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STUDY OF LEVEL OF SERUM LOW DENSITY LIPOPROTEIN (LDL) CHOLESTEROL IN PATIENTS WITH HELICOBACTER PYLORI INFECTION

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ABSTRACT

Objective – To study the level of serum LDL cholesterol in patients with H. Pylori infection and compared with control group who are age and BMI matched.

Material & methods - This study was prospectively conducted on age and BMI matched 60 patients (30 cases and 30 controls) presented to the Department of Medicine in Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu from november 2009 to October 2010 with the chief complaints of upper gastrointestinal symptoms. 60 patients enrolled in the study were divided into cases and control depending upon rapid urease test .The baseline characteristics of age, sex, height, weight and BMI were comparable in two groups. The maximum number of patients in group I (cases) was in age group of 35-45 years and in group II (control) in 25-35 years. 30 males and 30 females were recruited in whom mean height, weight and BMI were statistically insignificant. Among laboratory parameters, fasting plasma sugar and fasting serum lipid profile were estimated. We excluded the patients who had risk factors for dyslipidemia in order to be able to clearly assess whether infection with H.pylori raises serum LDL cholesterol of patients or not. The Statistical Package for SocialSciences (SPSS) version 13.0 was utilized to analyze the results. Parametric variables are presented as means ± standard deviation . An analysis using the SpearmanCorrelationwasperformedtoevaluatetheexistenceofassociations between H.pylori infection and LDL levels. Logistic Regression analysis, involving the statistically significant variables identified by the Spearman Correlationwasperformedtoevaluatetheprobabilityofraised LDL levels in presence of H.pylori infection investigated in this study. Chi square test is used to analyses the number of patients in two groups and 't' test for equality of means. P values < 0.05 were considered statistically significant.

Results- The difference in fasting plasma sugar level in two groups was statistically insignificant, but marked variability was seen in levels of serum lipid profile. The level of serum total cholesterol in cases v/s control group was significantly high 205.93 ± 13.17 mg/dl v/s 169.27 ± 16.44. Similar significant rise in the levels of serum LDL cholesterol was noted in cases (134.53 ± 11.88 mg/dl) v/s control (98.30 ± 13.78 mg/d1), The difference in the levels of I-IDL cholesterol and triglycerides was statistically insignificant in the twogroups.

Conclusion- The study found an association between H. pylori infection and altered serum lipid profiles. Infected subjects have a significant increase intotal cholesterol and LDL cholesterol levels compared to uninfectedsubjects. In view of the gravity of acute coronary events and salvageability on timely management, the infection with H. pylori can be a modifiable risk factor and further studies are needed to see the impact of early treatment of infection on acute coronaryevents.

KEYWORDS : H pylori ; LDL cholesterol ; urease test ; Dyslipidemia ; acute coronary events

INTRODUCTION

Uppergastrointestinaltractsymptomsarecommoncomplaintsofthepatients presenting in the outpatient department, commonly diagnosed as Acid Peptic Disease, Gastro-Oesophageal Reflux Disease or Peptic ulcer. A gram negative, microaerophilic rod bacterium called campylobacter pyloridis (Helicobacter pylori) has been incriminated as a causative agent for such symptoms[1]. The association of H.pylori with various extra-gastric conditions has been a matter of research. Commonly studied is association between H.pyloriandcardiovascularevents.Althoughthemechanismof actionofcoronary arterial wall is unknown, however it could resemble the gastric endothelial damage by this germ involving proinflammatory cytokines and cag A cytotoxin resulting in endothelial injury, macrophage transformation and thrombosis[2]. Infection with H.pylori induces long standing low grade persistent inflammatory stimulus which express selectin/integrin for leucocyte recruitment and endothelial dysfunction, thereby losing its ability to produce nitric oxide. These factors contribute to pathogenesis of atherosclerosis and coronary artery disease. H.pylori raises the gastric pH resulting in reduced folate absorption and levels in the body which inhibit methionine synthase reaction resulting in increased concentration of homocysteineinblood, whichisknowntobetoxictoendothelialcellsandan independent risk factor for atherosclerosis[3]. Current field of research is association of H.pylori infection with raised atherogenic lipid profile (LDL Cholesterol)[4]. Low grade persistent inflammation caused by H.pylori produces various cytokines. These cytokines raise serum lipid concentration and shift them to more atherogenic profile by activation of adipose tissue lipoprotein lipase, stimulation of hepatic fatty acid synthesis, influencing lipolysis and increased expression of procoagulant substances such as fibrinogen and platelet activating factor-1[5]. We conducted a study with the aimtoknowtheeffectofH.pyloriinfectiononserumLDLCholesterollevels,as defining the relationship between H.pylori and LDL will enhance our understandingaboutwhetherH. pyloriwouldbecomplementaryorredundant in causing dyslipidemia leading toatherosclerosis.

