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COMPARISON OF LEVELS OF LACTATE DEHYDROGENASE ENZYME [LDH] IN SALIVA OF THE PATIENTS WITH ACUTE MYOCARDIAL INFARCTION [AMI] AND CHRONIC PERIODONTITIS [CP]—A BIOCHEMICAL STUDY

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ABSTRACT

Background: Literature reveals that Periodontal disease could be a risk factor for cardio vascular disease. Available meta-analyses find significant heterogeneity which lead to the need for further observational and interventional studies. Host response to periodontal disease include the production of number of enzymes that are released by stromal, epithelial or inflammatory cells. They are associated with either cell injury or cell death. Lactate dehydrogenase [LDH] is the one among those enzymes and it is an intracellular enzyme released by the inflammatory cells during tissue destructive phases. Metabolic changes in the periodontium could be regulated by these enzymatic changes. LDH enzyme activities are higher in chronic periodontitis and in myocardial infarction. Estimation of the iso-enzymes of lactate dehydrogenase in serum is a well-established laboratory procedure for helping diagnose acute myocardial infarction.

Objective: The present study was designed to compare the levels of LDH in saliva of the patients with Acute Myocardial Infarction with Chronic Periodontitis, [G-A], Systemically healthy with Chronic Periodontitis [G-B], and Systemically and Periodontally healthy subjects [G-C].

Materials and methods: A total of 30 subjects 10 AMI with Chronic Periodontitis, and 10 Systemically healthy with Chronic Periodontitis and 10 Systemically and Periodontally healthy were recruited. Clinical Periodontal measurements were recorded and stimulated whole saliva was collected. The patients with AMI were examined after 3-4 days after admission to the coronary care unit. The activities of LDH enzyme levels were measured spectrometrically after centrifuging the collected salivary samples, by the optimized kinetic method of deutsche Gessellschaft Fur Klinische Chemie [DCKC].

RESULTS: The saliva of patients with AMI and Periodontitis had significantly higher LDH enzyme activities. Similarly the saliva of patients with Chronic Periodontitis also have higher levels of LDH enzyme activities. LDH enzyme activities correlated significantly in both test groups. LDH enzyme levels are significantly lower in saliva of Systemically and Periodontally healthy patients.

CONCLUSION: The present study showed higher levels of LDH in both Acute myocardial infarction [AMI] patients and Chronic Periodontitis [CP] patients. This could prove strong association between the two diseases. Number of samples in this study was less which could be a limitation. Further longitudinal studies with larger number of samples could confirm the association. Hence this estimation of LDH levels in saliva could be a non invasive method to detect acute myocardial infarction [AMI] and chronic periodontitis [CP].

KEY WORDS: Host Response, Lactate Dehydrogenase, Confounding factor, Thrombo embolic events, Acute Coronary Syndrome.

INTRODUCTION

Periodontal diseases are the second most common oral diseases next to dental caries and are considered as an inflammatory disorder that damages tissue through the complex interaction between periodontopathic bacteria and the host defense system. Microbial biofilm adhering to teeth, serves as a slow delivery system of oral pathogens into the systemic circulation leading to a chronic microbial challenge and downstream effects as a consequence of an altered immune response.

Cardiovascular atherosclerotic disease is a major contributor to the global disease burden.[1] Its pathogenesis is an area of intensive research. Inflammation is a major contributor to the risk for CVD. Destructive periodontal disease is also associated with chronic inflammation and has drawn the interest of the dental researchers towards identifying a link between this disorder and CVD[1]

Lactate dehydrogenase is a tetrameric protein found in all living cells and acts in the glycolytic cycle catalyzing the reversible reaction between pyruvate and lactate. It is elevated during tissue destructive phases, like myocardial infarction, rheumatic disease and acute leukemia. LDH activities are also higher in chronic periodontitis.[2] The present study was designed to compare the levels of LDH in saliva of patients with Acute Myocardial Infarction[AMI] and Chronic Periodontitis[CP] and to explore the possibility of using LDH as a biochemical marker of Periodontal disease and Myocardial infarction and as a reliable diagnostic aid.

MATERIALS AND METHODS

A total of 30 subjects [10 AMI with Chronic Periodontitis, 10 systemically healthy with Chronic Periodontitis and 10 systemically and periodontally healthy patients] were recruited. AMI patients were recruited from

coronary care unit in government medical college, Chennai. The other patients were recruited from the pool of patients presenting at the department of Periodontics, Thai Moogambigai Dental college, Chennai. The subjects were briefed about the study and informed consent was obtained and ethical committee approval was obtained. The subjects were assigned in three groups as,

Group A — AMI patients with Chronic Periodontitis.

