ISSN 2348-0319 International Journal of Innovative and Applied Research [2023]
(Volume 11, Issue 04)
16-25

Journal home page: http://www.journalijiar.com

INTERNATIONAL JOURNAL
OF INNOVATIVE AND APPLIED RESEARCH

RESEARCH ARTICLE

Article DOI: 10.58538/IJIAR/2026
DOI URL: *http://dx.doi.org/10.58538/IJIAR/2026*

MARKERS OF ATHEROGENICITY AND INFLAMMATION IN H.PYLORI INFECTED PEPTIC ULCER PATIENT

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Manuscript Info

Manuscript History
Received: 28 February 2023
Final Accepted: 13 April 2023
Published: April 2023

Keywords:
Peptic Ulcer, H. Pylori, Lipid Profile, MDA, C-Reactive Protein

Abstract

Peptic ulcer has been implicated in the pathogenesis of some non-gastric pathology, especially in cardiovascular disease. This study is aimed at determining the levels of markers of atherogenecity and inflammation in H. pylori infected peptic ulcer patients. A total of 60 subjects were recruited for the study of which 40 were subjects with peptic ulcer (20 are peptic ulcer patients with H.pylori and 20 are peptic ulcer patients without H. pylori) while 20 were healthy subjects. Five (5mls) of fresh venous blood was collected from all the participants by venepuncture using sterile needle and syringe. It was dispensed into clean plain sample container, and allowed to cloth and retract. The serum were separated into plain containers and stored at -20°c prior to use. All reagents were commercially purchased and the manufacturer's operational instructions were strictly followed. Lipid profile, malondialdehyde and C-reactive protein was determined using the following procedures. Lipid profile was determined using enzymatic method, malondialdehyde was determined using enzymatic method while C-reactive protein was determined using ELISA method. All values were expressed as mean ± standard deviation. The statistical analysis was carried out using student's t-test. Values with level of significance ($p<0.05$) was considered to be statistically significant. There was a significant increase ($p=0.002$, $p=0.005$, $p=0.000$, and $p=0.000$ respectively) in the mean value of total cholesterol (181.73± 16.50)mg/dl, triglyceride (114.04±19.07)mg/dl, MDA (3.63±0.58)mmol/L and C-reactive protein (4.32±0.97)ug/ml in Peptic Ulcer Patients without H.pylori when compared to controls (152.00±13.90)mg/dl, (82.76±16.50)mg/dl, (2.14±0.32)mg/dl and (1.78±0.37)ug/ml respectively. The mean value of HDL was significantly reduced ($p=0.000$) in Peptic Ulcer Patients without H.pylori (36.93±7.25)mg/dl when compared to control (55.46+ 4.94)mg/dl. There was a significant increase ($p=0.001$, $p=0.003$, $p=0.000$, and $p=0.000$ respectively) in the mean value of total cholesterol (241.14±44.90)mg/dl, triglyceride (136.36±30.65)mg/dl, MDA (4.71±0.54)mmol/L and C-reactive protein (6.09±1.03)ug/ml in Peptic Ulcer Patients with H.pylori when compared to controls (152.00±13.90)mg/dl, (82.76±16.50)mg/dl, (2.14±0.32)mg/dl and (1.78±0.37)ug/ml respectively. The mean values of HDL was significantly

reduced (p=0.000) in Peptic Ulcer Patients with H. pylori (31.32± 5.96)mg/dl when compared to control (55.46±4.94)mg/dl. There was a significant increase (p=0.007, p=0.003 and p=0.006 respectively) in the mean value of total cholesterol (241.14± 44.90)mg/dl, MDA (4.71±0.54)mmol/L and C-reactive protein (6.09±1.03)ug/ml in peptic ulcer patients with H.pylori when compared with Peptic Ulcer Patients without H. pylori (181.73±16.50)mg/dl, (3.63±0.58)mmol/L and (4.32±0.97)ug/ml respectively. There was no significant difference (p=0.128 and p=0.140 respectively) in the mean value of triglyceride (136.36±30.65)mg/dl and HDL (31.32±5.96)mg/dl in Peptic Ulcer Patients with H.pylori infectionwhen compared to Peptic Ulcer Patients with H.pylori infection (114.04±19.07)mg/dl and (36.93±7.25)mg/dl respectively Though there was some differences in the individual results. H. pylori infected peptic ulcer is associated with increased level of total cholesterol, triglyceride, malondialdehyde and C-reactive protein and a decreased level of HDL. From these results, there is a clear indication of inflammation and dyslipidaemia, which suggest acute association of H.pylori infection with cardiovascular diseases in peptic ulcer patients.