AIMS AND OBJECTIVES

We studied the level of serum LDL cholesterol in patients with H.pylori infection and compared with control group who are age and BMI matched.

MATERIAL AND METHODS

Thisstudywasprospectivelyconductedonage andBMImatched 60patients (30 cases and 30 controls) presented to the Department of Medicine in Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu from november 2009 to October 2010 with the chief complaints of upper gastrointestinal symptoms. Among them, patients who had H.pylori infection were categorised as Group I (cases) and who did not have H.pylori infection were categorised as Group II (control). Fasting serum LDL cholesterol levels of two groups were compared.

INCLUSIONCRITERIA- Patients presented with upper gastrointestinal complaints likedyspepsia,hearburn and sour eructation; Age group more than 25 years.

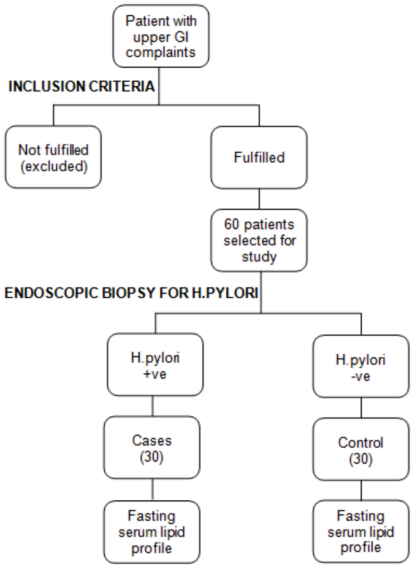
EXCLUSION CRITERIA- Alcohol intake more than 30gm. per day; Cigarette smoking; Hypertension;Diabetes mellitus; Hypothyroidism; Obesity (BMI>30kg/m^2); Liver and renal failure; Cardiovascular disorder; History of intake of Hypolipidemic drugs (statins), drugs which modify lipid profile (beta blockers, diureticsandaminodarone). Adetailedhistoryofsymptoms,clinical examination, laboratory investigation including blood sugar, renal function tests, liver function tests, ECG and upper gastrointestinal endoscopy with biopsy based rapid urease test were done. After excluding other pathology, thebaselinecharacteristicsofenrolledpatients (age,sex, weight,height,BMI, blood pressure, fasting plasma glucose) were matched and the levels of LDL cholesterolofH. pyloripositivepatientwerecomparedwithH.pylorinegative patients and analysedstatistically.

LIPID ESTIMATION METHODOLOGY :- Three millilitre of blood was collected with sterilised syringes from each patient. The blood was immediately transferred to clean vials and allowed to clot. The serum was separatedfromthebloodandit wasusedforlipidanalysis,byfullyautomatic Dimension RL Max auto analyser and semiautomatic RA 50 auto analyser. The levels of serum lipid are normally assessed by Enzymatic Methods.

Determination of H.pylori infection :- Subject enrolled for the study underwent endoscopic tissue biopsy of the gastric mucosa for determination of H.pylori infection by rapid urease test. Pronto dry kit is used for that. It detects the activity of urease enzyme of H.pylori in biopsy sample. Biopsy is incubatedinamediumcontainingureaandpHsensitivecolourmarker;urease hydrolyses urea to carbon dioxide, thereby changing the colour of the medium. It has sensitivity of 100% and specificity of 96.8% and accuracy of 96.8%.

Statistical Analysis- The Statistical Package for Social Sciences (SPSS) version 13.0 was utilized to analyze the results. Parametric variables are presentedasmeans ±standarddeviation.TheMann-Whitneytestwasusedto analyze the sample divided into two groups related to presence of absence of H.pylori infection. An analysis using the Spearman Correlation was performedtoevaluate theexistenceofassociationsbetweenH.pyloriinfection and LDL levels. Logistic Regression analysis, involving the statistically significantvariablesidentifiedbytheSpearmanCorrelationwasperformedto evaluatetheprobabilityofraisedLDLlevelsinpresenceofH.pyloriinfection investigated in this study. Chi square test is used to analyses the number of patients in two groups and 't' test for equality of means. P.values < 0.05 were considered statisticallysignificant.

