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Original Article

Lactate Dehydrogenase: A Pragmatic Diagnostic Tool for Periodontitis and Diabetes

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ABSTRACT

Background: Many biomarkers were evaluated in the last few years for different sort of diseases, among them some may have the common biomarkers. Salivary lactate dehydrogenase is used as a bio marker for diagnosing periodontitis as well as diabetes. The current study tries to find the correlation between periodontitis and diabetes as they share the same biomarker. **Methods:** A cross sectional study was conducted on 90 patients, dividing into 3 groups based on the inclusion and exclusion criteria. The clinical parameters like, gingival index, oral hygiene index- simplified, depth of periodontal pocket, and clinical attachment loss were recorded. Saliva of these patients was collected and the levels of LDH are examined in those samples for further analysis. **Results:** All of the clinical indicators, including GI, OHI-S, PPD, CAL and levels of HbA_{1c} showed a significant difference. All clinical indicators, as well as HbA_{1c} levels, were found to be greatest in Group B (PD+DM) patients. Salivary LDH levels were also shown to follow a similar pattern, with Group B having the highest levels, followed by Group A, then Group C. The subjects' HbA_{1c} levels and salivary LDH levels were shown to have a significant correlation. **Conclusion:** Salivary LDH can be used as a biomarker to detect any tissue damage or inflammation that transpires throughout an illness. The identification of this enzyme might be a pragmatic diagnostic tool for early diagnosis of periodontitis and diabetes. To affirm the outcomes and employ the test in future, further research on LDH should be done in larger sample sizes.

Key words: Lactate dehydrogenase, Biomarker, Saliva, Periodontitis, Diabetes.

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INTRODUCTION

Several biomarkers have been investigated in recent years for various diseases; some of the diseases share the common biomarkers. Biomarkers can be obtained from serum, saliva, and gingival crevicular fluid. Biomarkers can be used to diagnose a variety of disorders. Lactate dehydrogenase is a cytoplasmic enzyme practically found in all of the body's tissues. From necrotic cells, it is discharged into the extracellular environment.[1] Lactate dehydrogenase is released from damaged cells at the sites of cell death, and it can aid in the early identification of a variety of disorders. It is utilized to diagnose periodontitis as a bio marker.[2] Periodontitis and diabetes share the common biomarker; hence there is indeed a correlation between the two.

Periodontitis, an inflammatory condition of periodontium which destructs supporting structures of tooth and can also lead to several systemic disorders. It is caused by microorganisms that lead to periodontal defects, such as pockets, gingival recession, mobility, and teeth-supporting alveolar bone. Diabetes mellitus is a disorder caused due to lack of insulin production and/or chronic hyperglycemia. This condition may affect the organs like eyes, heart, brain, lungs, pancreas, kidneys, including the salivary glands. Long-term hyperglycemia causes the production of AGEs (advanced glycation end products), which can cause diabetic complications due to AGE accumulation in plasma and tissues.[3] Periodontitis is the sixth major complication of diabetes.[4]

Many bio markers are present in saliva in the case of salivary gland involvement, like Lactate Dehydrogenase (LDH), Alkaline Phosphatase (ALP), Aspartate and Alanines Aminotransferases (AST), Creatine Kinase (CK), and Acid Phosphatase (ACP). They are used to diagnose diabetes mellitus as well as periodontitis. By comparing salivary lactate dehydrogenase levels in different groups of individuals, a correlation between chronic periodontitis and type 2 diabetes mellitus can be established.

This corresponding study was done to evaluate the salivary lactate dehydrogenase (LDH) levels in patients suffering from periodontitis with and without diabetes and trying to find out whether diabetes has any influence on periodontal tissues systemically.

