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Original Article

Dentistry Section

Salivary IgA versus HIV and Dental Caries

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ABSTRACT

Introduction: The inter-relationship of Human Immunodeficiency Virus (HIV) infection and dental caries as well as Salivary Immunoglobulin-A (S-IgA) level appear to remain under explored while a manual and electronic search of the literature was made. Hence, the present study was undertaken to assess the relationship of S-IgA and dental caries status in HIV positive children.

Aim: The aim of this study was to find out the relationship of S-IgA antibody with dental caries by measuring the concentration of IgA in saliva of HIV positive and negative children and determine the dental caries status in HIV positive and HIV negative children, which may help in treatment planning and prevention of the same.

Materials and Methods: A total of 28 HIV positive children aged between 6-14 years and 28 age matched HIV negative children were included in this study and both samples were randomly selected from the same Non-Governmental Organization (NGO). The HIV status of both these samples was confirmed from their medical records provided by the NGO. Only 2cc of unstimulated saliva was collected from both groups in special tubes coded numerically using the method described by Collins and Dawes and the samples were analyzed to measure the concentration of IgA using commercially available ELISA kit (DRG Diagnostics, Germany). Examination of dental caries was carried out according to WHO criteria (1997) using a flat mouth mirror and CPI probe.

Results: In HIV +ve group mean S-IgA level was calculated as 81.61 ± 6.20 µg/ml, mean DMFT was 3.86 ± 3.37, mean deft was 4.75 ± 2.86. In HIV -ve group mean S-IgA level was calculated as 145.57 ± 17.83µg/ml, mean DMFT was 2.54 ± 0.69, mean deft was 2.43 ± 2.01.

Strong-ve correlation between S-IgA and DMFT ($r = -0.781$, $t = 6.38$, $p < 0.001$) and negative but Not Significant (N.S.) correlation ($r = -0.19$, $t = 0.99$, $p > 0.05$) between S-IgA and deft was found in HIV +ve group. Strong –ve correlation between S-IgA and DMFT ($r = -0.655$, $t = 4.42$, $p < 0.001$), S-IgA and deft ($r = -0.942$, $t = 14.32$, $p = <0.001$) was found in HIV-ve group.

Conclusion: This study suggests that the individuals who are suffering from IgA deficiency in general, are more susceptible to dental caries than normal individuals.

Keywords: Child, deft index, DMFT index, Immunodeficiency, Immunoglobulin

INTRODUCTION

It has been established that dental caries is a disease of microbial etiology [1]. Although dental caries can be associated with various microorganisms including actinomyces, lactobacilli, and streptococcal species, there is an overwhelming relationship between the presence of a *Streptococcus mutans* and the initiation of carious lesion in both animals and man [1]. Naturally occurring secretary antibodies to *Streptococcus mutans* have been demonstrated in human secretion, which may afford similar protection against dental caries. If these naturally induced antibodies are effective in controlling oral disease, then individual deficient in immunoglobulin synthesis would be expected to exhibit increased incidence of dental caries [1]. Several studies have demonstrated that secretory Immunoglobulins A (IgA) has biologic activity, including viral neutralization and bacterial opsonisation and inhibition of colonization of local surfaces. Thus, it has become apparent that stimulation of the local secretory IgA system could interfere with the pathogenesis of *Streptococcus mutans* infection and therefore, might be effective in preventing experimental dental caries [2]. Secretory IgA, the predominant salivary immunoglobulin, is mostly produced by local gland associated immunocytes, depending on the local activated CD4+ cells. Human Immunodeficiency Virus (HIV) infection with subsequent immune suppression leads to a decrease in CD4+ cells and is associated with a decrease in the T-helper/inducer cell dependent IgA production [3]. Lower IgA concentration has been found in unstimulated whole saliva and stimulated parotid saliva in HIV patients [4,5]. Controversy remains till now in the relationship between HIV infection, mucosal immunity and dental caries. Many studies reveal that there is higher prevalence of dental caries in HIV infected children than in normal children [6-10]. The inter-relationship of HIV infection and dental caries as well as Salivary-IgA (S-IgA) level appear to remain under explored while a manual and electronic search of the literature was made. Hence, the present study was undertaken to assess the relationship of S-IgA and dental caries status in HIV positive children.

The aim of this study was to find out the relationship of S-IgA antibody with dental caries by measuring the concentration of IgA in saliva of HIV positive and negative children and determine the dental caries status in HIV positive and HIV negative children, which may help in treatment planning and prevention of the same.