Figure A: Showing flow of patients in the study



OBSERVATIONS

Following observations were made during the study:
Demographic features of 60 patients divided into cases and control group are as under:

Baseline Characteristics	Group I (Cases) n=30	Group II (Control) n=30	P-value
Age (yrs)	38.63 ± 8.49	37.70 ± 8.68	0.675
Sex (m/f); n (%)	17/13; (57/43)%	13/17; (43/57)%	0.302
Height (metres)	1.653 ± 0.055	1.658 ± 0.054	0.724
Weight (kg)	60.80 ± 6.34	61.37 ± 8.36	0.768
BMI (kg/m^2)	22.26 ± 2.06	23.24 ± 1.73	0.125
systolic BP (mm Hg)	13.4 ± 4.76	130.2 ± 4.14	0.863
Diastolic BP (mm Hg)	82.8 ± 3.84	82 ± 3.71	0.416

P value <0.05 is statistically significant.

Laboratory parameters of patients of two groups are as under

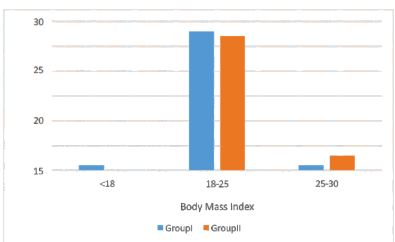
Variables (mg/dl)	Group I (cases)	Group II (control)	P value
Plasma glucose (F)	97.53 ± 6.46	96.8 ± 4.59	0.614
Total cholesterol	205.93 ± 13.17	169.27 ± 16.44	<0.001
HDL cholesterol	41.97 ± 5.84	41.83 ± 5.38	0.927
LDL cholesterol	134.53 ± 11.88	98.30 ± 13.78	<0.001
Triglycerides	146.83±22.80	147.67 ± 30.338	0.905

P value <0.05 is significant

The baseline characteristics of two groups are comparable as shown in the above table and P value statistically insignificant except for total cholesterol and LDL cholesterol.

BMI BASED DISTRIBUTION OF PATIENTS OF TWO GROUPS

BMI (Kg/m^2)	Group I		Group II	
	n	%	n	%
<18	1	3.3	0	0
18-25	28	93.3	27	90
25-30	1	3.3	3	10



In group I (cases): 1 patient (3.3%) has BMI of <18, 28 patient (93.3%) has

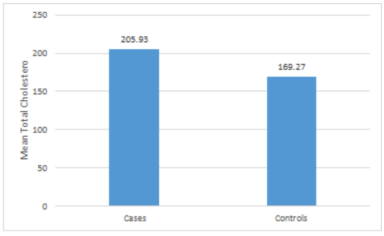
in range of 18-25 and 1 patient (3.3%) in 25-30 range.In group II (control): no patient has BMI <18, 27(90%) patients has in range of 18-25 and 3(10%) patients in 25-30 range.
Maximum number of patients lies in normal BMI range of 18-25 in both groups.
The BMI in two groups was statistically insignificant.

COMPARISON OF TOTAL CHOLESTEROL IN TWO GROUPS

Group	N	Total Cholesterol Mean ± SD(mg/dl)	't' value	P value
Cases	30	205.93 ± 13.17	9.535	<0.001***
Controls	30	169.27 ± 16.44		

***p< 0.001; Highly Significant

Mean Total CholesterolTable shows the comparison of total cholesterol in two groups.



In group I(cases), among the 30 patients, the range of total cholesterol varies from 176 mg/dl to 228 mg/dl with Mean ± SD of 205.93 ±13.17

In group II (control), the range of total cholesterol varies from 148 mg/dl to 210 mg/dl in 30 patients with Mean ± SD of 169.27 ± 16.44 The 't' value is 9.535

The difference of serum total cholesterol in two groups were statistically highly significant with p value <0.001.

COMPARISON OF HDL IN TWO GROUPS

Group	N	HDL (mg/dl) Mean ± SD	't' value	P value
Cases	30	41.97 ±5.84	0.092	0.927^{NS}
Controls	30	41.83 ± 5.38		

NS: p > 0.05; Not Significant

Table shows the comparison of HDL cholesterol in two groups.

In group I of 30 cases, the level of HDL cholesterol varies from 32 mg/dl to 59 mg/dl with Mean ± SD of 41.97 ± 5.84
In group II of 30 controls, the level varies from 33mg/dl to 52 mg/dl with Mean ± SD of 41.83 ± 5.38
The 't' value for means is 0.092

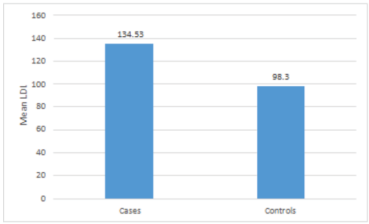
In the two groups difference of level of serum HDL cholesterol is statistically insignificant as p value is 0.927.