MATERIALS AND METHODS

This cross-sectional study, conducted on 90 patients visiting the outpatient section of Periodontology department, Peoples College of Dental Sciences and Research centre, Bhopal. Patients were selected and divided into 3 groups on the basis of inclusion criteria and exclusion criteria. Group A consisted of 30 subjects with chronic periodontitis without diabetes (PD), Group B consisted of 30 subjects with chronic periodontitis and diabetes (PD+DM), and Group C consisted of 30 Healthy subjects/control group(C). Patients suffering from moderate to severe periodontitis affecting more than 30% of sites. Patients within the age group of 25-60 years, systemically healthy subjects except type 2 diabetes mellitus, HbA_{1c} levels between 4% to 6% were considered under Groups A and C, levels between 6.5% - 8% were considered under Group

B, subjects with minimum of 20 natural teeth excluding third molars and with pocket depth ≥ 4mm. Active smokers, pregnant women and lactating females, subjects taking antibiotic or periodontal treatment in the previous 6 months except the oral hypoglycaemic agents, insulin therapy or both, major complications of diabetes, HbA_{1c} levels more than 8 were excluded. The clinical parameters like, gingival index, oral hygiene index- simplified, depth of periodontal pocket, and clinical attachment loss were recorded. Saliva of these patients was collected and the levels of LDH are examined in those samples for further analysis.

SPSS (Statistical Package for Social Sciences) software, version 28, IBM was employed for statistical analysis. The Kruskal-Wallis H test ("one-way ANOVA on ranks"), the Spearman correlation coefficient denoted by the symbol r Analysis of Variance (ANOVA) tests were used to analyze the variables. It tests the significance of difference between the means of more than two groups.

RESULTS

The mean age of the participants was found to be 40.82 ± 10.26 yrs, with a minimum of 22yrs and a maximum of 65 yrs. The Mean age of Group A, Group B, and Group C was 37.70 ± 8.86, 47.73 ± 8.51, and 37.03 ± 9.88 respectively. A comparison of mean age among all the groups is done and their difference is tested using Kruskal Wallis test, a statistically significant difference was observed between the groups with test statistic of 19.813, and $p<0.001$ [Highly significant].

The mean gingival index score of Group A, Group B, and Group C was 2.21 ± 0.35,2.28 ± 0.38, and 0.77 ± 0.48 respectively. On the basis of above values, Group B (PD+DM) shows higher value along with Group A (PD) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 56.535, and $p<0.001$ [Highly significant]. The mean OHI-S score of Group A, Group B, and Group C was 4.31 ± 0.91, 4.06 ± 1.02, and 1.52 ± 0.69 respectively. On the basis of above values, Group A (PD) shows higher value along with Group B (PD+DM) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 58.530, and $p<0.001$ [Highly significant]. The mean probing pocket depth score of Group A, Group B and Group C was 5.97 ± 0.91, 5.38 ± 0.70, and 2.77 ± 0.52 respectively. On the basis of above values, Group A (PD) shows higher value along with Group B (PD+DM) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 62.734, and $p<0.001$ [Highly significant]. The mean clinical attachment level of Group A, Group B, and Group C was 6.34 ± 0.97, 5.75 ± 0.72, and 3.07 ± 0.51 respectively. On the basis of above values, Group A (PD) shows higher value along with Group B (PD+DM) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 62.537, and $p<0.001$ [Highly significant]. [Table 1]

The mean HbA_{1c} levels of Group A, Group B, and Group C was 4.68 ± 0.52, 7.17 ± 0.55, and 4.51 ± 0.65 respectively. On the basis of above values, Group B (PD+DM) shows higher value along with Group A (PD) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 60.392, and $p<0.001$ [Highly significant]. The mean salivary lactate dehydrogenase

Table 1: Comparison of clinical parameters among groups.

