"COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"

BY

DR DEEPTHI PRADEEP PATIL KULKARNI

DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA.

In partial fulfilment of the requirements for the degree of

M.S. IN GENERAL SURGERY

UNDER THE GUIDANCE OF

DR. P. N. SREERAMULU

PROFESSOR

DEPARTMENT OF GENERAL SURGERY

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR – 563101

APRIL/MAY 2022

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR-563101

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled **"COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"** is a bona fide research work carried out by me underthe guidance of **Dr.P.N SREERAMULU, PROFESSOR** Department of General Surgery, Sri Devaraj Urs Medical College & Research center, Tamaka, Kolar.

Date:

Place: Kolar **Signature of the candidate**

Dr. DEEPTHI PRADEEP PATIL KULKARNI

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA,

KOLAR-563101

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"** is a bonafide research work done by **Dr. DEEPTHI PRADEEP PATIL KULKARNI** under my guidance and supervision in partial fulfillment of the requirement for the degree of M.S.in GENERAL SURGERY.

Date:

Place: Kolar

Signature of the Guide

Dr. P.N SREERAMULU

Professor

Department of General surgery,

Sri Devaraj Urs Medical College,

& Research Center, Tamaka, Kolar.

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR-563101

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"** is a bona fide research work carried out by **Dr. DEEPTHI PRADEEP PATIL KULKARNI** under the guidance of **Dr. P.N SREERAMULU,** Professor**,** Department of General Surgery.

Dr.K.KRISHNA PRASAD
Professor and Head
Department of General Surgery,
Sri Devaraj Urs Medical College
& Research Center,
Tamaka, Kolar.

Date:

Place: Kolar

Dr. P.N SREERAMULU
Principal and Dean
Sri Devaraj Urs Medical college
& Research Center, Tamaka
Kolar

Date:

Place: Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the ethics committee of Sri Devaraj Urs Medical College & Research Center, Tamaka, Kolar has unanimously approved **Dr. DEEPTHI PRADEEP PATIL KULKARNI** Post-Graduate student in the subject of **GENERAL SURGERY** at Sri Devaraj Urs Medical College, Kolar to take up the dissertation work entitled **"COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"** to be submitted to **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA.**

Date:

Signature of Member Secretary

Sri Devaraj Urs Medical

College & Research center, Tamaka,

Kolar–563101

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTER, TAMAKA, KOLAR, KARNATAKA

COPY RIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the Sri Devaraj Urs Academy of Higher Education and Research Center, Kolar, Karnataka shall have the rights to preserve, use and disseminate this dissertation/thesis in print or electronic format for academic /research purpose.

Date:

Place: Kolar

Signature of the candidate

Dr. DEEPTHI PRADEEP PATIL KULKARNI

Post graduate student

Department of General Surgery

Sri Devaraj Urs Medical College

Kolar.

Drillbit Softtech India Pvt. Ltd

Certificate of Plagiarism Check for Dissertation

Author Name	Dr. DEEPTHI PRADEEP PATIL KULKARNI
Course of Study	MS- GENERAL SURGERY
Name of Guide	DR. P. N. SREERAMULU
Department	GENERAL SURGERY
Acceptable Maximum Limit	10%
Submitted By	librarian@sduu.ac.in
Paper Title	COMPARATIVE STUDY OF ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE
Similarity	6%
Paper ID	436785
Submission Date	2021-12-28 15:15:59

Signature of Student

Signature of Major Advisor
Dr. P.N. Sreeramulu
Professor of Surgery
KMC No: 35832
Date:.....Time.....

Head of the Department
Prof. & HOD of Surgery
Sri Devaraj Urs Medical College,
Tamaka, KOLAR-563101.

University Librarian
28/12/21

Co-Ordinator, UG & PG Program
Co-Ordinator,
Faculty of Medicine,
Sri Devaraj Urs Academy
of Higher Education & Research,
Tamaka, Kolar- 563103

* This report has been generated by DrillBit Anti-Plagiarism Software

ACKNOWLEDGEMENT

Lucky are those who get to meet great people, luckier are the few who are privileged to work under them and imbibe priceless insight of life.

It is my pleasant privilege and honour to express my most humble and deep sense of gratitude to **Dr. P. N SREERAMULU** Professor, Department of General Surgery, Sri Devraj Urs Medical College And Research Centre, Kolar for his masterly guidance, invaluable advice, painstaking supervision, wholehearted encouragement, inspiration from the very inception to the completion of this study.

I am indebted to **Dr. K KRISHNA PRASAD.,** Professor and Head, Department of General Surgery, Sri Devraj Urs Medical College and Research Centre, Kolar, a teacher of inspiring genius and unstinting generosity for his overall guidance towards the progress of this dissertation.

I am grateful to **Dr. SRINIVASAN. D**, **DR. MOHAN KUMAR K, DR. PRAKASH DAVE, DR SHASHIREKHA. C**, Department of General Surgery, Sri Devraj Urs Medical College And Research Centre, Kolar, for their interest, involvement, critical evaluation and valuable suggestions rendered.

On the personal front, My special thank to my parents, Mr. **PRADEEP .G PATIL KULKARNI AND Mrs. SEEMA PATIL KULKARNI,** my sister **MEDHA P PATIL KULKARNI** for their unseen sacrifices, support and encouragement in every moment of my study. I

I am indebted to my beloved husband **Dr. GANESH ANANT RAO MUTALIK**, a compassionate, an ORTHOPEDIC SURGEON of consummate skills, a teacher of an

incomparable power of observation for his critical evaluation for perfection, valuable instruction and help throughout my study.

I also thank my in laws for their constant support and love, **Mr ANANT RAO MUTALIK, Mrs. PRERANA MUTALIK**.

I express my sincere thanks to **DR. VARSHA.A, DR. RAADHIKA RAJA** and **DR. BHAVANA CHOWDARY** for their support and encouragement.

It's my pleasure to thank **DR. ROHIT**, for his emotional anchor and upholding attitude throughout my post-graduation.

My sincere thanks to faculty and staff of Department of General Surgery, Department of General Surgery, Sri Devraj Urs Medical College and Research Centre, Kolar.

My heartfelt gratitude to all my colleagues who wholeheartedly supported me throughout my post graduation.

I would like to express my gratitude to the ALMIGHTY for his blessings.

Last but never the least my heartfelt gratitude to all those patients who have cooperated wholeheartedly in this study.

Signature of candidate

DR. DEEPTHI PRADEEP PATIL KULKARNI

LIST OF ABBREVIATIONS

HP	Helicobater pylori
APD	Acid peptic disease
Ca stomach	Carcinoma stomach
Cag A	Cytolytic Toxin A
DU	Duodenal Ulcer
ED	Erosive Duodenitis
ELISA	Enzyme Linked Immunosorbent Assay
GU	Gastric Ulcer
GERD	Gastroesophageal Reflux Disease
EG	Erosive Gastritis
H_2 blockers	Histamine 2 receptor blockers
NUD	Non-ulcer Dyspepsia
PPI	Proton Pump Inhibitors
RUT	Rapid Urease Test
Vac A toxin	Vacuolating cytotoxin A

TABLE OF CONTENTS

LIST OF TABLE

LIST OF FIGURES

ABSTRACT:

BACKGROUND:

APD is world wide health issue for the surgeons, mainly due to risk and associated complications like GU, DU, GIT perforation etc. this aims at early detection of disease which is caused by HP and intervention prevents the further complications.

METHODS:

This study is conducted in the endoscopic unit of department of General Surgery in R.L.Jalappa hospital and research centre in patients with APD in the year 2019-2021. All the patients suitable for the study in regards to the inclusion and exclusion crieteria are subjected to both the study until the samle size is achieved, with the prior agreement of the institutional ethical committee.

RESULTS:

All the participants are tested with RUT and ELISA and 87.60% had RUT positive and 86.78% had ELISA positive infection.RUT had sensitivity of 87.62% in predicting ELISA, specificity was 12.50%, with a total diagnostic accuracy of 77.69%. We treated 51.24% with the CMO kit and 48.76% with HP kit. On three-month follow up, 37.2% had recurrence of the disease with 33.87% in patients who are treated with CMO kit, and 40.68% among those treated with HP kit (p value 0.439).

Based on Chi square test /Fisher's Exact test our study concluded that RUT to have good accuracy for predicting HP infections and after three month follow up CMO kit treatment was found to have less recurrence rate.

Key words: Helicobacter pylori, acid peptic disease, rapid urease test, ELISA.

INTRODUCTION:

HP is highly prevalent in human population. It colonizes in the gastric epithelium in atleast ½ the world population.[1]In the developed countries, prevalence progressively ascends with age though the infection is acquired in the childhood.[2] Upto 93% and 87% of the duodenal ulcer and gastric ulcer are infected by HP respectively.

HP is a spiral, micro- aerophilic bacterium which on gram staining appears red/violet. It which was first discovered by Robin Warren and Barry Marshall in 1982 as the cause of gastritis and GU[2], a remarkable discovery in the olden days that revolutionized gastro-enetrology. Warren and Marshall, won Nobel prize for the great demonstration of HP infection. Prior to this discovery the stomach was assumed to be a sterile surface. "HP, formerly known as Campylobacter-pyloridis then Campylo-bacter-pylori''. Its exact mode of transmission is uncertain. HP was isolated from the human stomach and thus the mechanism by which it colonizes the stomach gastric epithelium demonstrated by few theories. HP is known to cause of APD, which forms as DU and GU. Also HP is regnised as class 1 carcinogen, as it leads to development of gastric adenocarcinoma, one of the world's morbid and mortality associated cancers[3].

Earlier HP was assumed to be caused due to psychological stress, irregular food habits, life style etc. but now its is well established fact that acid peptic disease is caused due to HP. Above mentioned factors acts as aggrevating factors.

APD is a cluster of gastrointestinal symptoms including pain abdomen, retrsosternal discomfort ,vomiting, nausea etc.. APD is multifactorial, long standing acid hyper section

is no longer considered as sole contributor. Most of the GU are due to defective mucosal protection or any factors that impair the intergrity of the gastric mucosa. HP; along with the risk factors smoking, alcohol consumption, prolonged non-steroidal anti inflammatory drugs/ steroid consumption, unhealthy dietary habbits, drug abuse also contribute to APD. Though the incidence of APD is in the reducing trend but the acute complications (perforation, obstruction, bleeding..)are still high. Calculation wise, HP incidence differs from one geographical location to another and may differ between different quality of life, ethnicity, social, etc of country[3].

There are several methods to detect the HP infection, both invasive and non-invassive, culture, histological staining, urease test, serological analysis. Early detection and eradication of HP leads to reduce in the incidence of complications of APD[4].

This study aimed at to detect and conclude the most sensitive and specific test among RUT in endoscopic sample and ELISA test for diagnosis of HP infection in APD. This study is conducted in the endoscopic unit, department of general surgery , R.L Jalappa hospital and research centre, Kolar.

This study will be conducted to compare, the Endoscopic Rapid Urease Test and Serology in the local population of Kolar to select the most sensitive, specific, rapid and reliable for the diagnosis of HP.

AIMS & OBJECTIVE

AIM:

TO COMPARE ENDOSCOPIC RAPID UREASE TEST WITH SEROLOGY OF HELICOBACTOR PYLORI INFECTION IN ACID PEPTIC DISEASE.

PRIMARY OBJECTIVES:

1. To proportionate the finding of Endoscopic Rapid urease test
2. To proportionate serological test to estimate the IgG levels
3. To compare the outcome to above test to determine the sensitivity and specificity.

SECONDARY OBJECTIVE:

1. To compare standard HP kit (amoxycillin 750mg BD, Tinidazole 500mg BD, Omeprazole 20mg BD)with clarithromycin 250mg BD, metronidazole 400mg TID, Omeprazole 20mg BD treatment

REVIEW OF LITERATURE:

In 19th century only the HP was prevent in the European countries.

The time between 1800 and 1950, nearly 150year, there was major changes in every aspect of HP infection and any changes in the clinical manifestations of HP.

Palmer sir identified that the microbe seen in gastric biopsies and it was entered GIT by oral route, after the publication in 1954.

On later days of In 1955, Kornberg and Davies discovered urease enzyme in stomach which was bacterial in origin.

Mr. Moynihan published his work on "PEPTIC ULCER" in 1910.

Leeberg and Lefevre also suggested that urease may be bacterial in origin in 1959, however none could reduce the connection between spiral microbe and enzyme urease in the stomach correlation until 1986.[6]

The introduction of fibreoptic gastroscopy during 1970's lead to the discovery of Helicobacter (formerly Campylobacter) pylori. For the first time it was fisible to see the mucosa of the stomach and duodenum and take guided biopsy specimens of the gastric antrum.

The role of gastric bacteria in the pathophysiology of APD disease was again studied in 1970's.

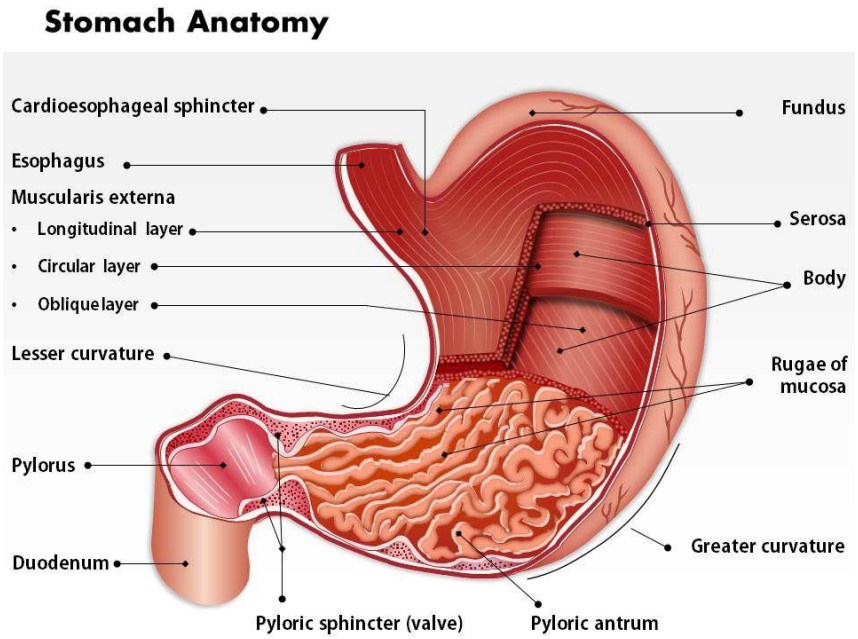
Mr.Steer and Mr.Collin-Jones were close in deducing the correlation of HP and APD from the endoscopic biopsy specimen but due to human error and faulty techniques, sterility of scope was not possible. It lead to growth of Pseudomonas aeruginosa[6] during 1975.

