THE PREVALENCE OF SALIVARY GLAND DISORDERS AND LICHEN PLANUS IN PATIENTS INFECTED WITH CHRONIC HEPATITIS C VIRUS

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ABSTRACT

This study was carried out to examine the oral health of Hepatitis C Virus infected patients. In particular, the prevalence of salivary glands disorders and Oral Lichen Planus. Eighty patients infected with HCV, who were not undergoing anti-viral treatment, were examined. The information collected from the patients included, demographic details together with perception of their oral health and access to dental care since they were diagnosed of hepatitis C. Both extra-oral and intra-oral examinations were conducted. Teeth present and visible caries were recorded, periodontal conditions were measured using a Community Periodontal Index of Treatment Need (CPITN) probe and denture fit and hygiene were assessed where appropriate. The soft tissues were examined and lichen planus was diagnosed clinically. The whole salivary flow rates were estimated using spitting technique. The oral health of this cohort was poor. Twelve patients had clinical evidence of oral lichen planus (OLP), though all were not confirmed histologically. The salivary flow rates were significantly lower ($p < 0.001$) than previously reported healthy controls. Of the 25 regular dental attenders, only 5 had encountered problems accessing dental care. Chronic HCV infected patients require significant oral health care and an effective oral health education is required for HCV-infected patients and their carers.

Key points: *Prevalence, lichen Planus, Salivary gland, CPITN probe*

INTRODUCTION

Hepatitis C virus, an enveloped, single-stranded RNA Virus was identified by choo et al (1989) in the USA and is now known to be the primary etiologic agent of parenterally transmitted non-A, non-B hepatitis world wide. The WHO estimates that about 3% of the world population (170-200 million people) are infected with HCV and are at risk of developing liver cirrhosis and / or liver cancer.[1]

Although there are certain well-defined risk factors for hepatitis C transmission such as a history of intravenous drug abuse, former transfusions of blood or blood products, or sex with an infected partner, in around 10% of patients with chronic HC no obvious risk factor can be found.[1] In Pakistan, India, italy, japan and Egypt, unsafe injectins and contaminated equipment used in healthcare related procedures and in USA and Australia, illegal use of injection drugs has been the prominent mode of transmission of HCV over the pas 30 years.[2]

Chronic Hepatitis C progresses, if at all, at a slow pace displaying no signs and symptoms during the first two decades after infection in most cases. However, chronic Hepatitis C leads to cirrhosis in around 30% of patients and is associated with increased risk of liver cancer.[3] The literature suggests that HCV-infected patients may frequently have Sjögren-like sialadenitis with mild clinical symptoms, whereas oral LP may be significantly associated with HCV infections in Southern Europe and Japan .[23]

Patients infected with HCV often present with extra-hepatic manifestations, possibly as a result of viral infiltration of tissues or immunological trigger mechanisms.[4] Examples include hashimoto's disease, cryglobulinaemia, and arthiritis, porphria cutanea tarda (PCT), LP, DM, Lymphomas, perphral neuropathy and

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salivary gland disorders.[5] In recent years, several authors have reported a relationship between OLP and chronic liver disease, especially hepatitis C. This association seems to be strong in Japanese and Mediterranean populations, probably due to the higher prevalence of HCV infections.[24] Mignogna et al found that 28.8 % of OLP patients were HCV positive.[25]

The role of Hepatitis C virus (HCV) infection in the causation of lichen planus (LP) is controversial as many studies from around the world, [3] including several studies from various parts of India, have shown contradictory results. This study was conducted to look for an association between Hepatitis C Virus infection and lichen planus in the university of Lahore Dental College.

METHODOLOGY

The study consisted of 80 patients (65 males and 15 females) with chronic hepatitis C virus infection, who came for dental treatments in the University of Lahore Dental Hospital, (Lahore, Pakistan) between July 2009 to February 2010. Their mean age was 35 years (range 20-70), although 55% were 25-35 years-old. All the patients were confirmed of having HCV-RNA by Reverse Transcription Polymerase Chain Reaction (RT-PCR) and absence of other concomitant liver disease, negative HIV testing, no prior interferon treatment, absence of any underlying diseases which could produce salivary gland disorders (Xerostomia, Sjogren's Syndrome, diabetes mellitus or other autoimmune diseases etc).

A short clerking form was used to collect relevant patient details. Specific questions relating to their diagnosis, route of infection and stage of disease were asked. Patients were also asked questions of dental relevance including their own oral health and access to dental care since they were diagnosed with hepatitis C.

An initial extra-oral examination was performed to identify any abnormalities of the temporomandibular joint, salivary glands and lymph nodes. Then an intra-oral examination carried out under standard torch light illumination. Teeth present were charted and visible carious lesions were recorded. The periodontal condition was assessed using a Community Periodontal Index of Treatment Need (CPITN) probe.[6] All soft tissues were examined including the palate, tongue, floor of mouth, Buccal mucosa and gingivae. Lichen planus was diagnosed clinically according to the criteria described by.[7]

Salivary flow rate was measured by means of spiting method. Stimulated whole saliva was collected between 10:00 a.m. and 12:00 noon, by a single investigator. Subjects refrained from eating, drinking, smoking and oral hygiene procedures for 90 minutes before salivary collection. The spitting method was employed, applying four drops (0.17g) of 0.1M citric acid on the anterior dorsal surface of the tongue every minute for a five-minute period.[8] The first two minutes were considered to be a period of gland accommodation,[9] so samples collected during this time were discarded. Whole stimulated salivary flow rate of >0.7 ml/min was considered normal.[10] Saliva samples were collected in a sterile container, measured for volume and stored at -80 C.