Group	Mean	Standard Deviation	Minimum	Maximum	Kruskal-Wallis test statistic	Significance
			Age (Years)			
Group A	37.70	8.86	27.00	60.00	19.813	$p<0.001$
Group B	47.73	8.51	29.00	65.00		
Group C	37.03	9.88	22.00	57.00		
			GI			
Group A	2.21	.35	1.60	2.90	56.535	$p<0.001$
Group B	2.28	.38	1.60	2.90		
Group C	.77	.48	.30	1.90		
			OHI-S			
Group A	4.31	.91	2.90	5.80	58.530	$p<0.001$
Group B	4.06	1.02	2.40	5.90		
Group C	1.52	.69	.40	2.80		
			PPD			
Group A	5.97	.91	4.20	7.40	62.734	$p<0.001$
Group B	5.38	.70	4.30	7.40		
Group C	2.77	.52	1.70	3.50		
			CAL			
Group A	6.34	.97	4.30	7.80	62.537	$p<0.001$
Group B	5.75	.72	4.40	7.70		
Group C	3.07	.51	2.10	3.80		
			HbA1c			
Group A	4.68	.52	3.70	5.80	60.392	$p<0.001$
Group B	7.17	.55	6.10	8.20		
Group C	4.51	.65	3.20	5.80		
			LDH			
Group A	940.18	90.36	698.70	1047.50	67.361	$p<0.001$
Group B	1080.61	113.85	897.60	1342.20		
Group C	326.49	60.83	189.40	432.30		

Table 2: Correlation between LDH levels and HbA_{1c} levels of Participants.

Spearman's correlation		Hba_{1c}
LDH	Correlation Coefficient	.604**
	Sig. (2-tailed)	.000
	N	90

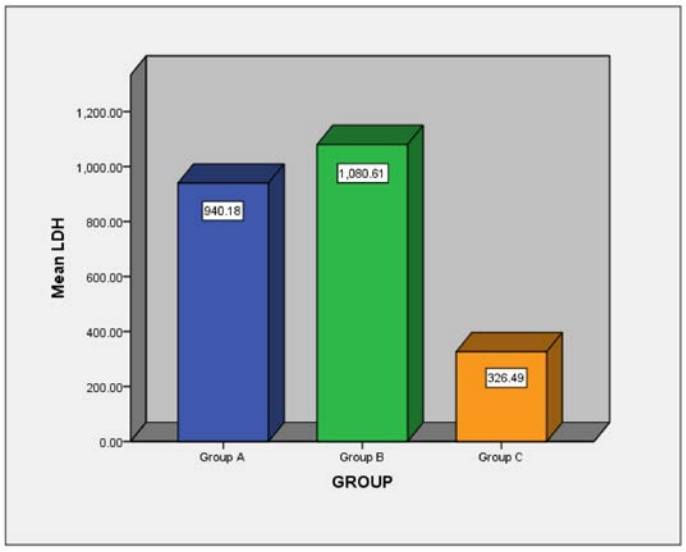

Figure 1: Bar graph showing comparison of LDH levels among groups.

levels of Group A, Group B, and Group C was 940.18 ± 90.36, 1080.61 ± 113.85, and 326.49 ± 60.83 respectively. On the basis of above values, Group B (PD+DM) shows higher value along with Group A (PD) as compared to Group C (Control). A statistically significant difference was observed between the groups with test statistic of 56.535, and $p<0.001$ [Highly significant]. [Table 1]

The correlation between LDH and HbA_{1c} levels is tested using spearman's correlation test and it was found to be strongly correlated with each other. The correlation coefficient was found to be 0.604, with a p value of <0.001. [Table 2] [Figure 1].

DISCUSSION

Diabetes and periodontitis are diseases that are commonly occurred in adults, which have a high prevalence in the population. In the United States, it is estimated that; 50% of the population is affected by periodontitis, and 7.8% suffer from diabetes. Type 2 DM is observed to be most common form.[5]

Quantifying biomarkers in saliva serve as an important tool to predict an individual's susceptibility to periodontitis. Costa *et al.*,[6] and Adriana Monea *et al.*,[7] in their study concluded that saliva analysis is an efficient and safe enough tool for diagnosis and evaluation of periodontal disease progression in type 2 diabetic patients.

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme essentially present in the body. LDH is released from damaged cells at the sites of cell death, and it can aid in the early identification of a variety of disorders. It is utilised to diagnose periodontitis as a bio marker. Periodontitis and diabetes share the same biomarker; hence there is indeed a correlation between the two.