MATERIALS AND METHODS

This cross-sectional analytical study was conducted in the Department of Pedodontics and Preventive Dentistry of Dr. R. Ahmed Dental College and Hospital, Kolkata, West Bengal, India, on 28 HIV positive children aged between 6-14 years and 28 age matched HIV negative children. Both samples were randomly selected from the same Non-Governmental Organization (NGO). The HIV status of both these sample was confirmed from their medical records provided by the NGO.

The selection criteria for the study samples were: Age between 6 to 14 years. No history of congenital and genetic problems, no history of any infection for last six months in case of control group, non tonsillectomized and ability to expectorate.

It was found that below 6 years of age the amount of secretory IgA present in the saliva is very less due to the immature lymph epithelial system and not reaching maturity until puberty. For this reason in the present study 6-14 years of age group was selected so that detectable amount of S-IgA could be found and very important time of mixed dentition period can be examined with evaluation of age related changes.

After taking the Ethical clearance from the Institutional Ethical Committee and delivering all the information regarding the study, a written consent of the legal care giver of children was taken. Saliva collection and dental examination were done in their own settlement on the same day. After collection of saliva, dental examination was done. To minimize possible food debris and stimulation of salivation, children were asked not to drink (except water) or eat anything one hour before saliva collection. Only 2cc of unstimulated saliva was collected from both groups in special tubes coded numerically using the method described by Collins and Dawes [11] (In this method, the child was asked to pool the saliva in the floor of the oral cavity and asked to spit intermittently) between 10 to 12 a.m. The samples were stored in the ice box, sent to the laboratory without any information regarding HIV positive and negative groups were leveled on the tube, thereby reducing the investigator bias and stored at -20°c until antibody analysis. Examination of dental caries was carried out according to WHO criteria (1997) [12] after allowing the children to sit on a chair under proper illumination using a flat mouth mirror and CPI probe.

Antibody levels were measured by solid-phase ELISA, performed in 96-well, flat-bottomed plates coated with anti-IgA (DRG Diagnostics, Germany) [13]. This test is based on simultaneous binding of human IgA to two antibodies, one monoclonal immobilized on microwell plates, and the other, polyclonal conjugates with Horseradish Peroxidase (HPR). Supernatant obtained after centrifuging the saliva sample which was diluted with IgA assay buffer and incubated at room temperature for one hour. TMB substrate solution is added after simple solid-phase washing and incubated at room temperature for 15 minutes. Stop solution is added after maximum colour development and this colour is compared with the colour of a series of standard with known level of IgA provided by the manufacturer to calculate the IgA concentration in the saliva sample which was expressed in µg/ml.

STATISTICAL ANALYSIS

Statistical significance of differences of each characteristic between two groups was tested by 'student's t-test' and p-value less than 0.05 was considered for checking the level of significance. Pearson's correlation coefficient test was used to find out the correlation of salivary IgA with dental caries.

RESULTS

In HIV +ve group mean S-IgA level was calculated as 81.61 ± 6.20 µg/ml, Range 6.98-90, CV 7.6, mean DMFT was 3.86 ± 3.37, Range 2-13, CV 87.13, mean deft was 4.75 ± 2.86, Range 0-8, CV 60.21 with mean age of samples being 9.53 ± 2.10 [Table/Fig-1].

In HIV-ve group mean S-IgA level was calculated as 145.57 ± 17.83 µg/ml, Range 120-182, CV 12.25, mean DMFT was 2.54 ± 0.69, Range 1- 4, CV 27.17, mean deft was 2.43 ± 2.01, Range 0-6, CV 82.72 with mean age of samples being 9.53 ± 2.10 [Table/Fig-2].

	Age(years)	Salivary IgA µg/ml	Caries index	
			DMFT	deft
Mean	9.53	81.61	3.86	4.75
S.D	2.10	6.20	3.37	2.86
Range	6-14	6.98-90	2-13	0-8
C.V	22.04	7.6	87.13	60.21

[Table/Fig-1]: Distribution of various variables in HIV +ve group. n=28
S.D; standard variation, C.V; coefficient of variation, DMFT; decayed, missing and filled teeth index, deft; decayed, extracted and filled teeth index, n; number of samples per group.

	Age(years)	Salivary IgA µg/ml	Caries index	
			DMFT	deft
Mean	9.53	145.57	2.54	2.43
S.D	2.10	17.83	0.69	2.01
Range	6-14	120 – 182	1 – 4	0 - 6
C.V	22.04	12.25	27.17	82.72

[Table/Fig-2]: Distribution of various variables in HIV –ve group. n=28
S.D; standard variation, C.V; coefficient of variation, DMFT; decayed, missing and filled teeth index, deft; decayed, extracted and filled teeth index, n; number of samples per group.

