivary flow rate is an accurate measure of salivary gland functionality. The objective of the study was to determine the association between hepatitis B virus infection and salivary flow rates.

Methods: This case-control study included 76 patients diagnosed with hepatitis B virus infection and 48 control participants. Socio-demographics and times of diagnosis for the case group were obtained using a standardized questionnaire and with the aid of patients' records. The unstimulated salivary flow rate was determined for all participants using the suction method and recorded as volume per time (mls/min). Data was presented using frequencies and proportions, with statistical significance set at $p < 0.05$ while the 95% confidence level was used to construct confidence intervals around estimates.

Results: There was no significant difference between the distribution of ages and gender of participants in both groups. The average salivary flow rate of the cases was 0.12mls/min, and was significantly lower ($p = 0.000$) than the control group with a mean value 0.48mls/min. The distribution of salivary flow rate differed significantly across the duration of initial diagnosis ($p = 0.007$).

Conclusion: The present study shows a substantial association between hepatitis B virus infection and salivary gland hypofunction, and there appears to be a correlation of the hypofunction with the chronicity of the disease.

Keywords: Unstimulated saliva, hepatitis B virus. Case-control

INTRODUCTION

Saliva is a hypotonic solution and a mixture of secretions of salivary acini, gingival crevicular fluid and mucosal exudates (Zhang et al., 2016). The analysis of salivary glands status can be carried out accurately by evaluation of unstimulated salivary secretion.

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Although several factors such as body hydration status, drugs, and circadian rhythm (Bhattarai et al., 2018) may affect the unstimulated saliva, it is

commonly preferred to the evaluations of stimulated whole saliva, since biomarkers may become diluted in the latter (Fenoll-Palomares et al., 2004; Priya et al., 2017).

A simple and efficient way of accessing the functionality of the salivary glands is by measuring the salivary flow rate (SFR), SFR refers to the amount of saliva produced cumulatively from all the glands in a specified amount of time, and it is expressed as ml/min. At rest, SFR will range from 0.25 to 0.35 ml/min, and can increase with the influence of stimulation to 1.5 ml/min (Carda et al., 2006).

Viral hepatitis, like several other viral diseases, can be associated with oral manifestations and specifically, salivary gland diseases such as xerostomia and sialadenitis. Although the underlying pathophysiology has not been fully understood, it has been linked to immune complex sequelae and liver dysfunction (Bagewadi et al., 2015). Substantial progress has been made in establishing the diagnostic relevance of oral fluids in hepatitis B virus infection (Hutse et al., 2005; Ghosh et al., 2015; Gharavi & Esmaeili, 2020), yet, there is a relative gap in reports of its oral manifestations. For instance, there are more reports linking oral manifestations, specifically, salivary gland disorders with hepatitis C virus compared to hepatitis B virus infection (Grossmann et al., 2010; Jeffers & Webster-Cyriaque, 2011; Rahayuningtyas & Setiadhi, 2019). Thus, this study is aimed at determining the association between hepatitis B virus infection and salivary glands functionality.

MATERIALS AND METHODS

This case-control study included 76 patients diagnosed with hepatitis B virus infection and 48 control participants. Socio-demographics and times of diagnosis for the case group were obtained using a standardized questionnaire and with the aid of patients' records. The case group was further subcategorized into acute infection and chronic infection by six months' cut-off timeline from the first diagnosis.

For the salivary flow rates determination, participants were made to sit upright, asked to rinse their mouths with water to remove food debris. Participants were then asked to lie on the dental chair, a single wooden spatula was used as a bite prop, to allow saliva to pool at the floor of the mouth for 5 minutes. Thereafter, the whole unstimulated saliva was aspirated with the aid of a

sterile plastic pasture pipette into a graduated 15ml Falcon tube, and the volume was measured and recorded. Salivary flow rate is documented as volume (mls) per time (minute) (mls/min).

The data collected were screened for completeness and entered into IBM SPSS version 21.0 software. The categorical variables sex, associated oral lesions, were presented using frequencies and proportions. The level of statistical significance was set at $p < 0.05$ while the 95% confidence level was used to construct confidence intervals around estimates.