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Introduction:-

Peptic ulcer is a disease characterized by ulceration of the walls of the stomach and the duodenum (Luck, 2008). Peptic ulcers are pathological conditions affecting the gastrointestinal tract. Malignancies of the Gastro-intestinal tract are relatively resistant to radiation therapy and chemotherapy has also had modest benefit, whereas an effective therapy still remains elusive in the treatment of gastroduodenal ulceration(Asemota et al., 2023; Ikpenwa et al., 2022; Amadi et al., 2021; Anyiam et al., 2022). One of the common denominators for the genesis of these diseases is the involvement of free radicals (Fridovich, 2016).

Signs and symptoms of a peptic ulcer can include one or more of the following:Abdominal pain, classically epigastric strongly correlated to mealtimes. In case of duodenal ulcers the pain appears about three hours after taking a meal; Bloating and abdominal fullness; Waterbrash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus - although this is more associated with gastroesophageal reflux disease); Nausea and copious vomiting (Fink, 2011); Loss of appetite and weight loss; Hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting; Melena (tarry, foul-smelling feces due to presence of oxidized iron from hemoglobin); Rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis, extreme, stabbing pain, and requires immediate surgery (Snowden, 2008); A history of heartburn, gastroesophageal reflux disease (GERD) and use of certain forms of medication can raise the suspicion for peptic ulcer.

Complications of peptic ulcer include**;** Gastrointestinal bleeding is the most common complication. Sudden large bleeding can be life-threatening. It is associated with 5% to 10% death rate (Snowden, 2008); Perforation (a hole in the wall of the gastrointestinal tract) often leads to catastrophic consequences if left untreated. Erosion of the gastro-intestinal wall by the ulcer leads to spillage of the stomach or intestinal content into the abdominal cavity. Perforation at the anterior surface of the stomach leads to acute peritonitis, initially chemical and later bacterial peritonitis. The first sign is often sudden intense abdominal pain such as Valentino's syndrome. Posterior wall perforation leads to bleeding due to the involvement of gastroduodenal artery that lies posterior to the first part of the duodenum. The death rate in this case is 20% (Fink, 2011); Penetration is a form of perforation in which the hole leads to and the ulcer continues into adjacent organs such as the liver and pancreas; Gastric outlet obstruction is a narrowing of the pyloric canal by scarring and swelling of the gastric antrum and duodenum due to peptic ulcers. The person often presents with severe vomiting and Cancer which is included in the differential diagnosis (elucidated by biopsy), Helicobacter pylori as the etiological factor making it 3 to 6 times more likely to develop stomach cancer from the ulcer.

Causes of Peptic Ulcer includes; H. pylori, NSAIDs, stress, diet and others which includes gastric ischaemia, drugs, metabolic disturbances, cytomegalovirus (CMV), upper abdominal radiotherapy, Crohn's disease, and vasculitis (Fink, 2011). Gastrinomas (Zollinger–Ellison syndrome), rare gastrin-secreting tumors, also cause multiple and difficult-to-heal ulcers. Amongst the causes of peptic ulcer, the H. pylori is the most common cause.

The diagnosis is mainly established based on the characteristic symptoms. Stomach pain is usually the first signal of a peptic ulcer. In some cases, doctors may treat ulcers without diagnosing them with specific tests and observe whether the symptoms resolve, thus indicating that their primary diagnosis was accurate.More specifically, peptic ulcers erode the muscularis mucosae, at minimum reaching to the level of the submucosa (contrast with erosions, which do not involve the muscularis mucosae) (Graham et al., 2011).Confirmation of the diagnosis is made with the help of tests such as endoscopies or barium contrast x-rays. The tests are typically ordered if the symptoms do not resolve after a few weeks of treatment, or when they first appear in a person who is over age 45 or who has other symptoms such as weight loss, because stomach cancer can cause similar symptoms. Also, when severe ulcers resist treatment, particularly if a person has several ulcers or the ulcers are in unusual places, a doctor may suspect an underlying condition that causes the stomach to overproduce acid (Fink, 2011).An esophagogastroduodenoscopy (EGD), a form of endoscopy, also known as a gastroscopy, is carried out on people in whom a peptic ulcer is suspected. It is also the gold standard of diagnosis for peptic ulcer disease. By direct visual identification, the location and severity of an ulcer can be described (Aid et al., 2014). Moreover, if no ulcer is present, EGD can often provide an alternative diagnosis.One of the reasons that blood tests are not reliable for accurate peptic ulcer diagnosis on their own is their inability to differentiate between past exposure to the bacteria and current infection. Additionally, a false negative result is possible with a blood test if the person has recently been taking certain drugs, such as antibiotics or proton-pump inhibitors.The diagnosis of Helicobacter pylori can be made by: Urea breath test (noninvasive and does not require EGD), Direct culture from an EGD biopsy specimen; this is difficult to do, and can be expensive. Most labs are not set up to performH. pylori cultures, Direct detection of urease activity in a biopsy specimen by rapid urease test (Fink, 2011), Measurement of antibody levels in the blood (does not require EGD). It is still somewhat controversial whether a positive antibody without EGD is enough to warrant eradication therapy, Stool antigen test and Histological examination and staining of an EGD biopsy.