Finally in 1982, scientist from Australia Mr.Robin Warren and Mr.Barry Marshall swallowed the HP bacteria and got APD hence proved the correlation and also established it firmly. They own Nobel prize for the great invention in 2005.

ANATOMY OF STOMACH:

The stomach is the dialated part of alimentary canal wit the capacity of 1500ml on an average. The stomach is relatively fixed at both ends but is very mobile in between. It tends to be high and transversely arranged in the short, obese person and elongated vertically in tall.it has four parts, fundus , body, pyloric antrum, pylorus with two orifice, cardiac orifice; between the esophagus and stomach which is a physiological structure, whose difuctioning leads to GERD and pyloric sphincter formed by the thickening of circular muscle in between stomach and duodenum; which checks the bile reflux and helps in maintains of gastric acidity p^H.

Figure no.1:

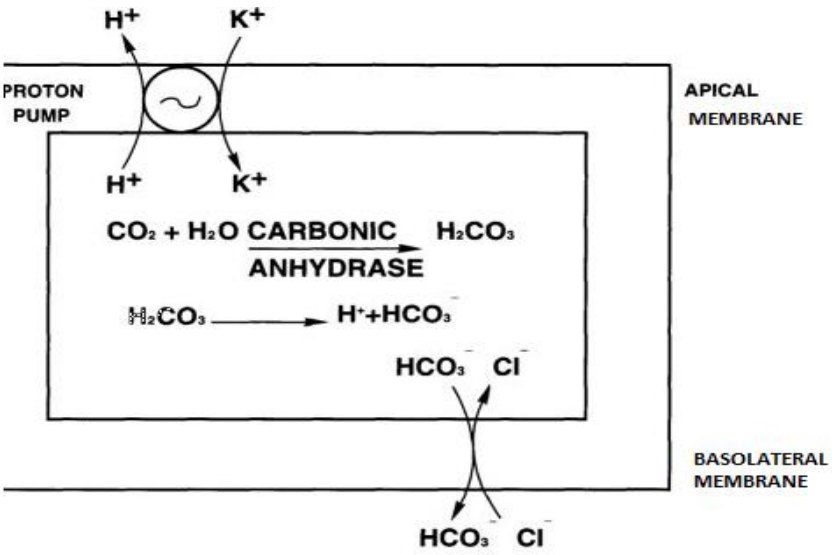


The stomach epithelium made up of gastric pits each composed of 4-5 gastric glands. The structure of the glands varies with different gastric parts. The cardiac orifice contains less than 5% of the total number of gastric glands; which includes mucous secreting cells and few parietal cells. The cardia and the fundus include acid secreting parietal cells and chief cells[1], whose function is to store and secret pepsinogen type A and C. In the pyloric region chief cells secrete pepsiongen C into the gastric lumen.

ACID SECRESTION IN STOMACH:

Gastric parietal cells in the mucosa secrete gastric hydro-chloric-acid into the stomach lumen. The acid secretion is stimulated mainly by acetylcholine from the postganglionic enteric neurons, gastrin from antral G-cells, histamine from enterochromaffin-like cells, and together with sensory induction by thought of food, sight, smell, taste, and swallowing of food. The inhibitor of the acid secretion is somatostatin secreted from D-cells in the corpus and pyloric part of gastric mucosa.

Figure no 2: Formation of Hcl in the parietal cell.



Gastric acid facilitates digestion of protein and absorption of nutrients such as iron, calcium, folic acid with vitamin B_{12}. Gastric acid also further inihibit microbial proliferation and enteric infection. Pepsin is activated by hydro-chlororic-acid and it metabolizes proteins into peptides. Pepsinogens are proenzymes of pepsin synthesized in chief cells and mucous neck cells. Pepsinogen in adults is detectable in two immunologic subtypes: pepsinogen A (PGI) and pepsinogen C (PGII). Whereas PGI is only synthesized in the oxyntic mucosa of the corpus, PGII is in most parts of the stomach and part of the duodenum too. When corpus atrophy develops, it leads to loss of chief cells and serum PGI can be observed.

Blood supply to the stomach by right gastric artery, short gastric artery with right and left gastric epiploic artery, venous drainage by right and left gastric veins and right and left epiploic veins. Lymphatic drainage is complicated, all the lymph from stomach eventually drain to celiac LN(lymphnode) situated in thse root of celiac truck.

HELICOBACTER PYLORI(HP):

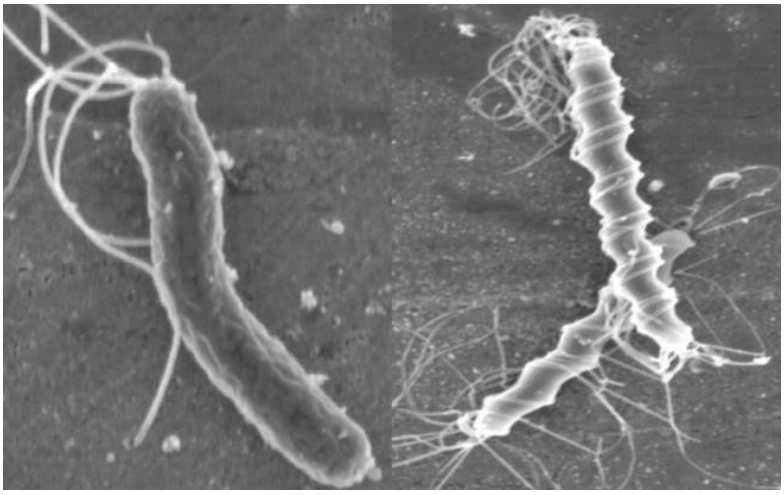
In the year 2005 Australian scientists Mr. Barry J. Mr.Marshall and Mr.J. Robin Warren, "for their discovery of the bacterium *Helicobacter pylori* (*HP*) and its role in gastritis and APD"[2].

HP belongs to 16s ribosomal RNA super family. BERGEY suggested that, HP belongs to group 2 of gram negative oraganism with the chacters:

1. Microaerophillic
2. Motile due to multiflagella
3. Helical
4. Gram negative
5. Catalase positive
6. Oxidase positive

7. Urease rapidly hydrolysing.

Figure no.3: Electronic microsope image of helicobacter pylori.



UNDERSTANDING THE PATHOPHYSIOLOGY OF HP INFECTION:

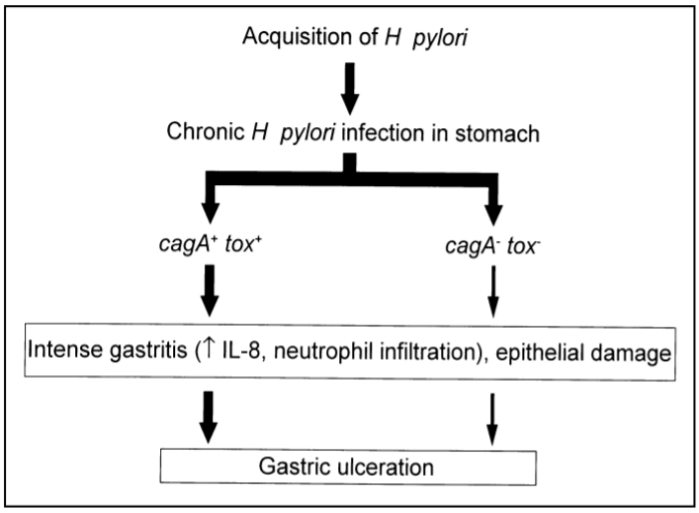
HP transmits the human body by oral route, clusters in the gastric epithelium and induces gastric inflammation. HP activated the platelet activation factor and other inflammatory mediators which not only cause inflammation but also further lead to ulceration. It stimulates the parietal cell gastric acid secretion and thus ultimately leading to APD.[9]

Now to know about the HP survival in the strong acid medium of stomach, HP produce large amount of basic enzyme urease. Microscopically the compound is metal containing enzyme. It is a hexameric molecule with two subunits of ureA and ureB. Urease enzyme producing gene is nine in number which code for both A and B proteins. Ureaes thus produced breaks the NH_4 which reacts with the hydro-chloric-acid and acts as a buffering agent . It creates a high Ph medium around the bacteria for its survival. The enzyme is also direct toxic to the gastric epithelial cells.[9,21,24] It is also

observed from recent studies that at a pH<2.5 and addition of pepsin increases the susceptibility of the bacteria.[60]

Now that the buffer environment is achieved for the bacterial survival , it seek for a host cell to reside. It has to break the phospholipid tough layer of epithelial cell , for that it produces phospholipase A and C2.there are many substances released from the ongoing inflammation , amongst them is reactive oxygen species, they direct the disrupt the membrane and leak of the cellular components.[9]

Thus establishing its residence in the gastric mucosal cell multiplies exponentially. It also suppress the gastric secreation by destroying the cells directsly and also indirectly inhibiting gastrin and hormone somatostatin which are suppressed by toxins and inflammatory mediators.[9]



Further the HP studies evoked the discovery of HP subtypes based on the virulence and also on the virulence of the HP. They are cag A, vac A. Basically the was cag A functioned by in vitro production of a vacuolating cytotoxin[42]. approximately 50% of HP strains produce this toxin, the cytotoxin induces cytoplasmic vacuolation in nearly all epithelial cell, spillage of the cellular content and cell death. Many studies have found

that infection with strains expressing vacuolating cytotoxin activity is more common among patients with APD patients than among HP-infected patients with superficial gastritis alone.The vacA genes present in both cytotoxin-producing and non-cytotoxin-producing strains represent multiple families of alleles that are significantly different from each other[51]. The regions of allelic diversity within vacA are localized to the signal sequence and the mid-region.

CagA has multiple effects on epithelial cells. These broadly include stimulating cell proliferation through mitotic signaling pathways such as the PI3 kinase–AKT28, 29, SHP2, GRB2 and MEK–ERK,30-32 and ß-catenin–WNT pathways. 33-35 CagA also reduces epithelial cell apoptosis by interfering with tumor suppressors such as p5336, 37 and RUNX338. CagA alters epithelial cell polarity through direct interactions with the polarity protein MAP/microtubule affinity-regulating kinase 2 (MARK2 or PAR1b)s and disrupts assembly and signaling through the cell junctions. These direct effects of CagA on epithelial cells could promote cancer development, because transgenic mice and zebrafish engineered to express CagA develop carcinomas when in absence of inflammation35, 43. In addition to its direct effects on epithelial cells, CagA and the T4SS activate inflammatory, NF-kB-dependent signaling22, 44-46 that leads to recruitment of inflammatory cells, reactive oxygen species-induced damage,47-49 and wound healing responses, which are all oncogenic. These findings and the epidemiological data linking.

CagA to gastric cancer risk, have led to the definition of CagA as a bacterial oncoprotein43. CagA's effects on epithelial cells are reversible and do not become permanent unless the target cells acquire mutations. CagA therefore induces cellular

transformation only in special circumstances, by inducing accumulation of multiple genetic variants over time. One particularly intriguing emerging concept is that a combination of CagA's signaling functions promotes cell de-differentiation or reprogramming of epithelial cells into more immature, stem-like cells that could be more prone to transformation.

Over the years, our understanding of CagA's function has evolved from its discovery as a bacterial antigenic protein epidemiologically associated with disease to a sophisticated signaling molecule that controls fundamental aspects of epithelial biology. In recent years, several groups have begun to investigate the potential pathogenicity of CagA, along with the cellular context in which CagA exerts its effects in vivo.

Vac A also has the potency to cause vaculation by relase of toxins.

Several bacterial adhesins have been epidemiologically implicated in disease and affect CagA delivery. The T4SS, per se, has biologic activities independent of CagA. Several component of the TFSS needle, such as CagL, CagY and CagI, for example, bind ß1 integrins to facilitate CagA delivery to epithelial cells. Since integrins are baso-lateral protein complexes, inaccessible at the lumenal surface of the epithelium, it not well understood where and when CagA is delivered. The bacterial protease HtrA might be able to disrupt the epithelial junctions to allow the bacteria to reach integrins.

CagA's damages the epithelial cells reversibly and do not become irreversible/permanent till the target cells acquire mutations. Therefore CagA induces cellular transformation only in certain circumstances, by inducing accumulation of multiple genetic variants over time. One particularly interesting advancement concept is that a combination of CagA's

stimulating the functions on cell differentiation or reprogramming of epithelial cells into more immature, that is dysplastic changes of stem cells that could be more prone to transformation and mutation into malignancy.

Over a period, our knowledge about the CagA's function has evolved from its identification of the bacterial antigenic protein incidence , prevalence associated with disease to a newly advanced signaling molecule that controls fundamental aspects of epithelial molecular biology. Recently, several studies have initiated to investigate the potential virulance of CagA, along with the cellular metabolism in which CagA exerts its effects in vivo. CagA delivery to the host cell requires ten close contact with the T4SS and the host- epithelial cell membrane. The mechanisms of this reaction are being considered, but results have revieled the concept that bacterial adhesion to epithelial cells is a multi-step complex steps.

Many bacterial adhesions molecules have been epidemiologically identified in disease and affect CagA delivery[51]. The T4SS, per se, shows the biologic activities independent of CagA. Many component of the TFSS needle, such as CagL, CagY and CagI, for e.g, bind ß1 integrins to stimulate CagA delivery to gastric mucous cells[53]. Thus integrins are baso-lateral protein complexes, not accessible at the lumenal surface of the gastric mucosa, it not well clear where and when CagA is delivered. The bacterial protease HtrA might be able to disrupt the epithelial junctions to allow the bacteria to attach integrins[61].

Helicobacter and gastric carcinoma :

Several potential study have been developed and are still developing to investigate correlation of HP infection and its inflammatory response contribute to the uncontrolled proliferation and growth of long-lived cells and eventually carcinoma. These include

infection-induced poor-differentiation of terminally maturing epithelial cells into long lived, replicating cells; recruitment of mesenchymal stem cells to gastric glands during tissue injury. The repair and subsequent differentiation or mutation of these immature stem cells. The direct bacterial effects or inflammatory changes in the resident gastric progenitor and gastric mucosal precursor cells.

Since HP reside in the superficial mucus layer overlying the stomach lumen, and attachment to mucus pit cells. It is fissible that these poorly differentiated cells are the targets of oncogenic transformation. This would infere that gastric mucosal cells that are poorly-differented into replicating cells and acquisition of cancerous mutations, The cancer stem cell traits. Several studies have showed the evidence that CagA has reprogramming potential that could convert epithelial cells into a pluripotent stem cell-like state, and facilitate the of mutations. For e.g, cells expressing CagA or infected with CagA positive bacteria miss features of epithelial differentiation and undergo phenotypic and molecular changes associated with epithelial–mesenchymal transformation.