IgA µg/ml	Mean	S.D	Difference between averages		Statistical significance	
			$x_1 - x_2$	S.E	't'	p
HIV +ve group	81.61	6.20	- 63.96	3.567	17.94	<0.001
HIV-ve group	145.57	17.83				

[Table/Fig-3]: Comparison of mean value of salivary IgA level between HIV +ve and HIV–ve group. X; mean, SE; standard error, t; student's't' test result, p; probability.

DMFT	Mean	S.D	Difference between averages		Statistical significance	
			$x_1 - x_2$	S.E	't'	p
HIV + ve	3.86	3.37	1.32	0.65	2.03	<0.05
HIV – ve	2.54	0.69				

[Table/Fig-4]: Comparison of mean value of DMFT between HIV +ve and HIV–ve group . X; mean, SE; standard error, t; student's't' test result, p; probability.

deft	Mean	S.D	Difference between averages		Statistical significance	
			$x_1 - x_2$	S.E	't'	p
HIV + ve	4.75	2.86	2.32	0.66	3.51	<0.01
HIV – ve	2.43	2.01				

[Table/Fig-5]: Comparison of mean value of deft between HIV +ve and HIV–ve group. X; mean, SE; standard error, t; student's't' test result, p; probability.

The mean IgA level of HIV +ve group has been found lower than the HIV –ve group whereas DMFT, deft values were higher in HIV +ve group than HIV –ve group. Coefficient of variation (CV) of DMFT in HIV +ve group was higher than the HIV –ve group which indicate that DMFT of HIV +ve group shows greater variability than the HIV –ve group whereas deft of HIV –ve group shows greater variability than HIV +ve group. IgA, deft of HIV +ve group shows lower variability than HIV –ve group.

The statistical significance of the difference between the means of two groups were tested by student's 't' test and p -values less than 0.05 were considered as statistically significant.

As shown in [Table/Fig-3] the't' value was computed as 17.94. With 54 degree of freedom (df) this calculated value was compared with the table value at 5% level to find out the level of significance. The corresponding p-value was <0.001 which was highly significant. So there is a statistical difference present between the mean value of S-IgA in HIV +ve and HIV–ve group. From this result we can say that mean S-IgA level of HIV–ve group was higher than the HIV +ve group.

As shown in [Table/Fig-4] the 't' value was 2.03. With df 54, the corresponding p-value was <0.05. So we can say that difference of mean value of DMFT between the two groups were statistically significant at 5% level and mean DMFT of HIV +ve group was higher than the HIV –ve group.

Test between	HIV + ve		
	'r'	't'	p
S-IgA &DMFT	-0.781	6.38	<0.001
S-IgA & deft	-0.19	0.99	>0.05(N.S)

[Table/Fig-6]: Pearson Correlation values of salivary IgA (S-IgA) with dental caries in HIV +ve group.
'r'; Pearson correlation value, t; student's't' test result, p; probability, N.S; not significant. n; number of samples per group

Test between	HIV - ve		
	'r'	't'	p
S-IgA &DMFT	-0.655	4.42	<0.001
S-IgA & deft	-0.942	14.32	<0.001

[Table/Fig-7]: Pearson correlation values of salivary IgA (S-IgA) with dental caries in HIV –ve group.
n=28 'r'; Pearson correlation value, t; student's't' test result, p; probability, n; number of samples per group.

Data presented in [Table/Fig-5] shows that the't' value was 3.51. With 54 df the corresponding p-value was <0.01 which indicate the presence of statistically highly significant difference of mean deft between the two group. So it can be said that the mean deft of HIV +ve group was higher than the HIV –ve group.

As shown in [Table/Fig-6] the 'r' value of S-IgA vs. DMFT was computed as -0.781 which was significant at 0.1% level (t = 6.38, p<0.001, df 26). This result indicate a strong –ve correlation between S-IgA and DMFT in HIV +ve group.

Negative but Not Significant (N.S.) correlation (r = -0.19, t = 0.99, p>0.05) was found between S-IgA and deft in HIV +ve group.

From the [Table/Fig-7] we can see that all the 'r' values were negative and statistically strongly significant (p<0.001) in HIV –ve group. From the result we can say that decreasing level of S-IgA in HIV +ve group was responsible for increasing level of DMFT and deft comparative with the HIV –ve group [Table/Fig-6].

DISCUSSION

The infectious nature of dental caries proves the hypothesis that some form of our body immunity can regulate caries activity [14] and it was assumed that S-IgA was directly involved in the immunity to dental caries which prevents the adherence of cariogenic microorganisms to the tooth surfaces [15] and it also inhibit the activity of glucosyltransferases [16] which is essential for synthesis of extracellular glucans.