Once the diagnosis of H. pylori is confirmed, the first line treatment would be a triple regimen where pantoprazole and clarithromycin can be combined with either amoxicillinor metronidazole. This treatment regimen can be given for 7 until 14 days. However, its effectiveness of eradicating H. pylori has been reducing from 90% to 70%. However, the rate of eradication can be increased by doubling the dosage of pantoprazole or increase the duration of treatment to 14 days. Quadruple therapy (pantoprazole + clarithromycin + amoxicillin + metronidazole) can also be used. The quadruple therapy can achieve an eradication rate of 90%. If clarithromycin resistance rates is more than 15% in an area, the usage of clarithromycin should be abandoned (Akbar and El Tahawy, 2015). Instead bismuth containing quadruple therapy can be used (pantoprazole + bismuth citrate + tetracycline + metronidazole) for 14 days. The bismuth therapy can also achieve an eradication rate of 90% and can be used as second line therapy when the first line triple regimen therapy failed (Fink, 2011).

Helicobacter pylori is the most important cause of chronic active gastritis, gastric and duodenal ulcers and plays an important role in the development of gastric cancer and mucosa-associated lymphatic tissue (MALT) lymphomas (Kreiss et al., 2015).Various studies showed that the H. pylori presence in digestive system ulcers leads to changes in lipid profile included cholesterol, triglyceride and lipoproteins HDL-C and LDL-C (Iscan et al., 2008). As substances like Apo-A1 and Apo-B are the fundamental structures of plasma lipoproteins, there must be a relationship between changes of their levels in cardiac diseases and the increase of plasma lipids indices by H. pylori. An increase in Apo-B level will lead to an increase in the risk of cardiovascular disorders (Chimienti et al., 2013). Lipoprotein-A is present only in human and has many properties in common with low density lipoprotein. The mechanisms of metabolism and actions as well as atherogenic specifications of Lp (a) is not known clearly. Its serum levels will be increased by an increase in atherosclerosis risk and cardiovascular disorders (von Eckardstein et al., 2011).

Oxidative stress is an imbalance between the Reactive Oxygen Species (ROS) formation and the ability of the biological system to neutralize them or repair the resulting damage. Oxidative stress from oxidative metabolism causes base damage as well as strand breaks in DNA. The base damage is mostly indirect and caused by reactive oxygen species e.g. O_2^- (superoxide radical), OH (hydroxyl radical) and H_2O_2 (hydrogen peroxide) (Chandra et al., 2015). A free radical however is an atom, molecule or ion that has an unpaired valence electron (Hayyan et al.,

2016).Accumulation of MDA in H. pylori-infected gastric mucosa not only provides evidence of increased oxidative stress and lipid peroxidation, but may also have a carcinogenic role. MDA can react with DNA to form adducts and cross-links and has been shown to be mutagenic in bacterial and mammalian systems and carcinogenic to rats (Basu and Marnett, 2013). MDA induces a diverse spectrum of mutations, such as frameshift mutations and base pair substitutions in Escherichia coli. In humans, increased concentrations of lipid peroxidation products have been found in the serum of gastric cancer patients (Choi et al., 2009).

C-reactive protein (CRP) is an annular (ring-shaped), pentameric protein found in blood plasma, whose levels rise in response to inflammation (Logering et al., 2013). It is an acute-phase protein of hepatic origin that increases following interleukin-6 secretion by macrophages and T cells. CRP is synthesized by the liver in response to factors released by macrophages and fat cells (adipocytes) (Pepsy and Hirschfield, 2013). C-reactive protein (CRP) is the most commonly assessed marker of acute and chronic inflammation. The acute H. pylori infection induces mucosal infiltration dominated by neutrophil leucocytes. Within few weeks, the acute inflammation develops to chronic active inflammation dominated by neutrophils, macrophages (CD14), lymphocytes (CD4, CD8 and CD19) and plasma cells (Graham et al., 2011). The initiation of the inflammation may be caused by invasive H. pylori or water-soluble proteins passing the mucosal barrier (Enders et al., 2015). Several interleukins are involved in the inflammatory process in the gastric mucosa. Production of IL-8, a neutrophil chemotactic factor, by the gastric epithelial cells is stimulated by H. pylori.