The gingival index (GI) score and simplified oral hygiene index (OHI-S) shows a significant difference between the groups, but on comparing between the groups, Group B (PD+DM) shows higher value along with Group A (PD) as compared to Group C (Control), which was statistically highly significant with p value <0.001. This is due to less amount of plaque in healthy patients which increased gradually with the progress of the periodontal disease. The Mean gingival score was 2.21, 2.28 & 0.77, while simplified oral hygiene index score was 4.31, 4.06 & 1.52 for Group A, Group B and Group C respectively. These findings are in line with those of Javier Enrique Botero *et al.*,[8] who found that diabetes can exacerbate periodontal disease and have an impact on an individual's overall health. The current study's findings are also in acceptances with those of Abhinav Avinash Havle *et al.*[9]

The Probing pocket depth (PPD) and clinical attachment level (CAL) shows a significant difference between the groups, but on comparing between the groups, Group B (PD+DM) shows higher value along with Group A (PD) as compared to Group C (Control), which was statistically highly significant with p value <0.001. The Mean probing pocket depth score was 5.97, 5.38, and 2.77, while clinical attachment level (CAL) was 6.34, 5.75 and 3.07 for Group A, Group B and Group C respectively. These differences between the groups are consistent with studies by Morita *et al.*[10] which concluded that the elevated levels of HbA_{1c} were associated with developing periodontal pockets of more than 4 mm. The current study results are also in agreement with a study conducted by Abhinav Avinash Havle *et al.*,[9] and in a study conducted by Uma Sudhakar *et al.*[11] the PPD was observed to be greater in periodontitis patients with a significant difference.

The Mean HbA_{1c} score shows a significant difference between the groups, but on comparing between the groups, Group B (PD+DM) shows higher value when compared to Group C (Control) and Group A (PD), which was statistically highly significant with p value <0.001, according to the inclusion criteria of the groups. The salivary LDH levels were found to be the greatest in the Group B (PD+DM) along with Group A (PD) as compared to Group C (Control), which was statistically highly significant with p value <0.001. The results of the current study are consistent with many other studies in the literature.[9,11-13] In a study conducted by Barbara Malicka *et al.*,[13] the LDH levels in saliva were found to be significantly higher in patients with diabetes mellitus type 2. The salivary LDH levels were found to be highest in the patients with periodontitis in a study conducted by Janet Moradi *et al.*[12] The LDH can act a potential biomarker in early identification and diagnosis of both chronic periodontitis and type 2 diabetes mellitus.

There are certain limitations of the current study, the study is conducted on a limited sample size, further studies are needed with a higher sample sizes. Although a higher value of salivary LDH levels were noticed in the Group B (PD+DM). A separate analysis of the group containing only diabetes mellitus without periodontitis is not carried out in the current study, which might have showed much accurate results and helps in predicting a stronger conclusion. Etiology of chronic periodontitis was not considered in the inclusion criteria, which may affect the salivary LDH levels. The current study obtained a significant difference among age of the participants of all the groups, which may not be appropriate for comparison.

CONCLUSION

The legitimacy of lactate dehydrogenase, a salivary biomarker, was evaluated for its accuracy in detecting chronic periodontitis and diabetes. The results show that the mean salivary LDH levels differed considerably across the three study groups. Salivary LDH levels were pre-eminent in individuals with periodontitis and diabetes, followed by those with periodontitis in non-diabetic. As a result, salivary LDH can be used as a biomarker to detect any tissue damage or inflammation that transpires throughout an illness. The identification of this enzyme might

be a pragmatic diagnostic tool for early diagnosis of periodontitis and diabetes. To affirm the outcomes and employ the test in future, further research on LDH should be done in larger sample sizes.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PD: Periodontitis; **DM:** Diabetes Mellitus; **GI:** Gingival Index; **OHI-s:** Oral Hygiene Index-Simplified; **PPD:** Probing Pocket Depth; **CAL:** Clinical Attachment Loss; **LDH:** Lactate Dehydrogenase; **HbA_{1c}:** Glycated Hemoglobin.

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