Salivary flow was analyzed in relation to demographical, clinical and analytical variables by applying the two-tailed student's T-test, the chi-square test and logistic regression analysis. The salivary flow results were compared to those obtained from an age and sex matched HCV-negative healthy control group of 80 healthy volunteers. Informed consent from patients and healthy controls was taken.

RESULTS

The study group was comprised of 80 patients (65 males and 15 females) with a mean age of 35years (range 16-70years). In 71 cases, subjects were non-smokers, while 9 remaining patients smoked less than one packet of cigarettes a week. The mean duration of HCV infection was 7 $\pm$ 2 years, although this was determined only in 15 cases. The mean time lapsed from diagnosis of hepatitis C virus infection was 3.5$\pm$1 (1-8years). Routes of infection among the 80 patients were blood transfusion (55%), intra-venous drug user (20%), and unknown (25%).

No significant extra-oral abnormalities were detected on examination of the temporomandibular joist, salivary glands or cervico-facial lymph nodes.

Seventy of the 74 dentate patients had at least one decayed tooth requiring treatment (Table 1). To estab-

lish if this finding were linked to HCV infection and not merely a reflection of the poor dental health, the data were compared with the adult dental health study 1988.[11] Using the same age classification as adult dental health study, it was possible to establish that for each age group within the HCV cohort the proportion with decayed or unsound teeth was greater than in the general population (Table 1)

Due to poor oral hygiene many of the study population, about 70% of the patients had gingivitis. The CPITN score recorded was 1 (10%), 2 (70%), and 3 (20%), which was compared favorably with adult dental health study OPCS (office of the population census and surveys) data for the general population[11] and probably reflects the relatively large number of young people in the study group.

Twenty patients wore dentures (partial or complete dentures), six of them had erythematous candidosis (denture stomatitis), of which they were unaware. Sixteen of the 80 patients (20%), twelve males and four females, were diagnosed clinically with Oral Lichen Planus (OLP), compared with a normal population incidence of 1%. Two of these sixteen patients were HCV-RNA negative, six were infected with genotype 1, two with genotype 2, and six with genotype 3.

A number of other oral mucosal anomalies (Table 2) were noted in a further eighteen patients. These included frictional keratosis (fig 1), hyperplastic candidosis, angular cheilitis (fig 2), Buccal mucosal pigmentation, petechial haemorhages (fig 3), mucosal ulcers (fig 4) and inflamed sublingual salivary duct openings.