Group B — Systemically healthy patients with Chronic Periodontitis.

Group C — Systemically and Periodontally healthy patients.

The patients with AMI were examined after 3-4 days after admission to the Coronary Care Unit, Govt. General hospital, Chennai. Patients with Systemic disorders like diabetes, immunological disorders and pregnant and lactating females were excluded from the study. Clinical Parameters like Plaque index [PI], Bleeding on Probing [BOP] and Probing pocket depth [PPD] were recorded for all the groups and stimulated whole saliva was collected. The activities of LDH enzyme levels were measured spectrometrically after centrifuging the collected salivary samples, by optimized kinetic method of Deutsche Gesellschaft Für Klinische Chemie [DCKC].

STATISTICAL ANALYSES

One sample Kolmogorov Smirnov test was employed to show that the samples were drawn from normal population except the variable BOP. To compare the mean values between two groups, Student's t-test was employed for the variables LDH, PI and PPD. As BOP does not follow a normal distribution, to compare the mean value, Mann Whitney test was employed. The significance level was fixed at 5%.

RESULTS

Table no. 1 describes the Students t-Test to compare the mean values between group A and group B. The mean values of LDH – U/I in Group A was 1137.3 ± 221.6 and in Group B was 1014.5 ± 115.5 . Even though group A had a higher mean LDH value than group B, the mean values were not statistically significant ($P > 0.05$). The mean PI value in Group A is 2.53 ± 0.39 and in Group B it is 2.40 ± 0.32 , the mean was not statistically significant ($P > 0.05$).

Table no. 2 explains the Students t-Test which compares the mean values between group A and group C. The mean values of LDH – U/I in Group A was 1137.3 ± 221.6 and in Group C was 95.6 ± 14.55 . The mean values were statistically highly significant ($P < 0.001$). The mean PI value in Group A was 2.53 ± 0.39 and in Group C it was 0.87 ± 0.40 , the mean was statistically highly significant ($P < 0.001$).

Table no. 3 describes the Students t-Test which compares the mean values between group B and group C. The mean values of LDH – U/I in Group A was 1014.5 ± 115.41 and in Group C was 95.6 ± 14.55 . The mean values were statistically highly significant ($P < 0.001$). The mean PI value in Group A was 2.40 ± 0.323 and in Group C, it was 0.87 ± 0.403 . The mean were statistically highly significant ($P < 0.001$).

Table no. 4 explains the results of Mann-Whitney Test (Non Parametric) which was done to compare the BOP mean values between groups. The mean BOP values for group A and C was 3.853 and its P value was < 0.001 . The mean BOP values for group B and C was 3.827 and its P value was < 0.001 . Both were highly significant.

Table no. 5 describes Karl Pearson Correlations coefficient test results between LDH and other parameters. The correlation between LDH – U/I with PI was 0.940, indicating that there was a strong relationship between LDH and PI and it was statistically highly significant ($P < 0.001$). Similarly LDH is strongly correlated with PPD

and BOP with correlations 0.942 ($P < 0.001$) and 0.912 ($P < 0.001$) respectively.

Table no. 6 explains Karl Pearson Correlations coefficient test results between LDH and other parameters in each group. It shows the correlation values of LDH with PI, PD and BOP in each group. The correlation between LDH and other parameters were good and statistically significant in Group A and Group B. In Group C the correlations were moderate and not statistically significant.

DISCUSSION

Numerous markers in the saliva have been proposed as diagnostic tests for periodontal diseases, such as intracellular enzymes [LDH, AST, ALT]. These enzymes are included in the metabolic process of cells and are mostly present in cells of soft tissues. Their increased release from the damaged cells of soft tissues is a reflection of metabolic changes in the inflamed soft tissues.[3]

In the present study, LDH levels were higher in group I and group II when compared to systemically healthy subjects. Between group I and group II, it was more significant in group I (subjects who have both the AMI and Chronic Periodontitis). In the present study, there was a strong co-relation between the levels of LDH and other clinical parameters [PI, PD, BOP] as well. They were more significant in group I & II, when compared to group III indicating increased soft tissue damage.