The CagA can weakly stimulate the WNT signaling to ß-catenin and induce WNT target genes such as the transcription factor CDX133-35[85]. CDX1 further, induce the expression of several stemness-associated factors, such as SALL4 and KLF5, potentially making cells more stemcells. Relanvant with this observation, HP infection has been observed to promote ectopic expression of KLF5 in mouse acid producing gastric glands.

However, gastric mucus cells are short lived, with a life span of only 24-48hours, so their interactions with HP or inflammatory factors are for short duration. HP causes significant inflammatory responses throughout the depths of the glands as well as hyperplasia during periods of chronic gastritis, indicated by profuse cell division and apoptosis of normal gastric cells as well. This widens the number of proliferating cells into the antral region of the glands, potentially facilitating immature cells into contact

with the HP.

It is universally accepted that premalignant metaplastic cells undergo atrophic gastritis with loss of parietal cells and many well differentiated cells. Chronic atrophic gastritis is also associated by expansion of immature proliferating cells, which has been reproduced in a mouse model of atrophic gastritis in which parietal cells were genetically vanished. When HP was introduced into this mouse model of atrophic gastritis, a direct interaction between the HP and gastric progenitor stem cells was occurred leading to some of the bacteria were internalized by progenitor stem cells.

Recently, direct interactions between HP and gastric precursor stem cells have been noted, in stomach of mice devoid of atrophy but infected with HP, and in samples from asymptomatic, infected patients with superficial gastritis. By reconstructing the gastric glands in 3-dimensions using electronic microscopy, these reports explained a subpopulation of HP that rests deep in the gastric mucosal glands. The gland-associated bacteria are distinct from the free living bacteria in the surface gastric mucus in that they grow as microclusters that attach directly to epithelial junctions of gastric precursor cells in the isthmus and in antrum ; mainly to the base of the gastric glands.

Irrespective of whether or not HP infection progresses to carcinomatous changes in humans, the bacteria appear to have evolved specialized mechanisms to interact and interfere with the precursor stem cells and progenitor cells in the gastric glands of stomach. To avoid the gastric lumen, HP are able to reach the surface of the stomach, adhere to the epithelial cells, and even grow as attached micro-clusters directly on the epithelial junctions deep in the gastric glands of stomach. This gland-associated HP is more prominent in the isthmus as well as antrum areas which are rich in mitotic dividing progenitor cells, and occurs early during colonization of mice and in asymptomatic acid peptic disease patient, before developing of atrophic gastritis. It was recently reported

that, within 2 weeks of infection, and before the onset of chronic gastritis, HP infection of the gastric glands activated the antral LGR5+ stem cells, leading to a doubling of the number of stem cells per gland by two months of infection. The stimulation and expansion of plueripotent stem cells spatially correlates with glands occupied by gland-with HP, and mutant HP unable to colonize the glands don't activate the precursor stem cells. This is suggesting that direct interaction between the bacteria and these stem cells promotes this uncontrolled cell proliferation.

Upon all this, it clear that HP has evolved and acquired the strength to colonize a specialized near precursor and stem cells, and that it manipulates these cells for its multiplication and proliferation. Microscopic localization and interactions between the HP and the progenitor epithelium cells could therefore be an important variable in the pathophysiology of gastric cancer. A micro genetic material that could exist within gastric glandular units that is particularly vulnerable to the oncogenic carcinomatic effects of HP.

There are many other virulent, toxic genes such as OipA, babB, and the plasticity cluster are shown but their function is not clearly known[71] . These strains are less pathogenic and are isolated from India; compared to other Asian countries such as India.

SYMPTOMATOLOGY:

Patients with a APD are mostly asymptomatic but may manifest as symptoms same to those of gastroesophageal reflux disease(GERD) disoder, which include heartburn, epigastric pain, and referred pain to the back or left shoulder, nausea, loss of apetite, vomiting etc. Patients with a duodenal ulcer may aggrivated on hunger or have night time abdominal pain associated with the circadian secretion of gastric hydrochloric

acid. GU patients tend to present with post meal fullness, bloating, discomfort, abdominal pain, nausea, vomiting, and weight loss, malena and rarely upper GI bleed.

Patients presenting with an ulcer perforation will often describe a sudden onset pain initially in the epigastric pain then diffuse all over the abdomens quadrants. On clinical examination of the abdomen, patient will be dehydrated because of the third space loss, pallor may be present due to slow bleeding/ eroding of GU. They also presents with diffuse abdominal tenderness mainly in the epigastric and hypochodrium which then progresses to guarding and rigidity. APD patients may have tachycardia, tachypnea with or without hypotension secondary to peritonitis if ulcer is perforated.acute blood loss is rare etity, as the GU erodes the vessles, only posterior GU bleeds. Metabolic alkalosis as as a result of prolonged vomiting and dehydration, also the diaphragm irritation causes less of tidal volume while respiration, pain is the main culprite. Gastric outlet obstruction is a rare complication of APD, it occurs mostly due to healing of an ulcer with scar tissue. The diagnosis of APD and its associated complications may be missed clinically in the elderly, obese, or immunocompromised patient due to the presence of only minimal symptoms and can present in late stages.

MODIFIED JOHNSON CLASSIFICATION:

TYPE	LOCATION	ACID SECRETION
I	Lesser curvature, incisura	reduced
II	Body, incisura, duodenum	incresed
III	pylorus	incresed
IV	Lesser curature, OG juction	reduced
V	anywhere	reduced

DIAGNOSIS OF HELICOBACTER PYLORI(HP):

The gold standard for HP detection is histopathologic examination and/or culture of biopsy tissue obtained during upper gastrointestinal endoscopy. The gastric tissue biopsy can furtherbe used for enzyme activity (urease test) detection indicating presence of HP.

Endoscopy-based diagnosis is limited due to its expense in large studies, the time required for bacterial culture, and the need of endoscopy facilities. Further, sometimes in carcinogenesis process it can be difficult to accurately measure whether a patient was ever infected with HP using this method of detection, as atrophy may cause spontaneous disappearance of HP. But rapid urease test in the endoscopic biopsy sample has an advantage of dectection of urease relised from the HP and aids the faster identification of HP infection and further management. Another advantage being its rapidity. Results will be obtained in less time and are accurate.

The serological tests of measuring antibodies in the plasma or serum can be an alternative method for detection of HP and may also be used to measure previous infection. The performance of commercial serology tests varies mainly due to strain heterogeneity in different popultation. Therefore, validation of a serological test is necessary before it can be used diagnostically in a population. In addition to strain variation, other factors can cause misclassification and impair the performance of serological tests. For e.g, the test cut-off values might differ with patients age, and also sample storage duration can affect the titers.

In this study serological tests include conventional immunoglobulin (IgA) enzyme-linked immunosorbent assay (ELISA) can pick up HP strains contain the cytotoxin associated

gene pathogenicity island (cagPAI) and the CagA effector protein[4], which is known to cause more extensive inflammation in the stomach mucosa which may be missed by the conventional IgG ELISA tests. Compared to antibodies against HP cell surface antigens (Hp-CSA) the CagA antibodies persist much longer after eradication and are therefore a better indicator of a past infection[5, 6].

EPIDEMIOLOGY:

HP chronically infects more than half the world's populations[92]. The infection is generally introduced during childhood through oral-fecal contacts. In developing countries the prevalence of HP infection peaks at 80-100% during adolescence and then persists in these individuals throughout life. In contrast, the infection is acquired later in developed countries and cleared in about 10% of the cases; its prevalence also peaks at 50-70% during young adulthood and this peak prevalence is declining[7]. The adult prevalence of infection is deduced to be 82% in Eastern Europe, 71% in Japan, 62% in China, 60-70% in Jamaica, 62% in Central America, 62% in Mexican Americans, 52% in non-Hispanic blacks in the U.S., and 26% among non-Hispanic whites in the U.S.[8]. Suggested risk factors for HP infection include low socioeconomic status and presence of infected family members[9, 8].

BURDEN OF INFECTION IN INDIA:

India is a vast country known for its rich history, culture and food. It is also the prototype developing country with a vast rural population living in poverty. The prevalence of HP in the Indian subcontinent can be as high as 80 per cent or more in rural areas[92]. The most commonly recognized manifestation of HP infection in India is peptic ulcer disease, particularly duodenal ulcer disease, which outnumbers gastric ulcers between 8:1 and

30:1[25], calculated the point prevalence of active peptic ulcer disease at 3% with a lifetime prevalence of 9 per cent. As in other regions, the actual risk of a particular outcome from HP infection is predicated on the pattern of gastritis[7]. Antral predominant gastritis leaves an intact gastric corpus, poorly controlled acid secretion and promotes gastric and duodenal ulcer formation. In contrast, with pangastritis acid secretion often falls below the level needed to produce and sustain duodenal ulcer disease (*e.g*., approximately 12 mmol/h), gastric ulcer becomes more common than duodenal ulcer and the incidence of gastric cancer rises. Finally, atrophic pangastritis is the main precursor lesion associated with gastric cancer[27].

MATERIALS AND METHODS

STUDY SITE: This study was conducted in the endsopic unit of deprtment of General Surgery in R.L.Jalappa hospital and research centre, Kolar

STUDY POPLULATION: All the patients with APD patients undergoing upper GI endoscopy in R.L.Jalappa hospital and research centre were included in the study.

STUDY DESIGN: This study is Cohart study

STUDY SAMPLE: 121

SAMPLING METHOD: All the study subjects were recrited into block sampling by convient sampling till the sample size is reched.

STUDY DURATION: the study is conducted from noverber 2019 to august 2021.

INCLUSION CRITERIA:

•Patients above 18 year undergoing upper GI endoscopy

EXCLUSION CRITERIA:

•Patients who have undergone partial or total gastrectomy

•Patients who have received treatment for helicobacter pylori infection in past 6 months.

•Patients who are immunocompromised.

ETHICAL CONSIDERATION: The study was conducted after the approval from the institutional ethics committee. Informed/ written/verbal consents were taken from all the study participants. The risk and advantages of the study were conveyed. Patients identity is kept confidencial.

DATA COLLECTION TOOLS:

All the study subjects details were documented according to the study performa.

METHODOLOGY:

All the study subjects with symptoms of acid peptic disease were subjected to upper GI Endoscopy and biopsies will be obtained from antral mucosa of 121 study subjects.Rapid urease test(RUT) and Serology tests for H. pylori (ELISA) will be conducted accordingly.

A detailed history, thorough clinical examinations, before the endoscopy will be done.

All the cases will undergo rapid urease test and ELISA IgG antibody detection

All the cases results will be compared based on sensitivity and specificity to detect helicobacter infection.

All the cases are followed up for 3 months for the symptomatic relief after the treatment.

FOLLOWING INVESTIGATIONS WERE DONE:

•HB :

•RBC :

•PCV:

•WBC:

•PLATELETS:

•HIV

•HbsA

•RAPID UREASE TEST

•ELISA to detect Ab against H.pylori in the serum

STATISTICAL METHODS

Endoscopic findings, rapid urease test and ELISA results were considered as primary outcome variables. Recurrence was considered as Secondary outcome variable. Treatment (CMO kit and HP kit) was considered as Primary explanatory variable. Data was also pictorial analysed with appropriate bar-diagram, pie-diagram, cluster bar diagram and stacked bar diagram Descriptive statistics were used to analyze data in evidence with the study's objectives. Data were expressed as the mean, 95% confidence interval (CI; lower and upper bounds), median, minimum and maximum, and percentage, where appropriate. Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used.). ELISA test was taken as gold standard. Rapid urease test was taken as screening test. The sensitivity, specificity, predictive values and diagnostic accuracy of the screening test along with their 95% Class Interval were presented. P value < 0.05 was considered statistically significant. Data was analyzed by using SPSS software, V.22. (1).1. SPSS I. IBM SPSS Statistics Version 22 Statistical Software: Core System Users' Guide. SPSS Inc. 2014.

RESULT:

A total of 121 subjects were included in the final analysis.

Table 1: Descriptive analysis of age (in years) in study population (N=121)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C. I	
					Lower	Upper
Age (in years)	46.88 ± 14.83	48.00	18.00	80.00	44.21	49.55

The mean age was 46.88 ± 14.83 years, ranged from 18 to 80 years. (Table 1)

Table 2: Descriptive analysis of age group (in years) in the study population (N=121)

Age Group (in years)	Frequency	Percentages
Upto 40 years	38	31.40%
41 to 60 years	64	52.89%
61 years and above	19	15.70%

Among the study population, 38(31.40%) were aged upto 40 years, 64(52.89%) were aged between 41 years to 60 years and 19(15.70%) were aged 61 years and above. (Table 2&figure 1)

Figure 1: Bar chart of age group (in years) in the study population (N=121)

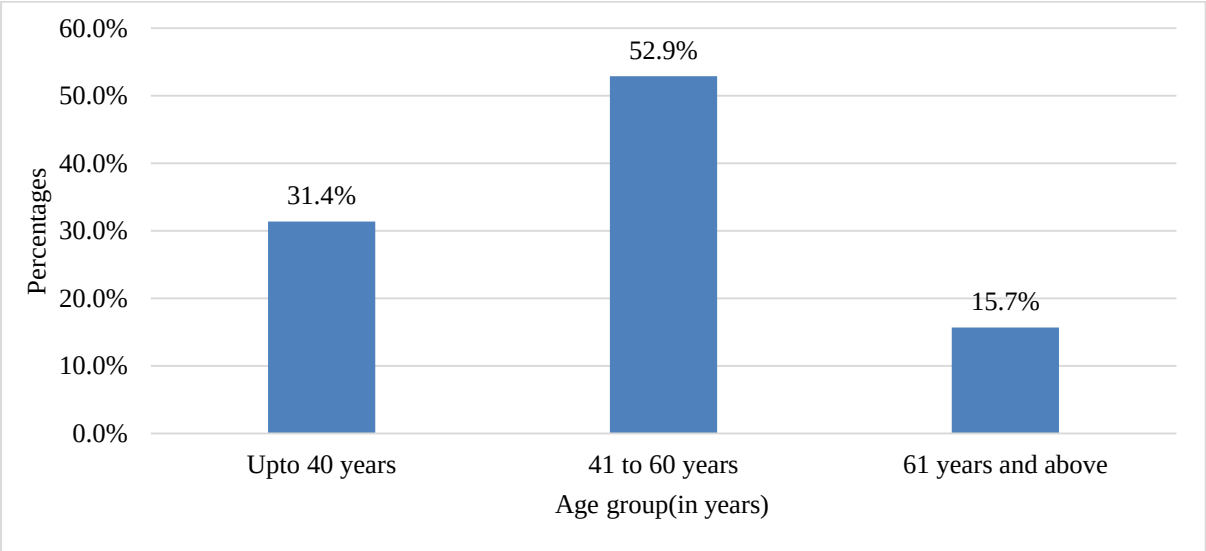


Table3: Descriptive analysis of gender in the study population (N=121)