RESULTS

There was no significant difference between the distribution of ages in both case and control groups ($p = 0.221$). The case group comprised 41 males (52.6%) and 37 females (47.4%) while the control participants consisted of 22 males (45.8%) and 26 females (54.2%) (Table 1).

The average SFR of the cases was 0.12mls/min (0.06 – 0.26) with the values ranging from 0.01 – 0.90 while that of the control group averaged 0.48mls/min (0.29 – 0.63) with the values ranging from 0.02 – 1.20. The saliva flow rate of the control group was significantly higher than that of the case group ($p = 0.000$) (Table 2). Figure 1 further illustrates that the majority of the participants in the case group has their SFR above 0.4mls/min and vice versa for the SFR of the control group.

The distribution of salivary flow rate differed significantly across the duration of initial diagnosis ($p = 0.007$). The mean SFR of the acute cases was 0.21mls/min and ranged from 0.04 – 0.46 while the chronic cases had a lower average SFR of 0.09mls/min.

In the case group, the average saliva flow rate of the males was 0.14 (0.07 – 0.30) while that of the females was 0.10 (0.05 – 0.20). The distribution of saliva flow rate did not differ between males and females in the case ($p = 0.209$) and in the control group ($p = 0.425$).

In the case group, there was no significant change in the saliva flow rate as age increased ($r_s = 0.03$, $p = 0.794$) while in the control group, there was a slight increase in the saliva flow rate with an increase in age although it was not significant ($r_s = 0.157$, $p = 0.286$).

Table 1: Demographic Characteristics of the Participants

Characteristic	Cases (N = 78) n (%)	Control (N = 48) n (%)
Age (years)		
Mean ± SD	39.9 ± 12.1	42.8 ± 14.0
Range	19 – 68	19 – 64
Gender		
Male	41 (52.6)	22 (45.8)
Female	37 (47.4)	26 (54.2)
Marital Status		
Single	26 (33.3)	25 (52.1)
Married	52 (66.7)	23 (47.9)

Table 2: Descriptive Statistics of Salivary Flow Rate (SFR) of the Participants

Character	Cases (n = 78)	Control (n = 48)	P-value
SFR			0.000**
Median (IQR)	0.12 (0.06 – 0.26)	0.48 (0.29 – 0.63)	
Range	0.01 – 0.90	0.02 – 1.20	