Number of studies were reported as the link between periodontal disease and acute myocardial infarction [4,5,6]. Acute coronary syndrome had higher plaque scores, gingival index and P. gingivalis count than stable patients. Studies have reported increased levels of LDH in recent AMI patients, suggesting severely damaged myocardial cells, which are the source for the increased LDH in serum and saliva. Studies have also been reported on increased levels of LDH levels in Chronic Periodontitis patients which again is an

inflammatory disorder. In the present study, LDH was found to be significantly increased in AMI with Chronic Periodontitis group alone. LDH an intracellular enzyme which catalyses the conversion of lactate to pyruvate, was increased in saliva in both AMI and Chronic Periodontitis. Smith et al [7] reported a study, in which, LDH levels were more in patients with increased probing depth compared to healthy probing depth. The results of their study and our study were similar. There is a growing evidence that poor oral health especially periodontitis increases the risk of acute myocardial infarction [8]. Thromboembolic events may be related to chronic oral infection. Number of hypothesis have been proposed regarding the relationship between these diseases.[9] It could be attributed to the common risk factor which are common to both the diseases with tobacco use as the main cofounding factor [10]. It could also be attributed to the periodontal pathogens that produce the endotoxins and pro inflammatory mediators by host monocytes, causing local and systemic destruction of connective tissue favoring platelet aggregation and thromboembolic events.[11]

Saliva is readily available and could be easily collected by simple, non invasive method without using any specialized equipments. The present study LDH assays were done using saliva. LDH assays may also be used to measure and detect the rate of progression of an inflammatory condtion. However, the LDH level may not be able to pinpoint the exact location of damage. It could also be used to detect the progression after treatment[3]. The potential of salivary biomarkers and their potential to provide screening diagnosis should be kept in mind. Targeted approaches that identify the key biomarkers linked to distinct biological phases of diseases are needed to generate the panels required to provide the sensitivity and specificity needed for accurate diagnosis. The present study has certain limitations. The number of participants were small, so it may not be representative of the total

population of CVS disease. Further longitudinal studies with larger sample sizes are needed for a more significant results.

CONCLUSION

The present study showed higher levels of LDH in both Acute myocardial infarction[AMI] patients and Chronic Periodontitis [CP] patients. This could prove strong association between the two diseases. Number of samples in this study was less which could be a limitation. Further longitudinal studies with larger number of samples could confirm the association. Hence this estimation of LDH levels in saliva could be an non invasive method to detect acute myocardial infarction [AMI] and chronic periodontitis [CP].

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TABLES

Table no 1: Students t-Test to compare the mean values between group A and group B

	Group	N	Mean	Std. Dev	t-Value	P-Value
LDH-U/I	Group-A	10	1137.30	221.644	1.554	0.143
	Group-B	10	1014.50	115.413		
PI	Group-A	10	2.53	0.392	0.810	0.429
	Group-B	10	2.40	0.323		
PD-mm	Group-A	10	5.80	0.789	0.896	0.382
	Group-B	10	5.50	0.707		
BOP	Group-A	10	2.50	0.527	0.885	0.388
	Group-B	10	2.30	0.483		

LDH-Lactate Dehydrogenase, PI-Plaque Index, PD-Probing depth, BOP-Bleeding on probing.

The mean LDH values are not statistically significant ($P > 0.05$) in both A & B groups. The mean PI value in Group A is 2.53 ± 0.39 and in Group B it is 2.40 ± 0.32 , the mean are not statistically significant ($P > 0.05$).

Table no 2: Students t-Test to compare the mean values between group A and group C

	Group	N	Mean	Std. Dev	t-Value	P-Value
LDH-U/l	Group-A	10	1137.30	221.64	14.830	<0.001*
	Group-C	10	95.60	14.55		
PI	Group-A	10	2.53	0.392	9.342	<0.001*
	Group-C	10	0.87	0.403		
PD-mm	Group-A	10	5.80	0.789	9.436	<0.001*
	Group-C	10	2.90	0.568		
BOP	Group-A	10	2.50	0.527	7.203	<0.001*
	Group-C	10	1.10	0.316		

LDH-Lactate Dehydrogenase, PI-Plaque Index, PD—Probing depth, BOP-Bleeding on probing

*Denotes, significant P value. The mean values of LDH – U/l in Group A is 1137.3 ± 221.6 and in Group C is 95.6 ± 14.55 . The mean values are statistically highly significant ($P < 0.001$). The mean PI value in Group A is 2.53 ± 0.39 and in Group C it is 0.87 ± 0.40 , the mean are statistically highly significant ($P < 0.001$).

Table no 3: Students t-Test to compare the mean values between group B and group C

	Group	N	Mean	Std. Dev	t-Value	P-Value
LDH-U/l	Group-B	10	1014.50	115.41	24.980	<0.001*
	Group-C	10	95.60	14.55		
PI	Group-B	10	2.40	0.323	9.367	<0.001*
	Group-C	10	0.87	0.403		
PD-mm	Group-B	10	5.50	0.707	9.067	<0.001*
	Group-C	10	2.90	0.568		
BOP	Group-B	10	2.30	0.483	6.573	<0.001*
	Group-C	10	1.10	.316		

LDH-Lactate Dehydrogenase, PI-Plaque Index, PD—Probing depth, BOP- Bleeding on probing

*Denotes, significant P value. The mean values of LDH – U/I in Group B is 1014.5 ± 115.41 and in Group C is 95.6 ± 14.55 . The mean values are statistically highly significant ($P < 0.001$). The mean PI value in Group B is 2.40 ± 0.323 and in Group C it is 0.87 ± 0.403 the mean are statistically highly significant ($P < 0.001$).