Gender	Frequency	Percentages
Male	90	74.38%
Female	31	25.62%

Among the study population, 90(74.38%) were male participants, 31(25.62%) were female participants. (Table 3&figure 2)

Figure 2: Pie chart of gender in the study population (N=121)

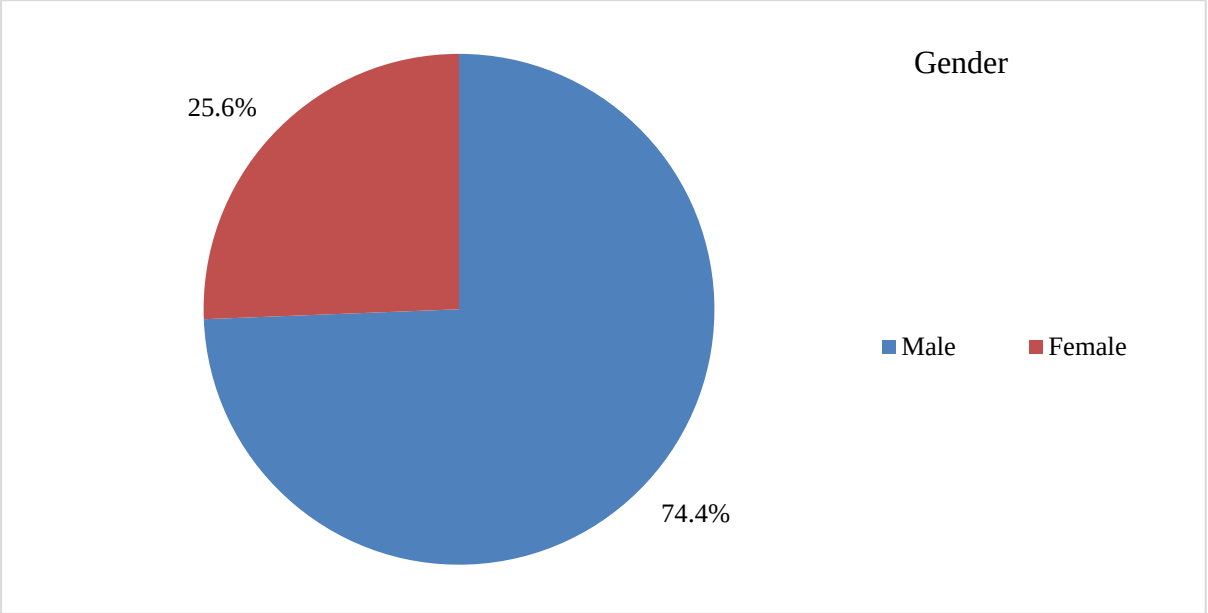


Table4: Descriptive analysis of occupation in the study population (N=121)

Occupation	Frequency	Percentages
Day time worker	98	80.99%
Night time worker	23	19.01%

In the study participants, 98(80.99%) were day time worker and 23(19.01%) were night time workers. (Table 4&Figure 3)

Figure 3: Pie chart of occupation in the study population (N=121)

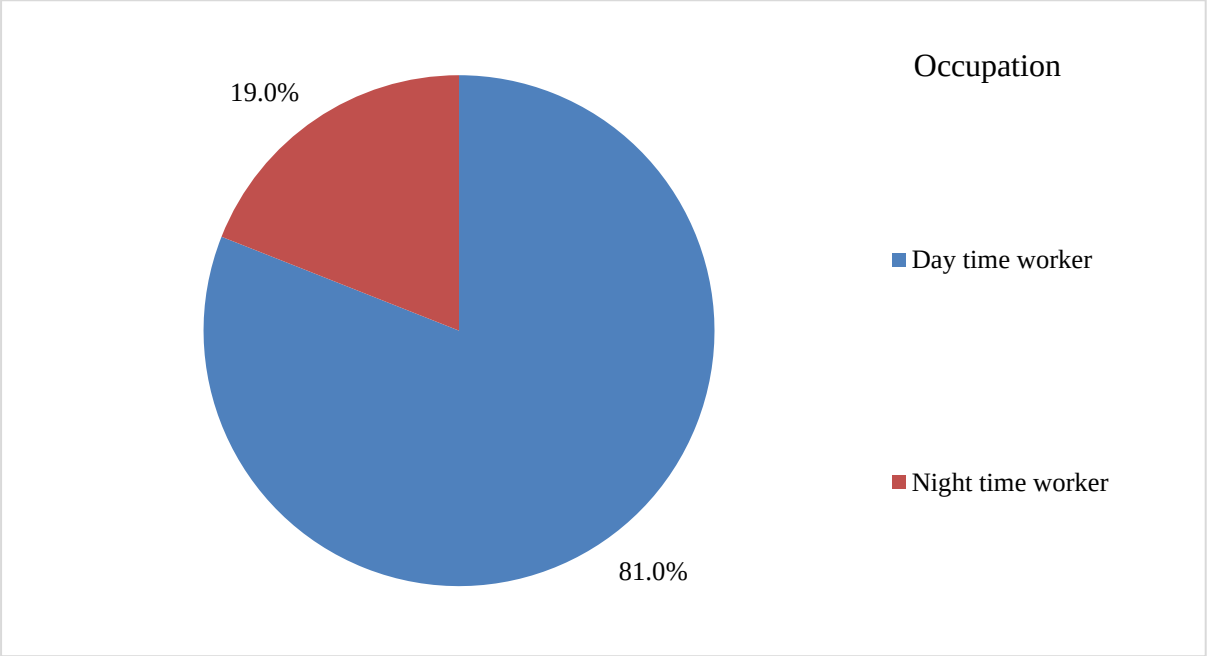


Table 5: Descriptive analysis of symptoms in the study population (N=121)

Symptoms	Frequency	Percentages
Pain abdomen	53	43.80%
Nausea	22	18.18%
Retrosternal discomfort	17	14.05%
Vomiting	17	14.05%
Heart burn	12	9.92%

As symptoms, 53(43.80%) had pain abdomen, 22(18.18%) had nausea, 17(14.05%) had retrosternal discomfort and vomiting for each and 12(9.92%) had 9.92%. (Table 5&figure 4)

Figure 4: Bar chart of symptoms in the study population (N=121)

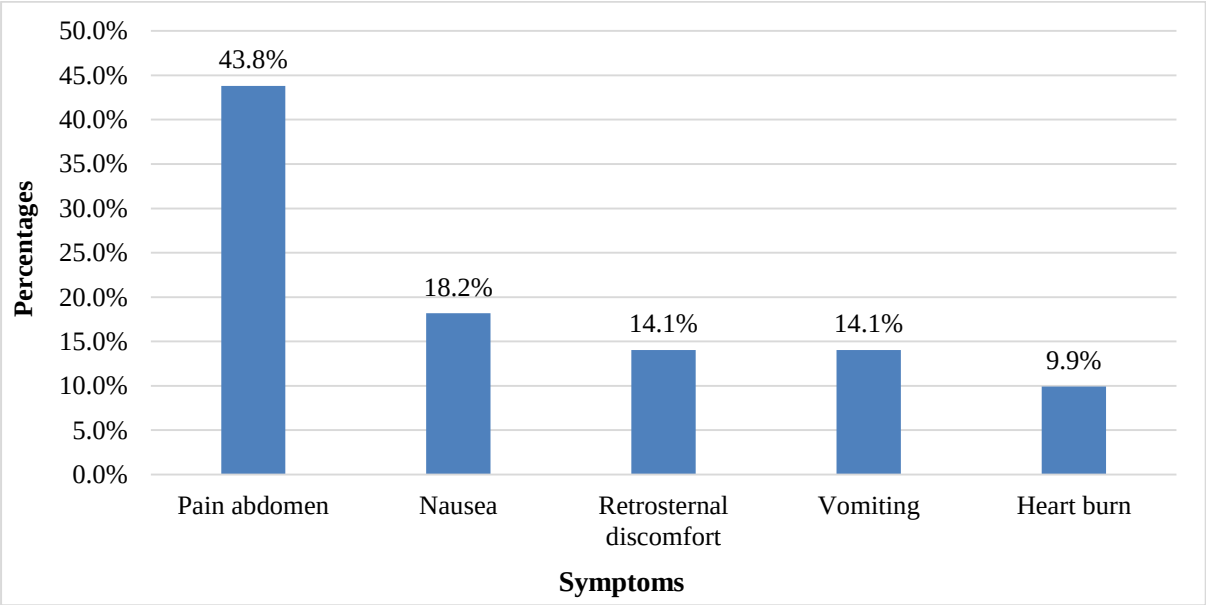


Table6: Descriptive analysis of duration of symptoms (in days) in study population (N=121)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C. I	
					Lower	Upper
Duration of Symptoms (in days)	1.04 ± 1.67	0.20	0.03	6.00	0.74	1.34

The mean duration of symptoms was 1.04 ± 1.67 days, ranged from 0.03 to 6 days. (Table 6)

Table 7: Descriptive analysis of comorbidities in the study population (N=121)

Comorbidities	Frequency	Percentages
Diabetic mellitus	28	23.14%
Hypertension	24	19.83%
Ischemic heart disease	2	1.65%

Comorbidities of study population reported as, 28(23.14%) with diabetic mellitus, 24(19.83%) with hypertension and 2(1.65%) with ischemic heart disease. (Table 7)

Table 8: Descriptive analysis of endoscopic finding in the study population (N=121)

Endoscopic Finding	Frequency	Percentages
Antral Gastritis	31	25.62%
Gastritis	19	15.70%
Biliary Gastritis	18	14.88%
Normal Study	18	14.88%
Pyloric Hyperaemia	16	13.22%
Diffuse Gastritis	14	11.57%
Diffuse Mucosal Erythema	4	3.31%
Mucosal Hyperaemia	1	0.83%

As per endoscopic findings, 31(25.62%) had antral gastritis, 19(15.70%) had gastritis, 18(14.88%) had biliary gastritis and normal study for each, 16(13.22%) had pyloric hyperaemia, 14(11.57%) had diffuse gastritis, 4(3.31%) had diffuse mucosal erythema and 1(0.83%) had mucosal hyperaemia. (Table 8)

Table 9: Descriptive analysis of rapid urease test in the study population (N=121)

Rapid urease test	Frequency	Percentages
Positive	106	87.60%
Negative	15	12.40%

Out of 121 participants, 106(87.60%) rapid urease test result was positive. (Table 9&figure 5)

Figure 5: Pie chart of rapid urease testin the study population (N=121)

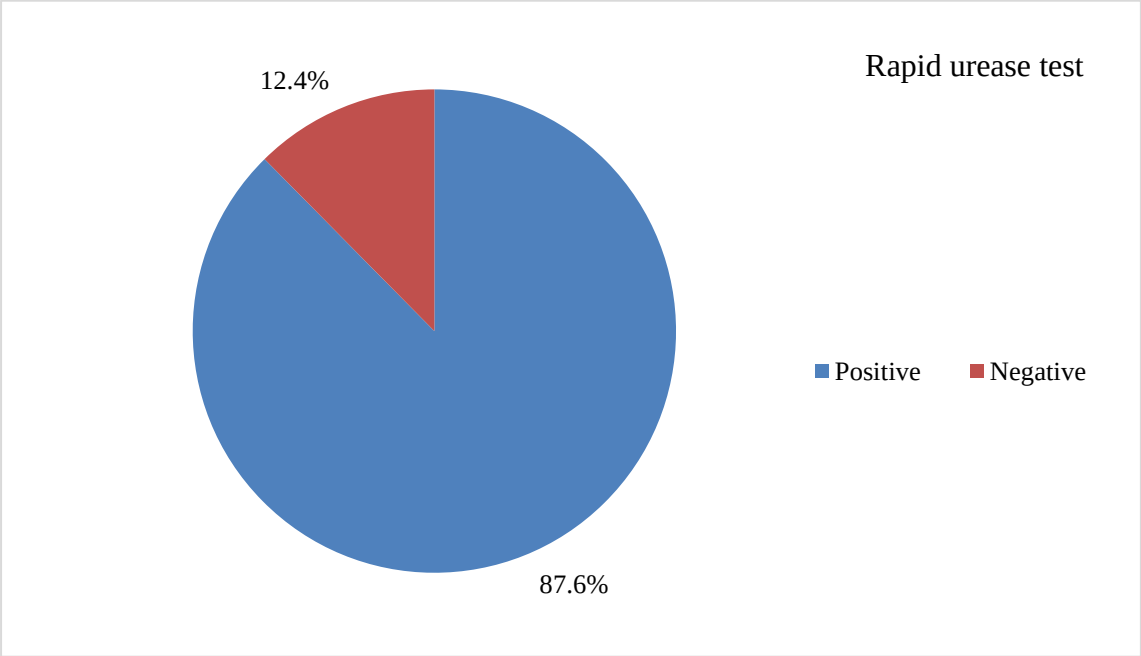


Table 10: Descriptive analysis of enzyme linked immunosorbent assay in the study population (N=121)

Enzyme linked immunosorbentassay	Frequency	Percentages
Positive	105	86.78%
Negative	16	13.22%

Out of 121 participants, 105(86.78%) had positive results in enzyme linked immunosorbent assay. (Table 10&figure 6)

Figure 6: Pie chart of enzyme linked immunosorbentassay in the study population (N=121)