SFR = Saliva flow rate, IQR = Inter-quartile range

** Significance at 99% confidence level.

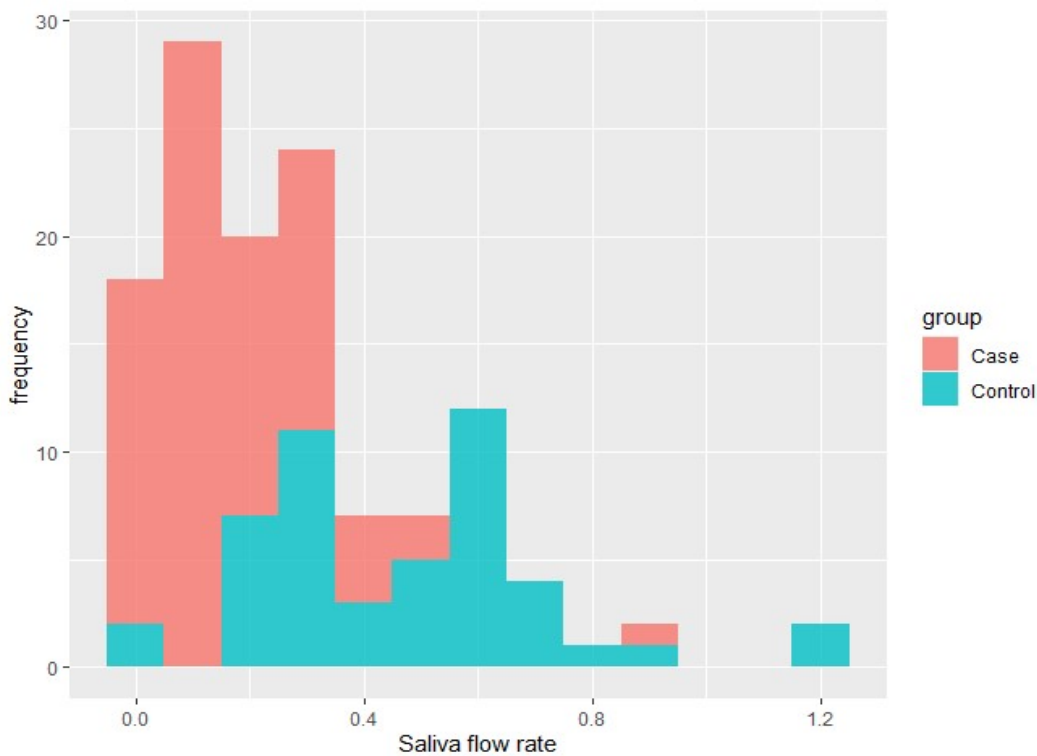


Figure 1: The distribution of saliva flow rate in both the case and control groups.

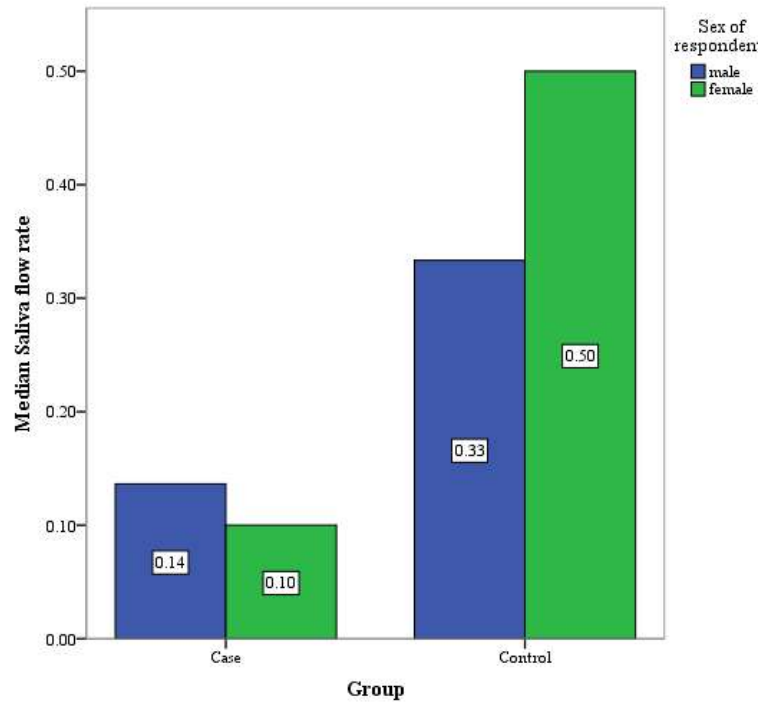


Figure 2: The average saliva flow rate of males and females in both the case and control groups.