COMPARISON OF LDL IN TWO GROUPS

Group	N	LDL (mg/dl) Mean ± SD	't' value	P value
Cases	30	134.53 ± 11.88	10.910	<0.001***
Controls	30	98.30 ± 13.78		

*** p< 0.001; Highly Significant

Mean LDLTable shows the comparison of LDL cholesterol in two groups.



30casestakeninstudyhaveserumlevelofLDLcholesterolrangingfrom110 mg/dl to 155 mg/dl with Mean ± SD of 134.53 ±11.88
Whereas in 30 control, the level of LDL cholesterol ranges from 72 mg/dl to 132 mg/dl with Mean ± SD of 98.30 ± 13.78
The 't' value is 10.910 and the difference in the levels of serum LDL cholesterol is highly significant as p value is <0.001.

COMPARISON OF TRIGLYCERIDES IN TWO GROUPS

Group	N	Triglycerides (mg/dl) Mean ± SD	't' value	P value
Cases	30	146.83 ±22.80	0.120	0.905^{NS}
Controls	30	147.67 ±30.38		

NS:p>0.05; Not Significant

Mean TGTable shows comparison of triglycerides in two groups.

In group I(cases): among 30 patients the range of triglycerides varies from 50 mg/dl to 175 mg/dl with Mean ± SD of 146.83 ± 22.80

IngroupII(controls):among30patientstherangevariesfrom94mg/dlto240 mg/dl with Mean ± SD of 147.67 ±30.38
The't' value is 0.120

Thedifferenceinlevelsofserumtriglyceridesintwogroupswerestatistically insignificant as p value is0.905.In our study, we have excluded the patients who had risk factors for dyslipidemia in order to be able to clearly assess whether infection with H.pylori raises serum LDL cholesterol of patients ornot.

RESULTS -

60 patients enrolled in the study were divided into cases and controldependinguponrapidureasetest.Thebaselinecharacteristicsofage, sex, height, weight and BMI were comparable in two groups. Themaximum numberofpatientsingroupI (cases)wasinagegroupof3545yearsandin group II (control) in 25-35 years. The number decreases with increasing age because of co-morbid conditions in older age group and patients fail to fit into inclusion criteria. 30 males and 30 females were recruited in whom mean height, weight and BMI were statistically insignificant. Among laboratory parameters, fasting plasma sugar and fasting serum lipid profile were estimated. The difference in fasting plasma sugar level in two groups was statistically insignificant, but marked variability was seen in levels of serum lipid profile. The level of serum total cholesterol in cases v/s control group was significantly high 205.93 ± 13.17 mg/dl v/s 169.27 ± 16.44. Similar significant rise in the levels of serum LDL cholesterol

was noted in cases (134.53 ± 11.88 mg/dl) v/s control (98.30 ± 13.78 mg/d1), The difference in the levels of I-IDL cholesterol and triglycerides was statistically insignificant in the two groups.**DISCUSSION**- The results of our study were comparable to various studies conducted worldwide over association of H.pylori with atherogenic lipid profile. Previous studies which have shown the association of H.pylori with atherogenic lipid profile are Ansari M et al (2000)[6] demonstratingrise

in levels of total cholesterol, LDL cholesterol and Total cholesterol/HDL ratio in H.pylori infected patients thereby suggesting association between H.pylori and dyslipidemia. This association was further supported by study conducted by Kucukazman M et al (2009)[7] in which levels of total cholesterol and LDL cholesterol were found to be significantly raised in H.pylori infected patients and HDL cholesterol and triglycerides levels were statistically insignificant. Papamichael KX et al (2009)[8] demonstrated association between H.pylori with dyslipidemia, specifically with raised total cholesterol and LDL cholesterol and decreased HDL cholesterol in H.pylori infected patients. The study promoted the hypothesis of inflammatory cytokines induced atherogenic modificationof lipid profile. Ugwuja et al (2009)[9] supported this association in pregnant women, in which they have concluded that H.pylori positive pregnant women had higher LDL cholesterol level than H.pylori negative women. The results of our study were in accordance with Sung et al (2005), [10]Chimienti G et al (2003).[11] Both had demonstrated the positive association between H.pylori infection and atherogenic lipid profile.Thestudy conducted by Chimienti G showed persistent inflammation plays a basic role in the pathogenesis of atherosclerosis by altering lipid profile. Helicobacter pylori, as an independent risk factor for acute coronary events were demonstrated in the study conducted by Kinjo K et al (2002)[12]. Studies conducted by Kanbay M et al (2005)[13] and Parente F et al (2000) [14]did not support the hypothesis. Although changes in level of HDL cholesterol and CRP levels were found in H.pylori infected patients but Kanbay M et al refuted any changes in LDL cholesterol levels. In our study we did not found any difference in HDL cholesterol and triglycerides level. The effect of H.pylori on these parameters of lipid profile is still controversial and need further studies. One of the mechanisms for difference in lipid profile in our study may be that H.pylori is a bacterial infection. Gallin JL et al (1969)[15] demonstrated that some infection may induce disturbances in serum lipid levels. It was further supported by Alvarez C et al (1986)[16] as they have clearly demonstrated return of serum lipid levels to normal range as the patient recovered from sepsis. Another mechanism may be that H.pylori generates persistent low grade inflammatory stimulus which alters the lipid profile in the body.