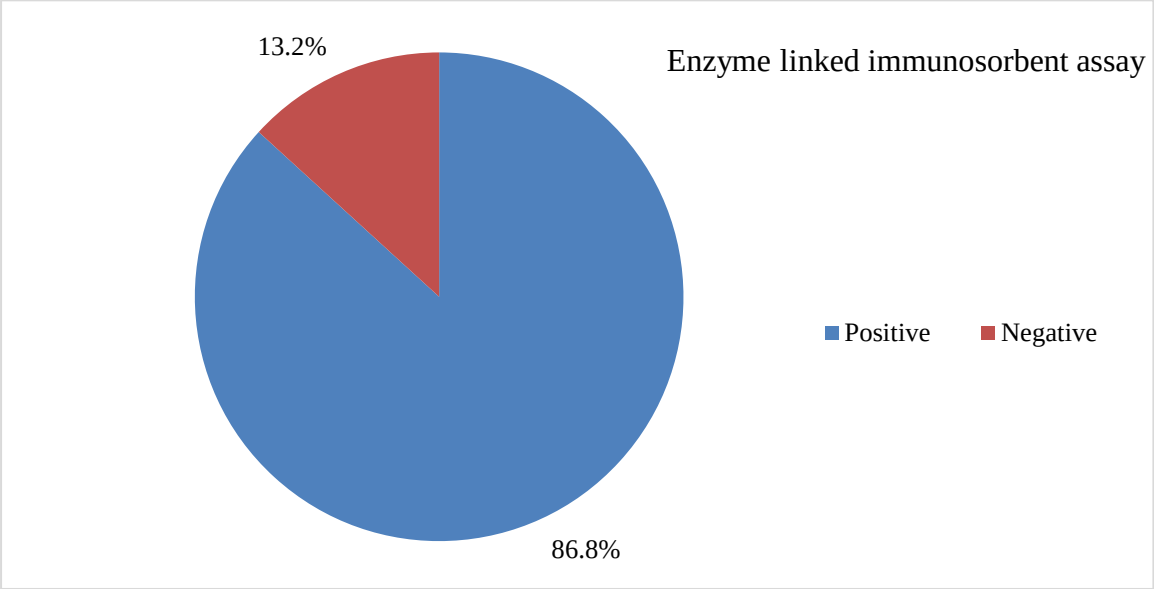


Table 11: Descriptive analysis of treatment in the study population (N=121)

Treatment	Frequency	Percentages
CMO KIT	62	51.24%
HP KIT	59	48.76%

Among the study population, 62(51.24%) were taken CMO kit and 59(48.76%) were taken HP kit. (Table 11&figure 7)

Figure 7: Bar chart of treatment in the study population (N=121)

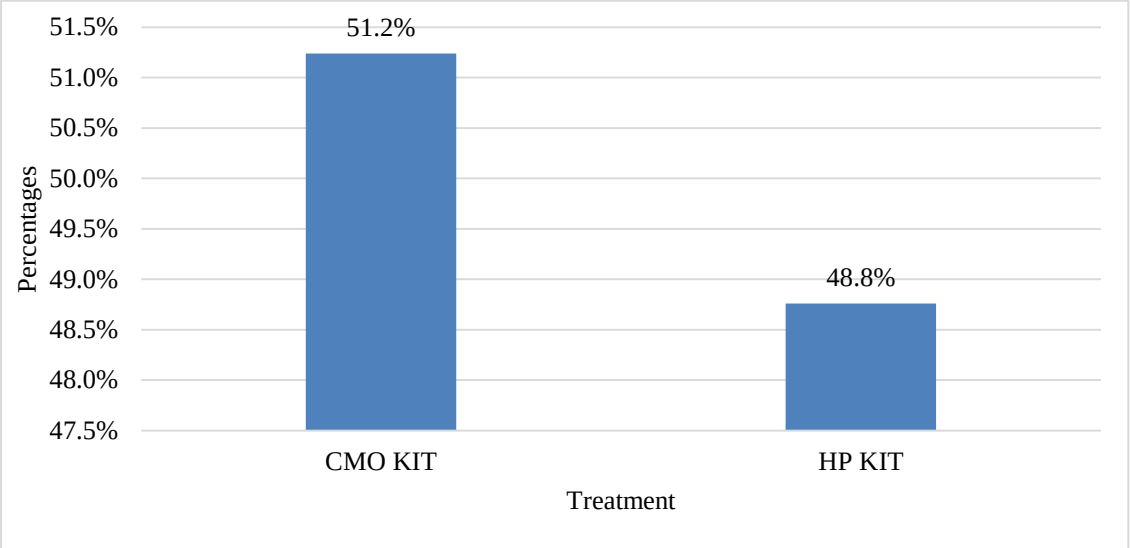


Table 12: Descriptive analysis of follow up symptom in the study population (N=121)

Follow up symptoms	Frequency	Percentages
Pain	12	9.92%
vomiting	10	8.26%
Nausea	7	5.79%
Retrosternal discomfort	7	5.79%
Recurrence	2	1.65%
Regurgitation	2	1.65%
Pain abdomen	2	1.65%
Asymptomatic	1	0.83%
Intermittent pain	1	0.83%
Pain reduced	1	0.83%
Nil	76	62.81%

Among the study population, 12(9.92%) had pain, 10(8.26%) had vomiting, 7(5.79%) had nausea and retrosternal discomfort for each, 2(1.65%) had recurrence, regurgitation and pain abdomen for each, 1(0.83%) had asymptomatic, Intermittent pain and Pain reduced for each as follow-up symptoms. (Table 12)

Table 13: Descriptive analysis of recurrence in the study population (N=121)

Recurrence	Frequency	Percentages
Yes	45	37.2%
No	76	62.80%

Out of 121 participants, 45(37.2%) had recurrence. (Table 13&figure 8)

Figure 8: Pie chart of recurrence in the study population (N=121)

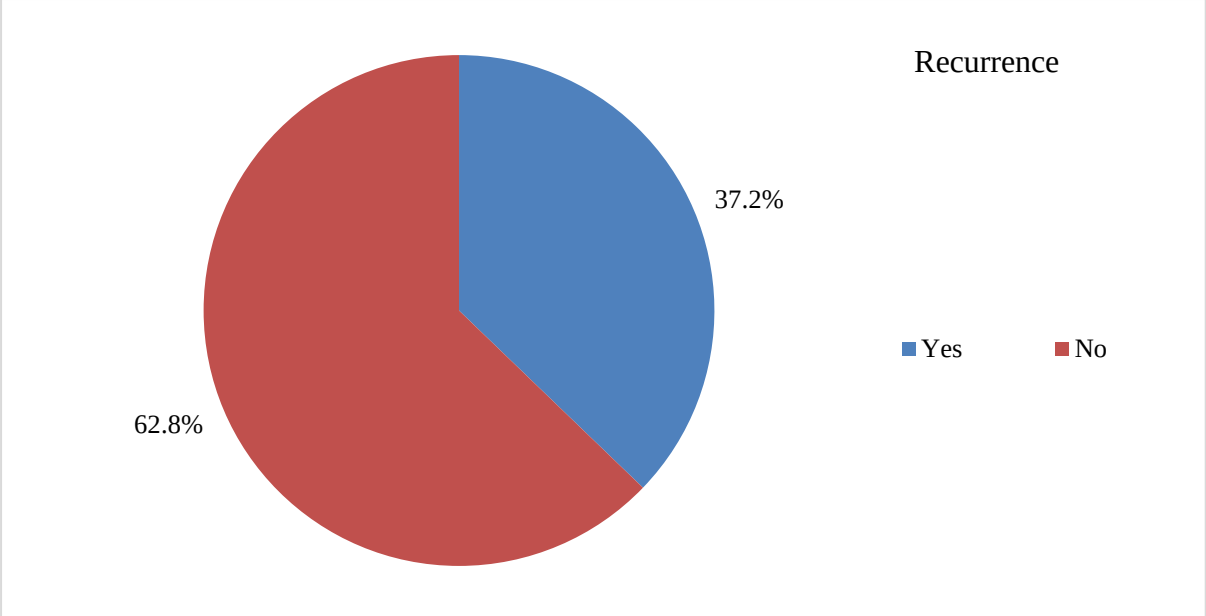


Table 14: Comparison of endoscopic finding between rapid urease test(N=121)

Endoscopic Finding	Rapid urease test	
	Positive	Negative
Antral Gastritis (N=31)	28 (90.32%)	3 (9.68%)
Gastritis (N=19)	15 (78.95%)	4 (21.05%)
Biliary Gastritis (N=18)	12 (66.67%)	6 (33.33%)
Normal Study (N=18)	18 (100%)	0 (0%)
Pyloric Hyperaemia (N=16)	14 (87.5%)	2 (12.5%)
Diffuse Gastritis (N=14)	14 (100%)	0 (0%)
Diffuse Mucosal Erythema (N=4)	4 (100%)	0 (0%)
Mucosal Hyperaemia (N=1)	1 (100%)	0 (0%)

*No statistical test was applied- due to 0 subjects in the cells

Among the antral gastritis finding, 28 (90.32%), in gastritis cases15 (78.95%), in biliary gastritis12 (66.67%), in normal people18 (100%), in pyloric hyperaemia14 (87.5%), in diffuse gastritis 14 (100%), indiffuse mucosal erythema cases 4 (100%)and in mucosal hyperaemiafindings 1 (100%) showed positive in Rapid urease test. (Table 14)

Table 15: Comparison of endoscopic finding between ELISA (N=121)

Endoscopic Finding	ELISA	
	Positive	Negative
Antral Gastritis (N=31)	24 (77.42%)	7 (22.58%)
Gastritis (N=19)	16 (84.21%)	3 (15.79%)
Biliary Gastritis (N=18)	17 (94.44%)	1 (5.56%)
Normal Study (N=18)	16 (88.89%)	2 (11.11%)
Pyloric Hyperaemia (N=16)	13 (81.25%)	3 (18.75%)
Diffuse Gastritis (N=14)	14 (100%)	0 (0%)
Diffuse Mucosal Erythema (N=4)	4 (100%)	0 (0%)
Mucosal Hyperaemia (N=1)	1 (100%)	0 (0%)

*No statistical test was applied- due to 0 subjects in the cells

Among the antral gastritis finding, 24 (77.42%), in gastritis cases 16 (84.21%), in biliary gastritis 17 (94.44%), in normal people16 (88.89%), in pyloric hyperaemia 13 (81.25%), in diffuse gastritis 14 (100%), in diffuse mucosal erythema cases 4 (100%) and in mucosal hyperaemia findings 1 (100%) showed positive in enzyme linked immunosorbent assay. (Table 15)

Table 16: Comparison of age group (in years) between recurrence (N=121)

Age Group (In Years)	Recurrence		Chi square	P value
	Yes	No		
Upto 40 years (N=38)	10 (26.32%)	28 (73.68%)	2.804	0.246
41 to 60 years (N=64)	27 (42.19%)	37 (57.81%)		
61 years and above (N=19)	8 (42.11%)	11 (57.89%)		

The difference in recurrence across differentage groups was estimated to be insignificant with a P- value of 0.246 with majority of 27 (42.19%)participants were aged between 41 to 60 yr of age group. (Table 16&figure 9)

Figure 9: Cluster bar chart of comparison of age group (in years) between recurrence (N=121)

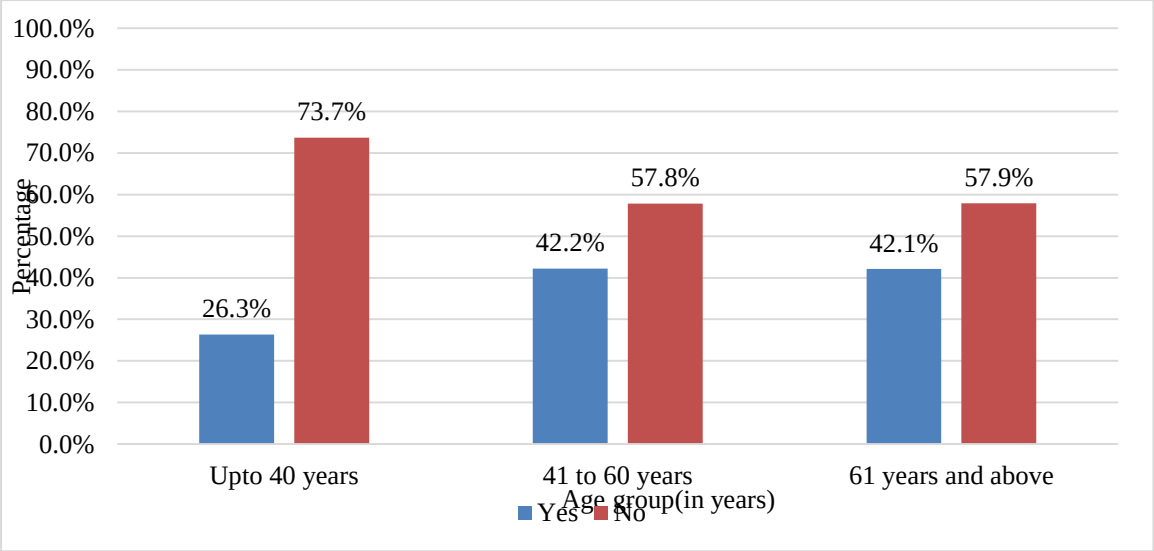


Table 17: Comparison of symptoms between recurrence (N=121)

Symptoms	Recurrence		Chi square	P value
	Yes	No		
Pain abdomen (N=53)	22 (41.51%)	31 (58.49%)	2.838	0.585
Nausea (N=22)	7 (31.82%)	15 (68.18%)		
Retrosternal Discomfort (N=17)	8 (47.06%)	9 (52.94%)		
Vomiting (N=17)	4 (23.53%)	13 (76.47%)		
Heart burn (N=12)	4 (33.33%)	8 (66.67%)		

The difference in recurrence across symptoms was seen to be insignificant with a P- value of 0.585 with majority of 22 (41.51%)participants had pain abdomen. (Table 17&figure 10)

Figure 10: Cluster bar chart of comparison of symptoms between recurrence (N=121)

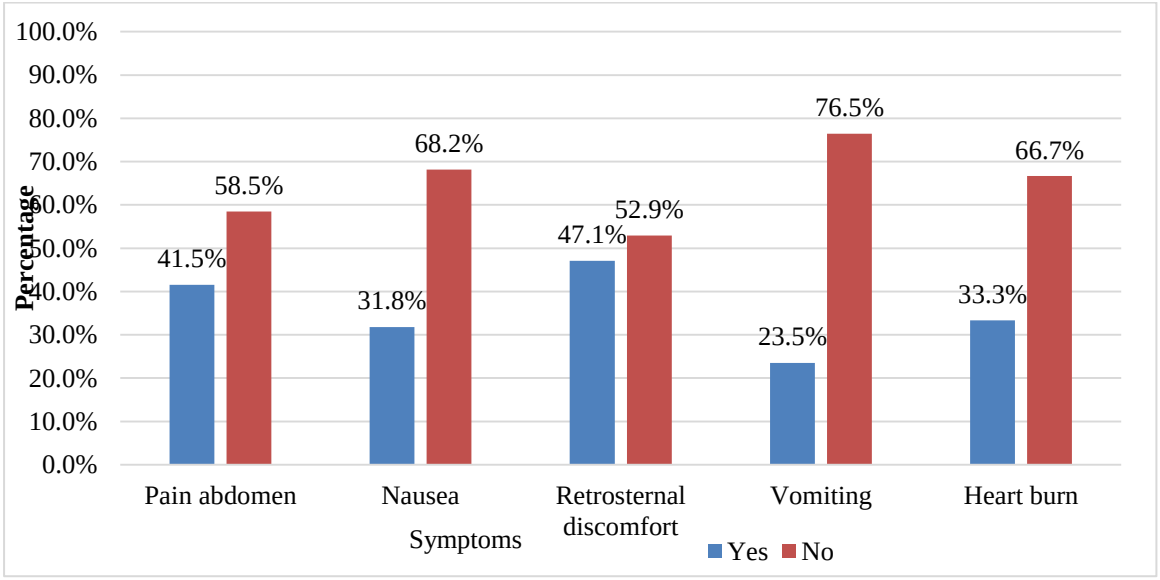


Table 18: Comparison of occupation between recurrence (N=121)