Table no 4: Mann-Whitney Test (Non Parametric) to compare the BOP mean values between groups.

Group	Z-Value	P-Value
Group-A vs Group-B	0.890	0.374
Group-A vs Group-C	3.853	<0.001*
Group-B vs Group-C	3.827	<0.001*

*Denotes significant p value.

P values are significant between group A and group C and between group B and group C

Table no 5: Karl Pearson Correlations coefficient between LDH and other parameters.

		LDH-U/I
PI	Correlation	0.940
	P-Value	<0.001
	N	30
PD-mm	Correlation	0.942
	P-Value	<0.001
	N	30
BOP	Correlation	0.912
	Sig. (2-tailed)	<0.001
	N	30

The correlation between LDH –U/I with PI is 0.940 indicating that there is a strong relationship between LDH and PI and it is statistically highly significant ($P < 0.001$). Similarly LDH is strongly correlated with PD-mm and BOP with correlations 0.942 ($P < 0.001$) and 0.912 ($P < 0.001$) respectively.

Table no: 6 Karl Pearson Correlations coefficient between LDH and other parameters in each group

		LDHa-U/l		
		Group-A	Group-B	Group-C
PI	Correlation	0.734	0.859	0.403
	P-Value	0.016	0.001	0.248
	N	10	10	10
PD-mm	Correlation	0.726	0.890	0.506
	P-Value	0.018	0.001	0.136
	N	10	10	10
BOP	Correlation	0.878	0.816	0.589
	P-Value	0.001	0.004	0.073
	N	10	10	10

The above table shows the correlation values of LDH with PI, PD and BOP in each group. The correlation between LDH and other parameters are good and statistically significant in Group A and Group B. In Group C the correlations are moderate and not statistically significant.

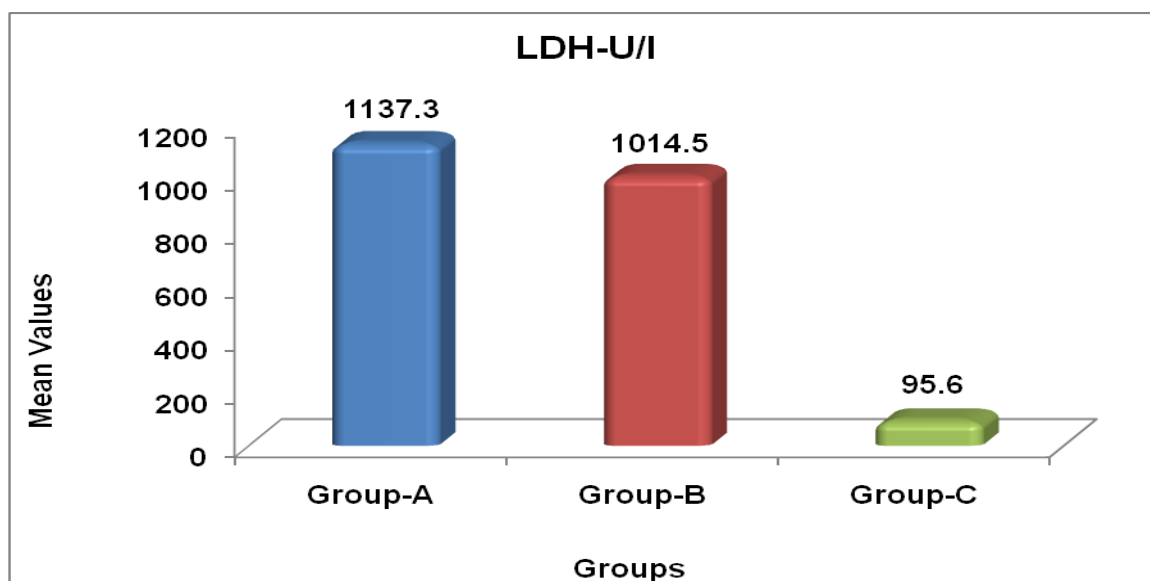
Figure: Comparison between LDH levels in all three groups.

Fig :1, explains LDH levels in Group A & B are more when compared with group C .

Group-A-AMI with Chronic Periodontitis,

Group-B-Chronic Periodontitis,

Group-C- Healthy Subjects.