CONCLUSION

Our study favours the proposed hypothesis of raised serum LDL cholesterol in H.pylori infected patients, as the basis for pathogenesis of acute coronary events. In this study, we have worked onone of the proposed mechanism of this association that is `Dyslipidemia inducedbyH.pyloriinfection'. Thisisacomparativestudyinwhichthelevels ofserumLDLcholesterolinH.pyloriinfectedpatientsarecomparedwiththe control group. The study found an association between H. pylori infection and altered serum lipid profiles. Infected subjects have a significant increase in total cholesterol and LDL cholesterol levels compared to uninfected subjects. These findings could identify a mechanism regarding H. pylori's role in atherosclerosis, as raised levels of LDL cholesterol is a risk factor for atherosclerosis and can precipitate acute coronary events. In view of the gravity of acute coronary events and salvageability on timely management, theinfectionwithH. pyloricanbeamodifiableriskfactorandfurtherstudies areneededtosee the impactofearlytreatme nto finfectiononacutecoronary events.

REFERENCES

1. John Del Valle: Peptic Ulcer Disease. Harrison's Principles of Internal Medicine 2008
2. Chimienti G, Russo F, Lamanuzzi B.L, Nardulli M, Messa C, Di LeoA:Helicobacterpyloriisassociatedwithmodifiedlipidprofile. Clinical Biochemistry 2003 July; 36(5):359-365
3. Markel HV: Department of Centenary Health Centre; Canada1996
4. Yavuz et al,Digestive disease sciences2008
5. Digestive disease sciences 2005 and world journal of gastroenterology2009
6. Ansari M, Ornrani M, Sayyah B, Ansari S: Effect of H.pylori infection on lipids patient with gastritis. African Journal of Microbiology Research 2010Jan;4(1):84-87
7. Kucukazman M, Bunyamin Yauz, Sacikara M: The relationship between Updated Sydney System Score and LDL cholesterol in patientinfected withH.pyloriinfection.DigestiveDiseaseSciences 2009;54:604-607
8. Papamichael KX, Papaioannou G, Helen K, Roussos A: H.pylori infection and endocrine disorder — Is there a link ? World Journal of Gastroenterology 2009 June;15(22):2701-2707
9. Ugwuja EI and Ugwu NC: Plasma lipid in Helicobacter pylori infected pregnant women. International Journal of Medicine and Medicinal Sciences 2009 May;1(5):224-226
10. Sung KC, Rhee EJ, Ryu SH: Prevalence of Helicobacter pylori infection and its association with cardiovascular risk factors in Korean adults. Int J Cardiol 2005 Jul;102(3):411-417
11. Chimienti G, Russo F, Lamanuzzi B.L, Nardulli M, Messa C, Di LeoA:Helicobacterpyloriisassociatedwithmodifiedlipidprofile. Clinical Biochemistry 2003 July; 36(5):359-365
12. Kinjo K, Sato H, Shiotani I: Prevalence of H.pylori infection and its link to coronary risk factors in Japanese patients with acute MI. Circulation Journal 2002 Sep;66(9):805-810
13. Kanbay M, Gurden G, Yucel M, Yilmaz U: Does eradication of Helicobacter pylori help normalise serum lipid and CRP levels. Digestive Disease and Sciences 2005 July;50(7):1228-1231
14. Parente F, Imbesi V, Cucino V: Helicobacter pylori Cag A seropositivity does not influence inflammatory parameters, lipid concentration and Haemostatic factors in healthy individuals. J Int Med 2000;247:213-217
15. Gallin JL: Chronic infections and Lipid profile. New England Journal of Medicine1969;1081-1086
16. Alvarez C, Ramos A: Lipids, Lipoprotein and Apolipoprotein in serum during infection. Clinical Chemistry 1986 Jan;32(1):142- 145