Occupation	Recurrence		Chi square	P value
	Yes	No		
Day time worker (N=98)	37 (37.76%)	61 (62.24%)	0.070	0.791
Night time worker (N=23)	8 (34.78%)	15 (65.22%)		

The difference in recurrence based on occupation was noticed to be insignificant with a P-value of 0.791 with majority of 37 (37.76%)participants were day time worker where night time workers showed very less recurrence with 8(34.78%). (Table 18)

Table19: Comparison of treatment between recurrence (N=121)

Treatment	Recurrence		Chi square	P value
	Yes	No		
CMO KIT (N=62)	21 (33.87%)	41 (66.13%)	0.600	0.439
HP KIT (N=59)	24 (40.68%)	35 (59.32%)		

Out of 62 participants using CMO kit, 21 (33.87%) developed recurrence and out of 59 participants using HP kit, 24 (40.68%) developed recurrence. The difference in the proportion of treatment between recurrence was statistically not significant (P value 0.439). (Table 2&figure 11)

Figure 11: Cluster bar chart of comparison of treatment between recurrence (N=121)

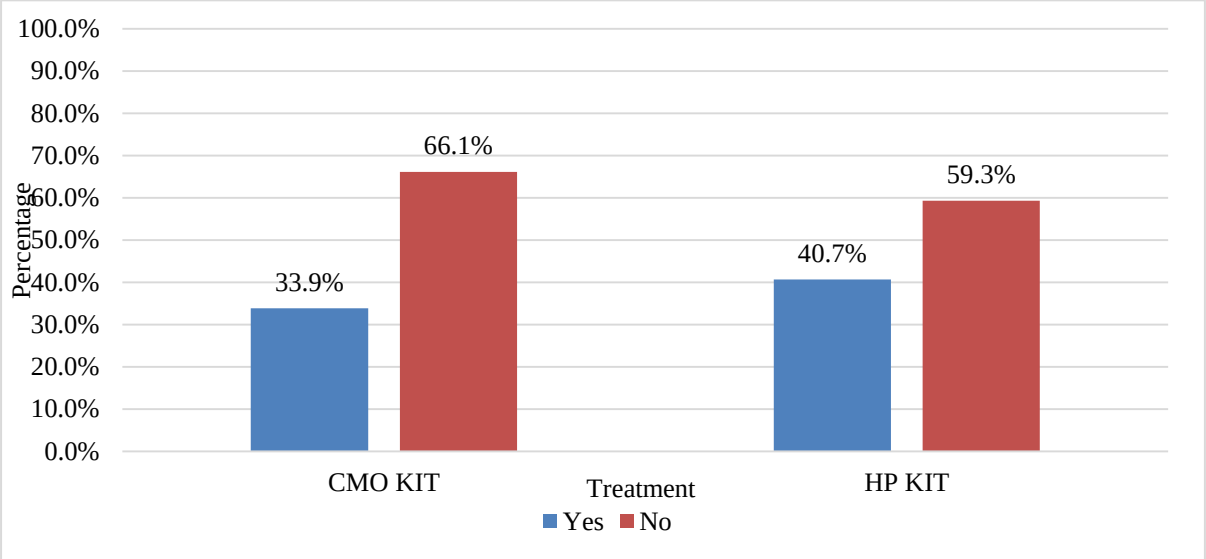


Table 20: Comparison of symptoms between treatment (N=121)

Symptoms	Treatment		Chi square	P value
	CMO KIT (N=62)	HP KIT (N=59)		
Pain Abdomen	29 (46.77%)	24 (40.68%)	1.031	0.905
Nausea	10 (16.13%)	12 (20.34%)		
Retrosternal Discomfort	9 (14.52%)	8 (13.56%)		
Vomiting	9 (14.52%)	8 (13.56%)		
Heart Burn	5 (8.06%)	7 (11.86%)		

Out of 62 participantsusing CMO kit, 29 (46.77%) had pain abdomen, 10 (16.13%) had nausea, 9 (14.52%) had retrosternal discomfort and vomiting for each and 5 (8.06%) had heart burn.

Out of 59 participantsusing HP kit, 24 (40.68%)had pain abdomen, 12 (20.34%)had nausea, 8 (13.56%) had retrosternal discomfort and vomiting for each and 7 (11.86%)had heart burn. The difference in the proportion of symptomsbetween treatment was statistically not significant (P value 0.905). (Table 2&figure 12)

Figure 12: Stacked bar chart of comparison of symptoms between treatment (N=121)

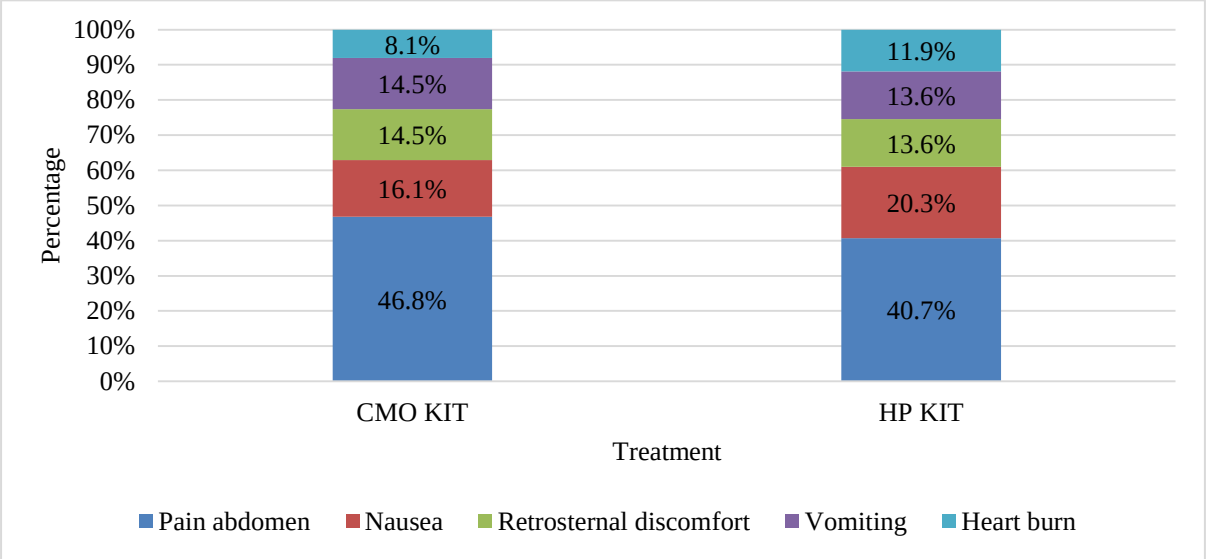


Table 21: Comparison of co-morbidities between treatment (N=121)

Comorbidities	Treatment		P value
	CMO KIT (N=62)	HP KIT (N=59)	
Diabetic mellitus	14 (22.58%)	14 (23.73%)	0.881
Hypertension	9 (14.52%)	15 (25.42%)	0.133
Ischemic heart disease	1 (1.61%)	1 (1.69%)	1.000

Out of 62 participants in CMO kit, 14 (22.58%) had diabetic mellites. Out of 59 participants in HP kit, 14 (23.73%) had diabetic mellitus. The variation in the proportion diabetic mellitus between treatment was statistically not significant (P value 0.881). Out of 62 participants in CMO kit, 9 (14.52%)had hypertension. Out of 59 participants in HP kit, 15 (25.42%)had hypertension. The variation in the proportion hypertension between treatment was statistically not significant (P value 0.133). Out of 62 participants in CMO kit, 1 (1.61%)had ischemic heart disease. Out of 59 participants in HP kit, 1 (1.69%)had ischemic heart disease. The variation in the proportion ischemic heart diseasebetween treatment was statistically not significant (P value 1.000). (Table 21)

Table 22: Comparison of ELISA with Rapid urease test (N=121)

Rapid urease test	ELISA		P value
	Positive (N=105)	Negative (N=16)	
Positive	92 (87.62%)	14 (87.5%)	1.000
Negative	13 (12.38%)	2 (12.5%)	

The difference in ELISA result between RUT results was found to be insignificant with a P- value of 1.000 with majority of 92 (87.62%)participants had rapid urease test. (Table 22)

Figure13: Stacked bar chart of comparison ELISA between rapid urease test (N=121)

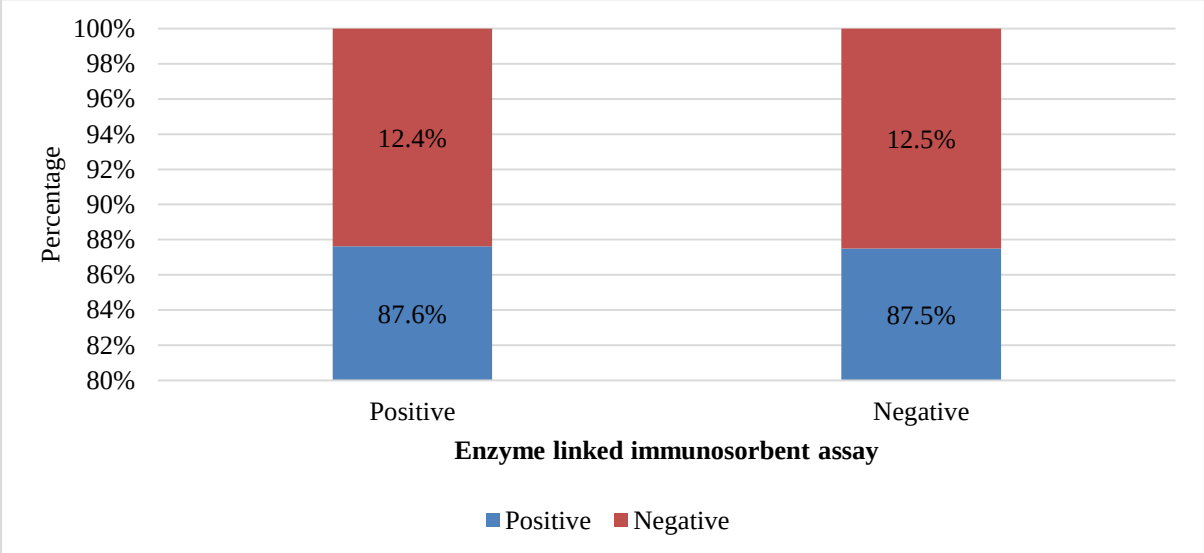


Table 23: Predictive validity of rapid urease test in predicting ELISA (N=121)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	87.62%	79.76%	93.24%
Specificity	12.50%	1.55%	38.35%
False positive rate	87.50%	61.65%	98.45%
False negative rate	12.38%	6.76%	20.24%
Positive predictive value	86.79%	78.83%	92.59%
Negative predictive value	13.33%	1.66%	40.46%
Diagnostic accuracy	77.69%	69.22%	84.75%

The rapid urease test had sensitivity of 87.62% (95% CI 79.76%to 93.24%) in predicting ELISA. Specificity was 12.50% (95% CI 1.55%to 38.35%), false +ve rate was 87.50% (95% CI 61.65%to 98.45%), false -ve rate was 12.38% (95% CI 6.76%to 20.24%), +ve predictive value was 86.79% (95% CI 78.83%to 92.59%),

-ve predictive value was 13.33% (95% CI 1.66%to 40.46%), and the total diagnostic accuracy was 77.69% (95% CI 69.22%to 84.75%). (Table 23)

DISCUSSION

Despite the fact that several methods for detecting HP infection have been established, the gold standard for detecting HP infection is still debated. None of the diagnostic approaches are completely foolproof or appropriate for all situations, and each has its own set of disadvantages. Despite the need for a quick and highly reliable test in clinical settings, there is currently no single test that can diagnose HP infection.[92] Invasive endoscopy, an excellent method that provides visualization of mucosa and biopsy of the upper gastrointestinal mucosa, remains the diagnostic gold standard. Bacterial culture is used to test biopsies for HP, which is the most reliable approach due to its high specificity. A RUT, a histological examination, and a (quantitative) enzymatic reaction of biopsies can all be used to establish the presence of HP.[83] Serology is especially appealing for pre-endoscopy and pre-treatment screening since it is straightforward, repeatable, and cost-effective, and it can also be done with stored samples. The ELISA; based detection of HP-specific IgG alone is the most often utilised serological test.[4] According to European [85] and United States of America guidelines[86], the first-line regimens for treating chronic HP infection in adults consist of a standard triple therapy including a proton pump inhibitor (PPI) with two antibiotics (clarithromycin and amoxicillin or metronidazole) or bismuth-containing quadruple therapy, given for 7–14 days. The current study is conducted to proportionate the RUT and ELISA and to find the validity of RUT in predicting ELISA test. A total of 121 patients with symptoms of acid peptic disease are included in the final analysis. We did upper GI endoscopy and obtained biopsies from the antral mucosa for RUT. Among them 51.24% were treated with CMO kit (clarithromycin 250mg BD, metronidazole 400mg TID, Omeprazole 20mg BD) and 48.76% with HP kit (amoxycillin 750mg BD, Tinidazole 500mg BD,

Omeprazole 20mg BD). All the cases were followed up for 3 months for the symptomatic relief after the treatment.