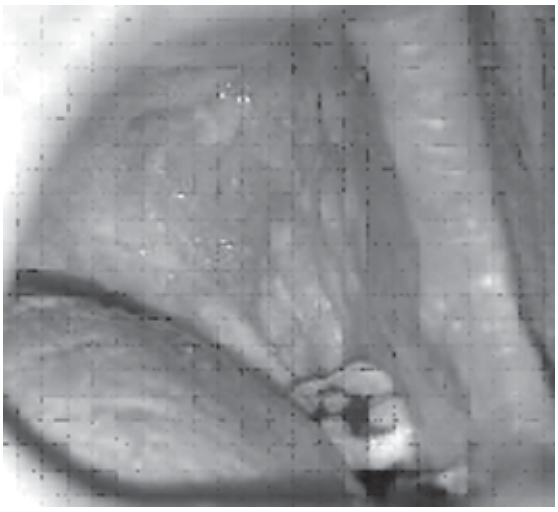

Fig 1: Frictional keratosis

Fig 2: Angular cheilitis

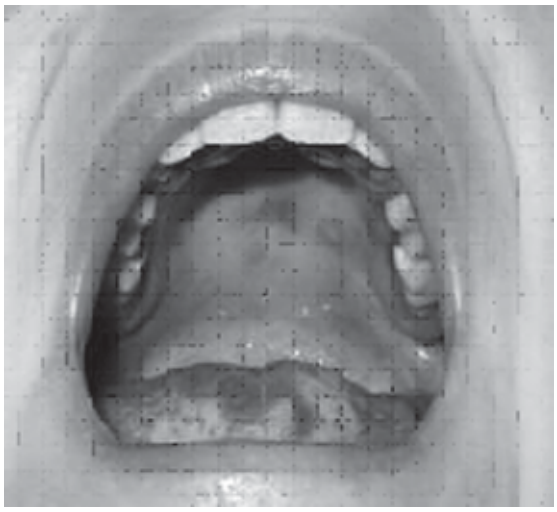

Fig 3: Petechial Haemorhage

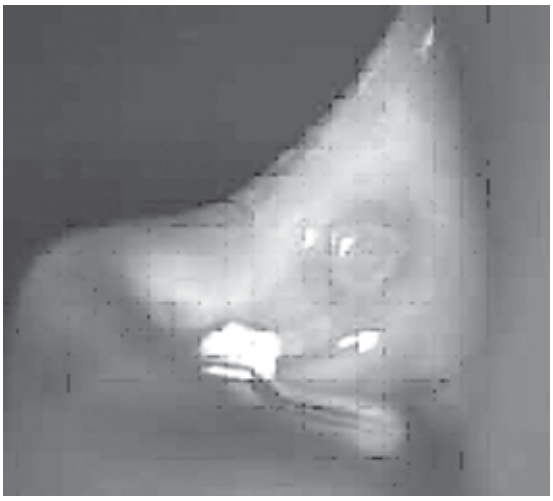

Fig 4: Mucosal ulcers

TABLE 1: CARIES INCIDENCE BY AGE GROUP AMONG THE COHORT OF 74 DENTATE PATIENTS WITH CHRONIC HEPATITIS C. THE OPCS FIGURES ARE PROVIDED TO ALLOW COMPARISON WITH THE GENERAL POPULATION

Age years	No. of patients	Pts. With Non-decayed teeth	Pts. With 1+ decayed teeth	% of Pts with decayed teeth	OPCS Value %
16-24	6	0	6	100	38
25-34	40	8	32	80	43
35-44	18	4	14	78	45
45-54	8	2	6	75	50
55-64	2	0	2	100	45
65+	0	0	0	0	47

TABLE 2: ANOMALIES AND NUMBER OF PATIENTS AFFECTED

Anomalies seen in patients	No. of affected patients	% of affected patients
Xerostomia	6	7.5
Hyposalivation	14	17.5
OLP	16	20
Frictional keratosis	20	25
Hyperplastic candidosis	18	22.5
Angular cheilitis	12	15
Buccal mucosal pigmentation	7	9
Petechial haemorrhage	16	20
Mucosal ulcers	22	27.5
Inflamed sublingual salivary duct	4	5

Six patients complained of oral dryness and Hyposalivation was demonstrated in 14 patients. The mean whole salivary flow rate in patients suffering from chronic HCV infection was 1.2+_0.5 ml/min (range 0.4-2.8). following categorization, the distribution of salivary flow rates amongst the 80 HCV patients was significantly different from values of 68 healthy controls [12] by a chi-square test of association ($p < 0.001$), with significantly more HCV infected patients demonstrating a flow rate of zero.

DISCUSSION

The spitting technique was used with a gustatory stimulus (citric acid drops), for whole stimulated saliva collection. The simplicity and reproductibility of this technique makes it a method of choice for whole saliva collection.[8] The main advantage of gustatory stimulation, over the chewing method is reduction in variability of salivary flow rates between individuals.[8]

The results demonstrated a significantly reduced salivary flow rate for the study group, compared with healthy controls.[12] There are a number of possible causes for a reduced salivary flow rate in hepatitis C infected individuals. The principal theories include infiltration of the salivary gland by the virus or a possible virus induced immune mechanism.[13] The role played by the saliva as a host defense mechanism is well recognized and xerostomia described may further predispose patients with HCV infection to both dental caries and oral soft tissue disease.

Another Significance in this study was the large number of patients on a methadone program. They presented high caries levels, especially in the cervical regions. A relatively high sugar content and prolonged oral contact time of methadone syrup predispose to rapid caries development. To allow cravings between methadone doses, chocolate and sugary snacks are eaten, also contributing to a higher caries incidence, as reported by sheedy.[14]

The high prevalence of OLP in cohort of HCV infected patients was surprising. No particular HCV genotype was detected in those patients with OLP. Although there does appear to be a consistency of association between HCV and OLP in some studies from southern Europe[15] and Japan,[16] such an association remains unproven in other geographical loca-

tions.[17,18,19,20] However, most of the studies have looked for HCV infection in patients with OLP, rather than seeking to identify OLP in cohorts of HCV infected patients. It should be noted that in this pilot study, the clinical diagnosis of OLP were not confirmed histologically. It was not possible in the environment where these patients were examined. There are limited data on the immunological aspects of HCV related to lichen planus. A number of possible pathogenic mechanisms have been suggested [13] including a cell-mediated cytotoxic response to an epitope shared by HCV and damaged keratinocytes[21] and a possible role for auto- antibodies directed towards epithelial epitopes.[22]

In summary, HCV may be a contributory cause in some patients, but it is neither necessary nor sufficient to cause OLP on its own.[13]

This study has shown that the oral health of many HCV infected patients is poor. Thus, access to dental treatment is an important issue. It was discouraging to hear that even within this small cohort, many patients had experienced discrimination and even refusal of treatment from dental surgeons following the diagnosis of HCV infection. In this pilot study, there was an association with oral dryness and OLP although these data require verification in a large-scale prospective study of the oral health of HCV infected patients. The lifestyle and neglected dental care of many of the HCV infected patients did not promote good dental health. There is need for more effective oral health promotion among both HCV infected patients and those caring for them and to ensure easy access of patients to appropriate dental care.

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