Certain studies showed that H. pylori infection induces an increase in the concentrations of serum lipid parameters and which is in turn associated to an atherogenic lipidic profile (Hoffmeister et al., 2011). However, there is no general consensus since other studies did not confirm these results (Zhu et al., 2012). In response to such pathogens, the stomach induces oxidative stress, which releases some inflammatory markers that might affect lipid parameters level. In particular, the bacterium Helicobacter pylori play a major role in eliciting and confronting oxidative stress in the stomach. Studies by Graham et al., (2011) has reported that C-reactive protein are involved in the inflammatory process in the gastric mucosa, but the authenticity of the report have not been validated. There is paucity of information on the level of atherogenic index, oxidative stress and inflammatory markers in peptic ulcer patients, therefore this study is aimed at determining the levels of markers of atherogenic index, oxidative stress and inflammatory markers in peptic ulcer patient.

Materials and Methods:-

Subjects:

The study was carried out at the medical-out patients department of Federal Medical Center Owerri, Imo state. A cross-sectional study was conducted in the month of October 2019 and all eligible subjects who filled the questionnaire and gave a written informed consent for the study period were sampled. A total of 60 subjects was used for the study. The 60 subjects were divided into two groups. Group 1 consists of 40 subjects suffering from peptic ulcer, while group 2 consists of 20 apparently healthy subjects.

Selection Criteria

Inclusion criteria

1. Subjects between 18 years and above.
2. Subjects suffering from peptic ulcer at the federal medical centre Owerri.
3. Subjects whose informed consent was obtained.

Exclusion criteria

1. Subjects below 18 years of age.
2. Subjects whose informed consent could not be obtained because they were skeptical about the research.

Sample Collection and preparation

Five (5mls) of fresh venous blood was collected from all the participants by venepuncture using sterile needle and syringe. It was dispensed into clean plain sample container, and allowed to clot and retract. Care was taken to prevent the blood sample from haemolysing. The blood samples in the plain container tubes were centrifuged for 10 minutes at 3000rev/min. The serum were separated into plain containers and stored at -20°c prior to use.All samples were analysed within 4 days of sample collection.

Laboratory Procedures

All reagents were commercially purchased and the manufacturer's operational instructions were strictly followed.

Determination of Total Cholesterol (TC), Using Total Cholesterol Assay Kit (Catalogue Number: STA-384)

Principle

The cholesterol is determined after enzymatic hydrolysis and oxidation. The indication quinoneimine is formed from hydrogen peroxide and 4-amino antipyrine in the presence of phenol and peroxidase. The absorbance of the resultant coloured solution read at 540nm against reagent blank is directly proportional to the concentration of total cholesterol in the sample. The enzymatic colorimetric determination of total cholesterol is based on the following reaction:

Cholesterol ester + H_2O $\xrightarrow{\text{Cholesterol esterase}}$ Cholesterol + Fatty acids

Cholesterol ester + O_2 $\xrightarrow{\text{Cholesterol esterase}}$ Cholesten-3-one + H2O

$2H_2O_2$ +Phenol +4-Aminoantipyrine $\xrightarrow{\text{Peroxidase}}$ Red quinine + 4H2O

Calculation

Total Cholesterol concentration (mg/dl)

$$= \frac{\text{Absorbance of sample x Concentration of standard}}{\text{Absorbance of standard}}$$

Concentration of standard => 200mg/dl

Determination of Triglyceride, using Triglyceride Assay Kit (Catalogue no: ab65336) Abcam

Principle

It is based on the enzymatic hydrolysis of triglyceride to form glycerol and fatty acids. The glycerol is then phosphorylated with the help of the presence of ATP to form glycerol-3-phospphate + ADP (Adenosine diphosphate). The glycerol-3-phosphate then further undergoes oxidation reaction to form dihydroacetone phosphate and hydrogen peroxide with the help of the enzyme glycerol-3-phosphate oxidase. The hydrogen peroxide then react with 4-amino antipyrine and 4-chlorophenol to form quinonimine and $4H_2O$ with the help of the enzyme peroxidase. The enzymatic determination of triglyceride is based on the following reactions:

Triglyceride + H2O $\xrightarrow{\text{Lipoprotein lipase}}$ Glycerol + Fatty acids

Glycerol + ATP $\xrightarrow[Mg^{2+}]{\text{Glycerol kinase}}$ Glycerol-3-phosphate + ADP

Glycerol-3-phosphate + O_2 $\xrightarrow{\text{GPO}}$ Violet coloured complex

$2H_2O_2$ + 4-Aminoantipyrine + TOPS $\xrightarrow{\text{POD}}$ Violet coloured complex

Calculation

Triglyceride concentration (mg/dl) =

$$\frac{\text{Absorbance sample x Concentration of Standard}}{\text{Absorbance of standard}}$$

Concentration of standard =< 200mg/dl

Determination of high density lipoprotein cholesterol (HDL- C) Using HDL-C Assay kit (Catalogue no: MBS744428)

Principle

The chylomicrons, VLDL and LDL, of the plasma are precipated by phosphotungstatic acid and magnesium ions. After centrifugation, HDL_S, are in the supernatant. The HDL content of the supernatant is measured by an enzymatic method.