The mean age of the study population is 46.88 ± 14.83 years with majority at 52.89% in the 41-60 years' age group. Our study group has a preponderance of male subjects with 74.38% males and 25.62% females. Most of them have day time working hours with only 19.01% working during the night. A study by Reddy. also had male predominance in their study group with 82 males and 28 females with maximum number of patients aged 26 years to 50 years.[7] In contrast Jalalypour study had more females patients in their study group with 43 males and 62 females with a mean age of 43 years.[8] Whereas, Pourakbari, studied both children and adults with mean ages 9.9 ±2.6 and 44.7 ±18.7 respectively. [9]On analysis of the age distribution, highest number of patients were seen belonging to the age group 31-40; with 57.14% patients from this age group in Maimbilly .'s study.[72]

Table comparing the patient's characteristics among various studies to present study

Studies	Sample size	Gender predominance	Age
Reddy.et al, [7]	100	82% male	26-50 years
Jalalypour et al, [8]	105	62% female	(mean age) 43years
Present study	121	74.38% males	41-60 years

Majority of patients with 43.80% complained of abdominal pain, followed by nausea in 18.18%, 14.05% had retrosternal discomfort, 14.05% had vomiting and 9.92%

complained of heart burn. The mean duration of symptoms was 1.04 ± 1.67 days. Comorbidities of study population are 23.14% had diabetic mellitus, 19.83% had hypertension and 1.65% had ischemic heart disease. On endoscopy, antral gastritis is found in 25.62%, 15.70% had gastritis, 14.88% had biliary gastritis, 13.22% had pyloric hyperaemia, 11.57% had diffuse gastritis, 3.31% had diffuse mucosal erythema and 0.83% had mucosal hyperaemia. 14.88% had a normal endoscopic evaluation with no abnormal findings.Majority of the cases were presented with chronic superficial gastritis (42%) followed by duodenal ulcer (37.33%) and Non ulcer dyspepsia was seen in 67% patients of dyspepsia in Rastogi.'s study.[81]

All the participants are tested with RUT and ELISA and 87.60% had RUT positive and 86.78% had ELISA positive infection. A study by Jalaypourused RUT, PCR and ELISA tests and patients with minimum 2/3 +ve tests (gold standard) considered as infected. According to this definition, 48.57% were positive for H. pylori, and 51.42% were diagnosed as uninfected.[88] another similar study by Reddy, did RUT, Grams staining, culture & serology IgG detection to all the cases and they observed that HP were detected more in antral gastritis case followed by DU. They found 58.1% positive with RUT, 51% positive with Grams staining, culture and 56.3% were positive on ELISA.[73 In] Maimbilly's study, RUT was positive in 82.35% and ELISA was positive in 80%.The patients between 31-40 years of age were found to be highly positive for RUT as well as serum IgG in their study.[80]

Among those with antral gastritis, 90.32% tested positive on RUT, and 77.42% on ELSIA. In patients with gastritis on endoscopy, 78.95% had RUT positive and 84.21% had positive ELISA; those with biliary gastritis 66.67% had RUT positive while a

whopping 94.44% had ELISA positive. Those with endoscopic findings of diffuse gastritis, diffuse mucosal erythema and mucosal hyperaemia, all tested positive for both the tests. HP has predilection towards gastric cells in antral mucosa so antral gastritis cases were predominant followed by duodenal ulcers, gastric ulcers, gastro duodenitis and carcinoma stomach in Reddy's study.[70] All patients who showed positive RUT within 30 minutes and serum H.pylori IgG level more than >30 IU/ml were suffering from gastritis in Maimbilly's study.[10]In Rastogi 's study, it was found that subjects with DU and GU had higher incidence of HP (91.07%), when compared to patients with gastritis (68.25%).[11]In their study, 52% of the dyspeptic patients were positive by RUT.

In Pourakbari's study, RUT showed sensitivity100% and 94% in children and adults, ELISA-IgG assays showed low sensitivity (29%) and high specificity (91%) in children. In adults, sensitivity and specificity was 62% and 80%, respectively using PCR as the standard test. Reddy's study reported that a combination of Grams staining smear examination, RUT and ELISA appear to be highly sensitive and specific for detection of H. pylori infection in patients undergoing endoscopy. They concluded that no single test can be considered sensitive or specific to detect or rule out H. pylori infection, so it is necessary to use a combination of tests.[70] Using PCR as standard, they found RUT had a sensitivity of 93.55% and specificity of 87.50%; while ELISA had a sensitivity of 75.75% and specificity of 72.72.%.[73]

According to Jalaypour.'s study, RUT test presented the best sensitivity of 92.16 %, but specificity of 90.74% and ELSIA showed 90.20% sensitivity and 61.11% specificity with standard being 2/3 tests being positive. They concluded that ELlSA is highly sensitive test for first-line identifies HP infection. [85] [s]Maimbilly, found that in patients with

symptoms of gastritis during the first visit in outpatient department, serum IgG estimation may be a useful tool to assess the severity of infection and need of medical treatment.[90] The RUT had a sensitivity of 100% and specificity of 58.54% when compared to cases that came positive by all three tests in Rastogi's study. On comparison of ELISA as a diagnostic test versus RUT, it had 100% sensitivity and 50% sensitivity.[91]In our study, the RUT had sensitivity of 87.62%in predicting ELISA, specificity was 12.50%, with a total diagnostic accuracy of 77.69%. This widen variation/range of sensitivity also specificity of the RUT as a marker of HP infection could be attributed to the lack of a gold standard to verify the association, causing researchers to compare it with different tests available from study to study. There are least studies in the literature which have compared the RUT and serology (ELISA) in predicting H-pylori infection. However, in our study we found RUT to be a good predictor of ELISA.

Cutler et al,[82] computed sensitivity, specificity, PPV, and NPV for ^{73}C UBT(C-urea breath test), serology, RUT, microscopic presence of H. pylori, in chronic and acute gastritis subjects using numerous tests taken collectively as gold standard. In terms of sensitivities and specificities, the predictive values were greater, with PPVs lower (UBT 0.99 versus 0.98, RUT 0.96 versus 1.0, serology 0.66 versus 0.95, and histology 0.94 versus 0.99). This conclusion could be explained by changes in the quantity and location of biopsies taken across the studies, as well as the fact that chronic gastritis was included among the diagnostic procedures in the referred study. Although this study found very minor difference in the accuracy among all diagnostic tests, the authors suggested RUT to be the first choice as it can be obtained within hours.[82] Similarly our study found RUT be useful in predicting the H-pylori infection in study population. In support to our study another similar study by Bruden, D,[83] aimed to compare the accuracy of ^{13}C urea breath

test (UBT), and immunoglobulin G antibodies to *HP* in serum. They found ^{13}C-UBT to outperform the antibody test for *H. pylori*.

The most important antibiotics in H. pylori treatment are clarithromycin, metronidazole, and amoxicillin. We treated 51.24% with the CMO kit (clarithromycin 250mg BD, metronidazole 400mg TID, Omeprazole 20mg BD)and 48.76% with HP kit (amoxycillin 750mg BD, Tinidazole 500mg BD, Omeprazole 20mg BD). On three-month follow up,37.2% had recurrence of the disease with 33.87% in patients who are treated with CMO kit, and 40.68% among those treated with HP kit (p value 0.439).At the end of 3 months follow up, 46.77% had pain abdomen in the CMO kit group and 40.68% in the HP kit group; 16.13% had nausea in CMO group and 20.34% in the HP kit group, with no statistically significant difference in the symptom recurrence between the two types of treatment (p 0.905). In a study in Karnataka, Shetty, noted increased resistance to metronidazole and levofloxacin, and a modest resistance to clarithromycin resistance.They found that metronidazole-, levofloxacin- and clarithromycin-based triple therapies can not be opted as Ist-line treatment in Karnataka.[94] In a randomized trial comparing Omeprazole + Amoxicillin + Clarithromycin (OAC group) versus Metronidazole (OAM group), clarithromycin was more effective than metronidazole in HP eradication.[75] In a study to compare the efficacy and tolerability of the first-line Helicobacter pylori first-line therapy, Nishizawa found that omeprazole, metronidazole, and amoxicillin was significantly more effective than that composed of lansoprazole, clarithromycin, and amoxicillin, without differences in tolerability.[76] In a pilot prospective open-label randomized controlled trial, comparing treatment with clarithromycin, amoxicillin, and esomeprazole, with levofloxacin, amoxicillin, and esomeprazole, it was found that Clarithromycin is slightly better than levofloxacin in treatment of H. pylori gastric infection, but both regimens show low effectiveness with

suboptimal eradication rates in our selected population.[87]Although in our study we found statistical insignificant results between the two treatment groups, the proportion of recurrence was less in CMO kit treatment.

Table comparing the aim , results and conclusion of various studies to present study

Studies	Aim	Sample size	Study population	Results	Conclusion
Jalalypour et al, [80] 2016	to comparatively evaluate invasive (rapid urease test and polymerase chain reaction) and non-invasive (enzyme-linked immunosorbent assay) tests in detection of infection with cytotoxigenic HP.	105	patients with GU	48.57% showed H-pylori +ve The sensitivity (92.16%) belonged to RUT. The sensitivities of other tests reflected PCR =88.24% and ELISA=90.20% PCR deduced to be the superior specificity (94.44%), and the specificities of the other tests including RUT=90.74 % and ELISA=61.11% the results of PCR and cag A-IgG ELISA depicted high rates of prevalence of cag +ve strain in the study population.	cag A was recommended as a target for PCR and non- invasive ELISA tests for detection of infection with toxigenic strains.
Falsafi, T et al,	Evaluated a homemade	50	30 children 20 adult	53% children wer +ve with	Home made kit was more

(2014)	HpSA kit developed by using the H. pylori antigens from Iranian-isolates for diagnosis of HP in the stool of infected patients			RUT,culture and biopsy Imported kit showed 57% +ve Home made kit showed 50%. Imported kit - Specificity 94%, sensitivity-86% Home made kit specificity 96%, sensitivity 98%	efficient over imported kit and biopsy in diagnosing Hpylori infection among Iran subjects
Cutler et al, (1995)	To compare the diagnostic accuracy of the easily available tests for diagnosis of HP.	268	-	Warthin-Starry staining had a best sensitivity and specificity, although CLO test, UBT, and IgG levels found not statistically different in declaring the accurate diagnosis. The absence of chronic antral inflammation was the best method to exclude infection. Stratification of results by clinical characteristics spotted that UBT & chronic gastric inflammation	The noninvasive UBT and IgG serology test are as accurate in predicting H. pylori status in untreated patients as the invasive tests of CLO and Warthin-Starry.

				found to be best predictors of HP status in older population than sixty years of age. IgA was a better predictor in white population.	
Present study	aimed at identifying the most sensitive and specific test among RUT and ELISA among patients of acid peptic disease attending Endoscopic Unit,	**121**	**-**	All the participants are tested with RUT and ELISA and 87.60% had RUT positive and 86.78% had ELISA positive infection. the RUT had sensitivity of 87.62%in predicting ELISA, specificity was 12.50%, with a total diagnostic accuracy of 77.69%.	RUT was found to be effective method for detection of H-pylori infections. CMO kit treatment was found to have less recurrence rate.

CONCLUSIONS

- This was a prospective study which had majority of subjects aged between 41-60years and male predominance was observed.
- The endoscopy findings found most with antral gastritis followed by gastritis, biliary gastritis, pyloric hyperaemia, diffuse gastritis, diffuse mucosal erythema and mucosal hyperaemia.
- Both RUT and ELISA was positive in majority of the subjects. Our study found RUT to have good accuracy for predicting HP infections.
- After a 3 month of follow up 37.2% had recurrence of the disease where 33.87% of patients with CMO kit, and 40.68% among those treated with HP kit. RUT was found to be effective method for detection of H-pylori infections.
- CMO kit treatment was found to have less recurrence rate.

Limitations:

Limitation of our study is the less number of the patients enrolled.

SUMMARY

There are several methods to detect the HP infection, both invasive and non-invasive, culture, histological staining, RUT, and serological analysis. Early detection and eradication of HP leads to reduce in incidence of complications of APD. This study aimed at identifying the best sensitive and specific test among RUT and ELISA among patients of acid peptic disease attending Endoscopic Unit, Department of General Surgery, R.L Jalappa Hospital and Research Centre, Kolar from March 2021 to September 2021. All the participants are tested with RUT and ELISA and 87.60% had RUT positive and 86.78% had ELISA positive infection.RUT had sensitivity of 87.62% in predicting ELISA, specificity was 12.50%, with a total diagnostic accuracy of 77.69%. We treated 51.24% with the CMO kit and 48.76% with HP kit. On three-month follow up, 37.2% had recurrence of the disease with 33.87% in patients who are treated with CMO kit, and 40.68% among those treated with HP kit (p value 0.439).

BABILOGRAPHY

1.Akbar DH, El Tahawy ATA, Helicobacter pylori infection at a university hospital in Saudi Arabia, prevalence, comparison of diagnostic modalities and endoscopic findings, Indian J PatholMicrobiol 2005; 48(2): 181-185.

2.Palmer KR, Penman ID, Brown SP, Alimentary tract and pancreatic disease. In: Haslett C, Chilvers ER, Boon NA, Colledge NR, Hunter JA. Davidson's Principles and Practice of Medicine 19th ed Edinburgh and Cambridge, London 2002: 747-783.

3.Logan RPH, Walker MM. Epidemiology and diagnosis of Helicobacter pylori, BMJ October 2001; 323: 920-922.

4.Aroori. S. Helicobacter pylori, Belfast City Hospital, Belfast, United Kingdom, Gastroenterology Today 2001 July-Sept 2001; 5: 131-133.

5.Glupezynski Y. Infection with Helicobacter pylori in: Hanser WJ, Sussman M (eds). Topley and Wilson's priciples of Bacteriology, Virology and Immunology. Volume 3 (Bacterial infections), 9th Edition Oxford: 581-591.

6.Windsor HM, O'Rourke Jani. Bacteriology and Taxonomy of Helicobacter pylori. In: Marshall BJ (ed). Gastroenterology. Clinics of North America, Helicobacter pyloriPart I.Saunders 2000; 29 (3): 633-647.

7.Atherton JC, Braser MJ. Helicobacter pylori infection. In: Kasper DI, Fauci AS, Long DL, Braunwald E, Hanser SL, Jameson JL (ed). Harrison's Principles of Internal Medicine 1: 16th edition, Mc Graw Hill 2004: 886-888.

8.Choudhuri G, Samir M. Epidemiology of Helicobacter pylori in India. Indian J Gastroenterol 2000; 19 (suppl.1): 53-55.

9.Berroteran A, Perrone M, Correti M ,Carazza ME, Tambazzi C, Goncalvez R et al. Detection of Helicobacter pylori DNA in the oral cavity and Gastroduodenal system of a Venezuelan population. J Med Microbiol 2002; 51: 764-77

10.Datta S, Chowdhury A, Mukhopadhyay AK, Bhattacharya SK, Berg DE, Nair GB. Molecular and Evolutionary genetics and drug resistance of the gastric pathogen, Helicobacter pylori, Indian J. Med. Res 2002; 115: 73-101.

11.Windsor HM, O'Rourke Jani. Bacteriology and Taxonomy of Helicobacter pylori. In: Marshall BJ (ed). Gastroenterology. Clinics of North America, Helicobacter pylori Part I.Saunders 2000; 29 (3): 633-647.