Although S-IgA antibodies have attracted a lot of interest for a number of years, their possible role in protection against dental caries is still not clear. Many studies have been performed to evaluate whether the presence or absence of caries can be correlated with the levels of total IgA in saliva.

The progressive deterioration of immune function associated with HIV infection might be expected to result in decreased IgA production; a T-cell dependent process. But the relationship between S-IgA and dental caries in children with HIV infection has not been well established. Hence, the present study was aimed at assessing the relationship of salivary IgA with dental caries status in HIV positive children.

The impact of HIV infection on salivary IgA level is unclear, with reports of both decreased and increased titers. Mandel I.D et al., [17] studied cohorts of HIV-infected and AIDS patients but detected no decrease in IgA secretion. In contrast, others reported higher but not significant concentration of total salivary IgA than the control group [3,18-21]. This increased immune reaction is most probably a response to the higher level of antigens present in the oral cavity of these patients, who suffer from opportunistic infections such as candidiasis.

In comparison with control group Challacombe SJ, Sweet SP [4], Sweet SP, Rahman D, Challacombe SJ [5], Muller F et al., [22] demonstrated reduced S-IgA concentrations in HIV infected patients. The present study report is in correlation with these studies [4,5,22]. Present study found lower S-IgA concentration in HIV positive group in comparison with the age matching healthy control group. This decreased lower IgA concentration can be possibly due to decrease in the levels of CD4+ T lymphocytes. Since, this cell has a pivotal role in the maturation of the secretory immune system, it is expected that this system would be altered in these patients.

Madigan A et al., found in a cross-sectional study that there was a higher prevalence of dental caries in the primary teeth of HIV-infected children as compared to their HIV negative sibling and in particular among children older than 6 years of age (7-14 years) [23].

Valdez IH, et al., reported a higher prevalence of dental caries (dft) in primary teeth of HIV-infected children (mean age 4.9±0.38) when compared to the national average for five-year-olds. They noted that primary dentition caries of HIV-infected children was 2.6-fold higher than the U.S. national average of 1.7 [24].

In a study of dental caries in HIV infected children in 1992 Howell RB et al., [25] reported that caries prevalence in HIV-infected children is very high, mainly in the primary dentition. They used non-infected siblings as controls to compensate for confounding factors. Srinivas RP et al., Sandeep Kumar et al., Shrikanth M et al., Sales Peres SHC et al., Arrive et al., also found the similar results in their studies [26-30].

The findings of the above studies [23-30] were in agreement with the result of our study. We found more dental caries in HIV infected group than the healthy control group and deft was more than DMFT in both the HIV positive and control group. These increased deft were possibly due to under developed immune system in lower age group who had more deciduous teeth compared to the higher age group patient as well as due to differences in composition between primary and permanent teeth.

Several investigations have suggested that secretory IgA in saliva may play a significant role in protecting dental caries. Legler DW et al., reported a high frequency of harbouring *Streptococcus mutans* and a greater susceptibility to dental caries in immunoglobulin–deficient patients [31]. Everhart DL et al., assumed a protective role for IgA antibody against caries development in a study of evaluation of dental caries experience and S-IgA in children aged 3-7years [32].

Orstavik and Brandtzaeg reported a statistically significant, negative correlation between the DMF score and IgA secretion rate in their study [33]. Lehtonen OJ et al., Camling E et al., Katz J et al., Fontnana M, et al., Bratthall D et al., Kirtaniya BC et al., Doifode & Damle, Golpasand Hagh L et al., in their study also demonstrated lower incidence of caries with higher salivary IgA concentration [34-41]. From this study they conclude that secretory IgA antibody in saliva provides protection against dental caries. The findings of the above studies are in agreement with the present study result. A negative correlation between S-IgA with dental caries in both the HIV positive and control group was observed in the present study. The result of this study suggests that immune dysfunction, regardless of type tend to predispose toward caries susceptibility. As IgA is the predominant immunoglobulin in saliva, it would be expected that patients deficient in this class of immunoglobulin would show a greater susceptibility to dental caries.

CLINICAL IMPLICATIONS

Passive immunization with IgA could reduce dental caries in those patients who are suffering from IgA deficiency.

LIMITATION

In the present study sample size was small and study was conducted at one time only and CD4 cell count was not included

in this study which have greater influence on the immunity, so further study is needed over a longer period of time with large sample size to obtain the accurate result.

CONCLUSION

This study suggests that the individuals who are suffering from IgA deficiency in general, are more susceptible to dental caries than normal individuals.

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