Calculations

Concentration of HDL cholesterol (mg/dl) =

$$\frac{\text{Absorbance of sample x Concentration of standard}}{\text{Absorbance of standard}}$$

Concentration of HDL Std =>100mg/dl

Evaluation of Malondialdehyde (By Albro Et Al., (1985).

Principle

Thoborbituric acid reacts with Malondialdehyde (MDA) an end product lipid peroxidation, under slight acidic condition to produce a red trimetrone complex which absorbs maximally at 532nun wave length with a spectrophotometer.

Equation of the reaction: Thiobarbituric acid + MDA acidic reddish trimethane complex

Determination of C-Reactive Protein Using ELISA Method (ABCAM ab99995)

Principle:

A known antibody is adsorbed on a solid phase, to which the test sample which may contain the antigen is added. During incubation, the antibody captures or binds the antigen to the solid phase. After washing enzyme labeled specific antibody is added at this stage the antigen molecule is sandwiched between two antibody molecule, one on the solid phase and the other on the enzyme label. On addition of the substrate, a colour change indicates that the enzyme labeled antibody is present on the solid surface.

Calculation:

Conc. of serum CRP= Absorbance of test X Concentration of Std
Absorbance of standard

The standard curve was constructed as follows: The absorbance for the standards (vertical axis) versus the standard concentrations (horizontal axis) was plotted on a linear graph paper.

Statistical Analysis

All values were expressed as mean ± standard deviation. The statistical analysis was carried out using student's t-test. Values with level of significance ($p<0.05$) was considered to be statistically significant.

Results:-

Table 1:- Mean Values of Total cholesterol, Triglyceride, HDL, MDA and C-reactive protein in Peptic Ulcer Patients without H.pylori infection (Test) Vs Apparently Healthy Subjects (Control).

Parameters	Peptic Ulcer Patients without H.pylori	Control	t-value	P-value
Total cholesterol (mg/dl)	181.73+ 16.50	152.00+ 13.90	3.37	0.002
Triglyceride (mg/dl)	114.04+ 19.07	82.76+ 16.50	3.40	0.005
HDL (mg/dl)	36.93+ 7.25	55.46+ 4.94	5.85	0.000
MDA (mmol/L)	3.63+ 0.58	2.14+ 0.32	6.20	0.000
C-reactive protein (ug/ml)	4.32+ 0.97	1.78+ 0.37	6.86	0.000

Key:
HDL: High Density Lipoprotein
MDA: Malondialdehyde
P<0.05: Significant
P>0.05: Not Significant

Table 1 showed that there was a significant increase (p=0.002, p=0.005, p=0.000, and p=0.000 respectively) in the mean value of total cholesterol (181.73± 16.50)mg/dl, triglyceride (114.04± 19.07)mg/dl, MDA (3.63±0.58)mmol/L and C-reactive protein (4.32±0.97)ug/ml in Peptic Ulcer Patients without H.pylori when compared to controls (152.00±13.90)mg/dl, (82.76±16.50)mg/dl, (2.14±0.32)mg/dl and (1.78±0.37)ug/ml respectively.
The mean value of HDL was significantly reduced (p=0.000) in Peptic Ulcer Patients without H.pylori (36.93±7.25)mg/dl when compared to control (55.46± 4.94)mg/dl.

Table 2:- Mean Values of Total cholesterol, Triglyceride, HDL, MDA and C-reactive protein in Peptic Ulcer Patients with H.pylori infection (Test) Vs Apparently Healthy Subjects (Control).

Parameters	Peptic Ulcer Patients with H.pylori	Control	t-value	P-value
Total cholesterol (mg/dl)	241.14+ 44.90	152.00+ 13.9	5.35	0.001
Triglyceride (mg/dl)	136.36+ 30.65	82.76+ 16.50	4.30	0.003
HDL (mg/dl)	31.32+ 5.96	55.46+ 4.94	8.59	0.000

MDA (mmol/L)	4.71+ 0.54	2.14+ 0.32	11.46	0.000
C-reactive protein (ug/ml)	6.09+ 1.03	1.78+ 0.37	11.11	0.000

Key:
HDL: High Density Lipoprotein
MDA: Malondialdehyde
P<0.05: Significant
P>0.05: Not Significant

Table 2 showed that there was a significant increase (p=0.001, p=0.003, p=0.000, and p=0.000 respectively) in the mean value of total cholesterol (241.14± 44.90)mg/dl, triglyceride (136.36±30.65)mg/dl, MDA (4.71±0.54)mmol/L and C-reactive protein (6.09±1.03)ug/ml in Peptic Ulcer Patients with H.pylori when compared to controls (152.00±13.90)mg/dl, (82.76±16.50)mg/dl, (2.14±0.32)mg/dl and (1.78±0.37)ug/ml respectively.