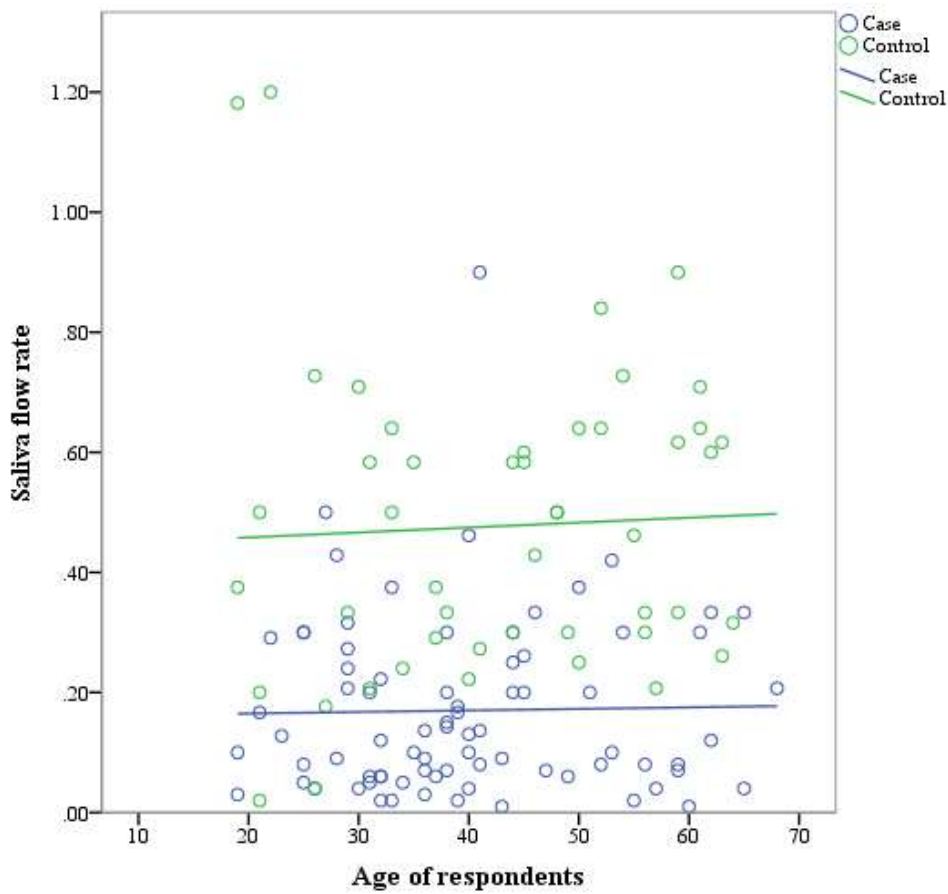


Figure 3: The relationship between saliva flow rate and age in both the case and control group.

DISCUSSION

Evaluation of unstimulated salivary flow rates has remained the fundamental and basic assessment of salivary function. The present study utilized the suction method, which only demands the passive participation of the participants and is reproducible. The paucity of reports in the literature about the salivary-glands sequelae of the hepatitis b virus disease processes has necessitated the need for this study to present a baseline and stimulate further explorations.

Similar to findings in a similar study amongst hepatitis C virus patients (Castro Ferreiro et al., 2002). there were no significant differences in the distributions of age and proportion of genders in the case and control groups.

In the present study, the significantly lower SFR amongst the hepatitis b virus-infected participants may be directly linked to virally induced salivary gland dysfunction even though the evidence is scarce. There is yet to be a consensus on the pathological mechanism of salivary dysfunction, however, complications of hepatitis B virus generally can be attributed to immune complex disorders, liver dysfunction and eventual liver failure (Bagewadi et al., 2015). This finding however is in variance with a similar study that compared SFR in patients with hepatitis C virus infection and healthy controls, where no significant difference in their SFR was observed (Castro Ferreiro et al., 2002). In a similar vein, Bagan et al reported no significant difference in SFR of patients with liver cirrhosis alongside their health control counterparts (Bagan et al., 1998). The average SFR of the chronic case group was 0.09mls/min below the hyposalivation threshold and differed significantly from that of the acute case group. No previous report had compared acute and chronic salivary gland manifestations of hepatitis b virus infection, however, it may be linked to the possibility of ensuing chronic liver dysfunction. Conversely, scores of studies have established no significant association of hepatitis B virus and Sjogren syndrome, a condition characterised by hyposalivation (Marcos et al 2009; Chen et al., 2012). Besides, the present study did not carry out assays to elicit the presence and absence of HBcAb IgM and HBcAb IgG respectively to clearly distinguish acute from chronic cases of hepatitis b virus (Li et al., 2020).¹⁷

The present study shows a substantial association between hepatitis B virus infection and salivary gland hypofunction, and there appears to be a correlation of the hypofunction with the chronicity of the disease. However, this study should stimulate further research to establish relationship

of salivary hypofunction with hepatitis B disease.

CONCLUSION

The present study shows a substantial association between hepatitis B virus infection and salivary gland hypofunction, and there appears to be a correlation of the hypofunction with the chronicity of the disease.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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