The mean value of HDL was significantly reduced (p=0.000) in Peptic Ulcer Patients with H.pylori (31.32±5.96)mg/dl when compared to control (55.46± 4.94)mg/dl.

Table 3:- Mean Values of Total cholesterol, Triglyceride, HDL, MDA and C-reactive protein in Peptic Ulcer Patients with H.pylori infection Vs Peptic Ulcer Patients without H.pylori infection.

Parameters	Peptic Ulcer Patients with H.pylori	Peptic Ulcer Patients without H.pylori	t-value	P-value
Total cholesterol (mg/dl)	241.14+ 44.90	181.73+ 16.50	3.28	0.007
Triglyceride (mg/dl)	136.36+ 30.65	114.04+ 19.07	1.64	0.128
HDL (mg/dl)	31.32+ 5.96	36.93+ 7.25	1.58	0.140
MDA (mmol/L)	4.71+ 0.54	3.63+ 0.58	3.62	0.003
C-reactive protein (ug/ml)	6.09+ 1.03	4.32+ 0.97	3.32	0.006

Key:
HDL: High Density Lipoprotein
MDA: Malondialdehyde
P<0.05: Significant
P>0.05: Not Significant
Table 3 showed that there was a significant increase (p=0.007, p=0.003 and p=0.006 respectively) in the mean value of total cholesterol (241.14± 44.90)mg/dl, MDA (4.71±0.54)mmol/L and C-reactive protein (6.09±1.03)ug/ml in Peptic Ulcer Patients with H.pylori when compared with Peptic Ulcer Patients without H. pylori (181.73±16.50)mg/dl, (3.63±0.58)mmol/L and (4.32±0.97)ug/ml respectively.
There was no significant difference (p=0.128 and p=0.140 respectively) in the mean value of triglyceride (136.36+ 30.65)mg/dl and HDL (31.32+ 5.96)mg/dl in Peptic Ulcer Patients with H.pylori infectionwhen compared to Peptic Ulcer Patients with H.pylori infection (114.04+19.07)mg/dl and (36.93+ 7.25)mg/dl respectively.

Discussion:-

Helicobacter pylori colonizes the stomach of at least half the world's population. It has been implicated in the pathogenesis of some gastric pathogenesis, especially in cardiovascular disease, but the mechanism is not yet understood.

The present study revealed that there was a significant increase (p<0.05) in the mean values of total cholesterol and triglyceride in peptic ulcer patients with and without H. pylori infection when compared to controls. Peptic ulcer causes the release of inflammatory cytokines which may have an essential role in the increase of total cholesterol and triglyceride. There is a general agreement that H. pylori infection itself modifies serum lipid profiles causingsystemic inflammatory response which induces changes in cholesterol (Ren et al., 2010). The study of Hoffmeistrer et al. (2011) was also showed that the cholesterol level was increased. Maisch, (2008) were in agreement with our findings.

In the present study, the mean value of HDL was significantly reduced (p<0.05) in peptic ulcer patients without H. pylori when compared to control. Systemic inflammation have been proven to alter the composition of HDL protein causing a decrease in the HDL levels (Rohrer et al., 2014). In addition, inflammation could transform HDL into a dysfunctional condition. These observations suggested that inflammatory cascades induced by H. pylori resulted in a

decrease in the HDL levels. Previous studies by Pilotto and Malfertheiner (2002), on patients with peptic ulcer showed that there is a significant decrease in HDL-C level.

The current study revealed that there was a significant increase ($p<0.05$) in the mean value MDA in peptic ulcer patients with and without H. pylori infection when compared to controls. H. pylori infection of the gastric mucosa stimulates influx of polymorphonuclear leukocytes, leading to the generation of reactive oxygen and nitrogen species. Cell membranes, which are rich in polyunsaturated fatty acids, are readily attacked by these compounds, producing fatty acid radicals and lipid hydroperoxides, which can decompose in complex ways, yielding more radical species and a wide range of compounds, notably malondialdehyde. Of these, MDA and 4-hydroxynonenal are the most common (Bartsch, 2009). MDA, which is also formed by the breakdown of prostaglandin endoperoxides, is a strongly genotoxic carbonyl compound that can react directly with DNA to produce a variety of adducts. This is consistent with the study carried out by Bartsch (2009).

The mean value of C-reactive protein was significantly increased ($p<0.05$) in peptic ulcer patients with and without H. pylori when compared to control. There are several possibilities for the mechanism underlying a causal role of H. pylori infection and increase level of C-reactive protein. First, H. pylori may have the direct effect on the structure and function of vascular endothelial cells. Extract of H. pylori has been reported to induce a disturbance of proliferation and apoptosis and to decrease viability of cultured vascular endothelial cells. The second possibility is the nutritional effect of H. pylori (Dixon et al., 2016). An infection from H. pylori may cause malabsorption of folate, vitamin B6, and vitamin B12. This nutritional defect could lead to failure of methylation by 5-methyl-tetrahydrofolic acid and subsequent hyperhomocysteinanemia, which is toxic to endothelial cells possibly triggers inflammatory processes and can lead to increase level of C-reactive protein.

The present study revealed that there was a significant increase ($p<0.05$) in the mean value of total cholesterol, MDA and C-reactive protein in peptic ulcer Patients with H.pylori when compared with peptic ulcer patients without H. pylori. This is a clear indication that the H. pylori infection is the cause of an increase in the level of total cholesterol, MDA and C-reactive protein. H. pylori has been reported to induce endothelial damages, disturbance of proliferation and release of inflammatory cytokines as confirmed with the increase in acute phase protein due to inflammation which causes an increase level of total cholesterol, MDA due to lipid peroxidation. This result is in agreement with the study conducted by Bartsch (2009).

There was no significant difference ($p>0.05$) in the mean values of triglyceride and HDL in peptic ulcer patients with H. pylori infectionwhen compared to peptic ulcer patients without H. pylori infection. Although there was individual differences in the level of triglyceride and in the HDL, which may also cause some systemic changes. This is in disagreement with the Study reported by Chimienti et al. (2013), they showed that peptic ulcer with and without H. pylori infection affects the serum lipid profile, causing increased level of triglyceride and decreased level of HDL in a way that can increase the risk of atherosclerosis.

Conclusion:-

H. pylori infected peptic ulcer is associated with increased level of total cholesterol, triglyceride, malondialdehyde and C-reactive protein and a decreased level of HDL. From these results, there is a clear indication of inflammation and dyslipidaemia, which suggest acute association of H.pyloriinfection with cardiovascular diseases in peptic ulcer patients.

References:-

1. Aid, I., Bentall, H. H., Mehigan, J. A., and Roberts, F. (2014). British Medical Journal, 2: 315-320.
2. Akbar, D.H. and El Tahawy, A.T. (2015). Helicobacter pylori infection at a university hospital in Saudi Arabia, prevalence, comparison of diagnostic modalities and endoscopic findings. Indian Journal of Pathology and Microbiology. 48 (2) 181-185.
3. Amadi, N. M., Achukwu, P. U., Onwukwe, S. O., Obeagu, E. I., Anoh, N. V., & Okpokwu, V. I. (2021). Anti Ulceration Efficacy of Boiled Aqueous Leaf Extract of Morinda lucida on Ethanol Induced Gastric Ulceration Rats. Journal of Pharmaceutical Research International, 33(47A), 164-175.
4. Anyiam, A. F., Obeagu, E. I., Obi, E., Omosigho, P. O., Irondi, E. A., Arinze-Anyiam, O. C., & Asiyah, M. K. (2022). ABO blood groups and gestational diabetes among pregnant women attending University of Ilorin Teaching Hospital, Kwara State, Nigeria. Int J Res Rep Hematol, 5, 113-21.

5. Asemota, E. A., Njar, V. E., Aguanah, I. T., & Obeagu, E. I. (2023). Distribution of ABO, Rhesus Blood Group and Helicobacter Pylori Infection among Secondary School Students in Calabar South Local Government, Cross River State, Nigeria. Madonna University journal of Medicine and Health Sciences ISSN: 2814-3035, 3(1), 32-45.
6. Bartsch, H. (2009). Exocyclic adducts as new risk markers for DNA damage in man. In: B. Singer and H. Bartsch (eds.), Exocyclic DNA Adducts in Mutagenesis and Carcinogenesis, Lyon. IARC Scientific Publications.150: –16.
7. Basu, A. K., and Marnett, L. J. (2013). Unequivocal demonstration that malondialdehyde is a mutagen. Carcinogenesis (London). 4: 331–333.
8. Chandra, K., Syed, S.A., Abid, M., Sweety, R. and Najam, A.K. (2015). Protection against fca induced oxidative stress induced DNA damage as a model of arthritis and in vitro anti-arthritic potential of costusspeciosus rhizome extract. International Journal of Pharmacognosy and Phytochemical Research 7(2): 383-389.
9. Chimienti, G., Russo, F., Lamanuzzi, B.L., Nardulli, M., Messa, C. and DiLeo, A. (2013). Helicobacter pylori is associated with modified lipid profile: impact on Lipoprotein (a). Clinical Biochemistry. 36: 359-365.
10. Choi YW, Park SA, Lee HW, Lee NG. Alteration of growth-phasedependent protein regulation by a Fur mutation in Helicobacter pylori. FEMS Microbiol Lett 2009; 294: 102–110.
11. Choi, M. A., Kim, B. S., and Yu, R. (2009). Serum antioxidant vitamin levels and lipid peroxidation in gastric carcinoma patients. Cancer Journal. 136: 89–93.
12. Dixon, M. F., Genta, R. M., Yardley, J. H. and Correa, P. (2016). and the participants of the International Workshop on the Histopathology of Gastritis. Classification and grading of gastritis. The updated Sydney system. America Journal of Surgical Pathology. 20: 1161–1181.
13. Enders, G., Brooks, W., von Jan, N., Lehn, N., Beyerdo¨rffer, E. and Hatz, R. (2015) Expression of adhesion molecules on human granulocytes after stimulation with Helicobacter pylori membrane proteins: comparison with membrane proteins from other bacteria. Infectious Immunonology. 63: 2473–2477.
14. Fink, G. (2011). Stress controversies: post-traumatic stress disorder, hippocampal volume, gastroduodenal ulceration. Journal of Neuroendocrinology. 23 (2): 107–17.
15. Fridovich, I. (2016). Biological effects of superoxide radical. ArchiveBiochemistry and Biophysics. 247: 1–11.
16. Graham, D.Y., Malaty, H.M., Evans Jr., D.G., Klein, P.D. and Adam, E. (2011) Epidemiology of Helicobacter pylori in an asymptomatic population in the United States. Effect of age, race, and socioeconomic status. Gastroenterology. 100: 1495–1501.
17. Hayyan, M., Hashim, M.A. and AlNashef, I.M. (2016). Superoxide ion. Generation and chemical implications. Chemical Reviews 116(5): 3029-3085.
18. Hoffmeister, A., Rothenbacher, D., Bode, G., Persson, K. and März, W. (2011). Current infection with Helicobacter pylori, but not seropositivity to Chlamydia pneumoniae or cytomegalovirus, is associated with an atherogenic, modified lipid profile. Arteriosclerotic Thrombotic Vascular Biology. 21: 427-432.
19. Ikpenwa, J. N., Aneke, C. C., Chukwueze, C. M., Chukwu, L. C., & Obeagu, E. I. (2022). Evaluation of Knowledge, Perception and Prevalence of Helicobacter pylori Infection among Students of Enugu State University of Science and Technology: A Multi-Disciplinary Approach. Sch J App Med Sci, 10, 1620-1627.
20. Iscan, A., Yiitolu, R., Ona, A., Vurgun, N., Ari, Z. and Ertan, P. (2008). Should children with infection be tested for lipid, lipoprotein and apolipoprotein. Japan Journal of Paediatrics. 40:47-51.
21. Kreiss, C., Blum, A.L. and Malfertheiner, P. (2015) Peptic ulcer pathogenesis. Current Opinion on Gastroenterology. 11: 25–31.
22. Logering, B.A., Gerke, P., Kreft, B., Wolber, E.M., Klinger, M.H., Fricke. (2013). The kidney as a second site of human C-reactive protein formation in vivo. European Journal of Immunology. 33:152-161.
23. Luck, G.D. (2008). Tumors of stomach. In: Feldman M, Sliesenger MH, Scharschmidt BF, editors. Gastrointestinal and liver diseases, 6th ed, vol. 1, Philadelphia, W. B. Saunders company. pp. 733–757.
24. Maisch, B. (2008). Coronary heart disease as inflammatory disease of the vascular bed? Etiology, sequela or misconception. Journal of Metabolic Medicine. 23:147-152.
25. Pepys, M.G. and Hirschfield, G.M. (2013). C-reactive protein: a critical update. Journal Clinical Investment. 111(12): 12.
26. Pilotto, A. and Malfertheiner, P. (2002). An approach to Helicobacter pylori infection in the elderly. Aliment.Pharmacological Thesis. 16: 683-691.
27. Rohrer, L., Hersberger, M. and von Eckardstein, A. (2014). High density lipoproteins in the intersection of diabetes mellitus, inflammation and cardiovascular disease. Current Opinion on Lipidology. 15(3):269–278.

28. Snowden, F.M. (2008). Emerging and reemerging diseases: a historical perspective. Immunological Reviews.225 (1): 9–26.
29. Von Eckardstein, A., Schulte, H., Cullen, P. and Assmann, G. (2001). Lipoprotein (a) further increases the risk of coronary events in men with high global cardiovascular risk. Journal of America College of Cardiology. 37: 434-439.
30. Zhu, J., Quyyumi, A.A., Muhlestein, J.B. and Nieto, F.J. (2012). Lack of association of Helicobacter pylori infection with coronary artery disease and frequency of acute myocardial infarction or death. America Journal of Cardiology. 89(2):155-158.