12.Atherton JC, Braser MJ. Helicobacter pylori infection. In: Kasper DI, Fauci AS, Long DL, Braunwald E, Hanser SL, Jameson JL (ed). Harrison's Principles of Internal Medicine 1: 16th edition, Mc Graw Hill 2004: 886-888.

13.Choudhuri G, Samir M. Epidemiology of Helicobacter pylori in India. Indian J Gastroenterol 2000; 19 (suppl.1): 53-55.

14.Berroteran A, Perrone M, Correti M ,Carazza ME, Tambazzi C, Goncalvez R et al. Detection of Helicobacter pylori DNA in the oral cavity and Gastroduodenal system of a Venezuelan population. J Med Microbiol 2002; 51: 764-770.

15.Molecular and Evolutionary and drug resistance of the gastric pathogen, Helicobacter pylori, Indian J. Med. Res 2002; 115: 73-101.

16.Abdou, A. M., Ahmed, M. M. E., Yamashita, Y., Kim, M., and Abdou, A. M. (2014). Immunoglobulin: A Natural Way to Suppress *H. pylori* in Humans. *Health, 6 (March)*, 781–791.

17.Aguemon BD, Struelens MJ, Massougbodji A, Ouendo EM. (2005): Prevalence and risk-factors for *H. pylori* infection in urban and rural Beninese populations. *Clinical Microbiology Infections*; 11:611–*7.*

18.Aguetoni Cambuí, C., and Mercier, H., (2009); Detection of urease in the cell wall and membranes from leaf tissues of bromeliad species. *Physiologia plantarum*, *136*(1), 86-93**.**

19. Alazmi, W. M., Siddique, I., Alateeqi, N., and Al-Nakib, B. (2010). Prevalence of *Helicobacter pylori* infection among new outpatients with dyspepsia in Kuwait. *BMC gastroenterology*, *10*(1), 14.

20. Allaker RP, Young KA, Hardie JM, Domizio P, and Meadows NJ. (2002); Prevalence of *H. pylori* at oral and gastrointestinal sites in children: evidence for possible oral-to-oral transmission. *Journal of Medical Microbiology*; 51:312–7.

21. Andersen, L.P., and Rasmussen, L. (2009). *H. pylori*-coccoid forms and biofilm formation. *FEMS Immunology and Medical Microbiology*, 56(2), 112-115.

22. Azevedo NF, Almeida C, Cerqueira L, Dias S, Keevil CW, and Vieira MJ. (2007): Coccoid form of *H. pylori* as a morphological manifestation of cell adaptation to the environment. *Applications Environmental Microbiology;* 73:3423–7.

23. Aziz, R. K., Khalifa, M. M., and Sharaf, R. R. (2015). Contaminated water as a source of H. pylori infection: A review. *Journal of advanced research*, *6*(4), 539-547.

24. Bauer, B., and Meyer, T. F. (2011). The Human Gastric Pathogen H. pylori and Its Association with Gastric Cancer and Ulcer Disease, *2011*.

25. Blaser, M. J., and Atherton, J. C. (2004). *H. pylori* persistence: biology and disease. *The Journal of clinical investigation*, 113(3), 321-333.

26. Braga, A. B., Fialho, A. M., Rodrigues, M. N., Queiroz, D. M., Rocha, A. M., and Braga, L. L. (2007). *H. pylori* colonization among children up to 6 years: results of a community-based study from Northeastern Brazil. *Journal of tropical pediatrics*, *53*(6), 393-397**.**

27. Brown LM (2000)."*H. pylori*: epidemiology and routes of transmission". *Epidemiology Revised* 22 (2): 283–97.

28.Huang, Y., Wang, Q. L., Cheng, D. D., Xu, W. T., and Lu, N. H. (2016). Adhesion and Invasion of Gastric Mucosa Epithelial Cells by *H. pylori*. *Frontiers in cellular and infection microbiology*, *6*.

29.Hunt, K., Adamson, J., Hewitt, C., and Nazareth, I. (2011). Do women consult more than men? A review of gender and consultation for back pain and headache. *Journal of health services research & policy*, *16*(2), 108-117.

30.Josenhans C, Eaton KA, Thevenot T, and Suerbaum S (2000). "Switching of Flagellar Motility in *H. pylori* by Reversible Length Variation of a Short Homopolymeric Sequence Repeat in flip, a Gene Encoding a Basal Body Protein". *Infectious Immunology* 68 (8): 4598–603.

31.Kaakoush, N. O., Castaño-Rodríguez, N., Mitchell, H. M., and Man, S. M. (2015). Global epidemiology of Campylobacter infection. *Clinical microbiology reviews*, *28*(3), 687-720.

32.Kahrilas, P. J. (2003). GERD pathogenesis, pathophysiology, and clinical manifestations. *Cleveland Clinic journal of medicine*, *70*(5), S4.

33.Kao, C. Y., Sheu, B. S., and Wu, J. J. (2016). *H. pylori* infection: An overview of bacterial virulence factors and pathogenesis. *Biomedical journal*, *39*(1), 14-23.

34.Kathleen G., Cindy M., Friedmann R (2002), Seroincidence of *H. pylori* infection in a cohort of rural Bolivia. Acquisition and analysis of possible risk factors. *Clinical Infectious Dis*eases; 35: 1059 – 1065.

35.Degnan, A. J., W. C. Sonzogni, and J. H. Standridge. 2003. Development of a plating medium for selection of *Helicobacter pylori* from water samples. Appl. Environ. Microbiol. 69:2914-2918.

36. Dixon, M. F. 2001. Pathology of gastritis and peptic ulceration, p. 459-469. *In* H. L. T. Mobley, G. L. Mendz, and S. L. Hazell (ed.), *Helicobacter pylori* physiology and genetics. American Society for Microbiology, Washington D. C.

37. Dunn, B. E., and S. H. Phadnis. 1998. Structure, function and localization of *Helicobacter pylori* urease. Yale J. Biol. Med. 71:63-73.

38. Dunn, B. E., N. B. Vakil, B. G. Schneider, M. M. Miller, J. B. Zitzer, T. Peutz, and S. H. Phadnis. 1997. Localization of *Helicobacter pylori* urease and heat shock protein in human gastric biopsies. Infect. Immun. 65:1181-1188.

39. Dye, B. A., D. Kruszon-Moran, and G. McQuillan. 2000. *Helicobacter pylori* infection and pathological periodontal conditions among adults in the United States. Amer. J. Epidemiol.151:59.

40. Dye, B. A., D. Kruszon-Moran, and G. McQuillan. 2002. The relationship between periodontal disease attributes and *Helicobacter pylori* infection among adults in the United States. Amer. J. Pub. Health. 92:1809-1815.

41. Eaton, K. A., D. R. Morgan, and S. Krakowka. 1992. Motility as a factor in the colonization of gnotobiotic piglets by *Helicobacter pylori*. J. Med. Microbiol. 37:123-127.

42. Eaton, K. A., S. Suerbaum, C. Josenhans, and S. Krakowka. 1996. Colonization of gnotobiotic piglets by *Helicobacter pylori* deficient in two flagellin genes. Infect. Immun. 64:2445-2448. 25

43. Enroth, H., and L. Engstrand. 1995. Immunomagnetic separation and PCR for the detection of *Helicobacter pylori* in waterand stool specimens. J. Clin Microbiol. 33:2162-2165.

44. Everhart, J. E., D. Kruszon-Moran, G. I. Perez-Perez, T. S. Tralka, and G. McQuillan. 2000. Seroprevalence and ethnic differences in *Helicobacter pylori* infection among adults in the United States. J. Infect. Dis. 181:1359-1363.

45. Gebara, E. C. E., C. Pannuti, C. M. Faria, L. Chehter, M. P. A. Mayer, and L. Lima. 2004. Prevalence of *Helicobacter pylori* detected by polymerase chain reaction in the oral cavity of periodontitis patients. Oral Microbiol. Immunol. 19:277-280.

46. Georgopoulos, S. D., A. F. Mentis, C. A. Spiliadis, L. S. Tzouvelekis, E. Tzelepi, A. Moshopoulos, and N. Skandalis. 1996. *Helicobacter pylori* infection in spouses of patients with duodenal ulcers and comparison of ribosomal RNA gene patterns. Gut. 39:634-638.

47. Giao, M. S., N. F. Azevedo, S. A. Wilks, M. J. Vieira, and C. W. Keevil. 2008. Persistence of *Helicobacter pylori* in heterotrophic drinking-water biofilms. Appl. Environ. Microbiol. 74:5898-5904.

48. Graham, D. Y., A. R. Opekun, M. S. Osato, H. M. T. El-Zimaity, C. K. Lee, Y. Yamaoka, W. A. Qureshi, M. Cadoz, and T. P. Monath. 2004. Challenge model for *Helicobacter pylori* infection in human volunteers. Gut 53:1235-1243.

49. Graham, D. Y., and M. S. Osato. 2000. *H. pylori* in the pathogenesis of duodenal ulcer: Interaction between duodenal acid load, bile, and *H. pylori*. Amer. J. Gastroenterol. 95:87-91.

50. Graham, D. Y., and Y. Yamaoka. 2000. Disease-specific *Helicobacter pylori* virulence factors: The unfulfilled promise. Helicobacter 5:S3-S9.

51. Han, Y. H., W. Z. Liu, Y. Z. Shi, L. Q. Lu, S. D. Xiao, and Q. H. Zhang. 2009. Gene expression profile of *Helicobacter pylori* in response to growth temperature variation. J. Microbiol. 47:455-465.

52. Ishihara, K., T. Miura, R. Kimizuka, Y. Ebihara, Y. Mizuno, and K. Okuda. 1997. Oral bacteria inhibit *Helicobacter pylori* growth. FEMS Microbiol. Lett. 152:355-361.

53. Joshua, G. W. P., C. Guthrie-Irons, A. V. Karlyshev, and B. W. Wren. 2006. Biofilm formation in *Campylobacter jejuni*. Microbiol.-Sgm 152:387-396. 26

54. Kelly, D. J., N. J. Hughes, and R. K. Poole. 2001. Microaerobic physiology: aerobic respiration, anaerobic respiration, and carbon dioxide metabolism, p. 113-124. *In* H. L. T. Mobley, G. L. Mendz, and S. L. Hazell (ed.), *Helicobacter pylori* physiology and genetics. American Society for Microbiology, Washington D.C. 55. Kersulyte, D., H. Chalkauskas, and D. E. Berg. 1999. Emergence of recombinant strains of *Helicobacter pylori* during human infection. Mol. Microbiol. 31:31-43.

56. Kikuchi, S., A. Ohgihara, A. Hasegawa, K. Miki, E. Kaneko, and H. Mizukoshi. 2004. Seroconversion and seroreversion of *Helicobacter pylori* antibodies over a 9-year period and related factors in Japanese adults. Helicobacter. 9:335-341.

57. Kitaeva, L. V., I. A. Mikhailova, D. M. Semov, S. N. Proshin, and V. Y. Kravtsov. 2008. Mucocytes with micronuclei and sowing with the coccoid forms of *Helicobacter pylori* in a mucous membrane of human stomach. Cell Tiss. Biol. 2:170-175.

58. Kivi, M., and Y. Tindberg. 2006. *Helicobacter pylori* occurrence and transmission: A family affair? Scand. J. Infect. Dis. 38:407-417.

59. Kurokawa, M., M. Nukina, and H. Nakanishi. 1999. Resuscitation from the viable but non culturable state of *Helicobacter pylori*. Kan. Zasshi. 73:15-19.

60. Kusters, J. G., M. M. Gerrits, J. A. G. VanStrijp, and C. VandenbrouckeGrauls. 1997. Coccoid forms of *Helicobacter pylori* are the morphologic manifestation of cell death. Infect. Immun. 65:3672-3679.

61. Kusters, J. G., A. H. M. van Vliet, and E. J. Kuipers. 2006. Pathogenesis of *Helicobacter pylori* infection. Clin. Microbiol. Reviews 19:449-490.

62. Li, C., P. R. Musich, T. Ha, D. A. Ferguson, N. R. Patel, D. S. Chi, and E. Thomas. 1995. High prevalence of H*elicobacter pylori* in saliva demonstrated by a novel PCR assay. J. Clin. Pathol. 48:662-666.

63. Liu, Z. F., C. Y. Chen, W. Tang, J. Y. Zhang, Y. Q. Gong, and J. H. Jia. 2006. Gene-expression profiles in gastric epithelial cells stimulated with spiral and coccoid *Helicobacter pylori*. J. Med. Microbiol. 55:1009-1015.

64. Malaty, H. M., A. El-Kasabany, D. Y. Graham, C. C. Miller, S. G. Reddy, S. R. Srinivasan, Y. Yamaoka, and G. S. Berenson. 2002. Age at acquisition of *Helicobacter pylori* infection: a follow-up study from infancy to adulthood. Lancet 359:931-935.

65. Donelli, G., P. Matarrese, C. Fiorentini, B. Dainelli, T. Taraborelli, E. Di Campli, S. Di Bartolomeo, and L. Cellini. 1998. The effect of oxygen on the growth and cell morphology of *Helicobacter pylori*. FEMS Microbiol. Lett. 168:9-15.

66. Dunn, B. E., G. P. Campbell, G. I. Perezperez, and M. J. Blaser. 1990. Purification and characterization of urease from *Helicobacter pylori*. J. Biol. Chem. 265:9464-9469.

67.Matz, C., D. McDougald, A. M. Moreno, P. Y. Yung, F. H. Yildiz, and S. Kjelleberg. 2005. Biofilm formation and phenotypic variation enhance predation-driven persistence of *Vibrio cholerae*. Proc. Nat.Acad. Sci. 102:16819-16824.

68. Melius, E., R. Wierzba, S. Davis, J. Sobel, B. Gold, A. Henderson, and J. Cheek. 2005. Risk factors for *Helicobacter pylori* in a rural community. Unpublished data. Centers for Disease Control, 55th Annual epidemic intelligence service conference, April 24-28, 2006.

69. Merrell, D. S., M. L. Goodrich, G. Otto, L. S. Tompkins, and S. Falkow. 2003. pH-regulated gene expression of the gastric pathogen *Helicobacter pylori*. Infect. Immun. 71:3529-3539.

70. Hazell (ed.), *Helicobacter pylori* physiology and genetics. American Society for Microbiology, Washington D. C.

71. Moss, S. F., and P. Malfertheiner. 2007. *Helicobacter* and gastric malignancies. Helicobacter 12:23-30.

72. Nakamura, H., H. Yoshiyama, H. Takeuchi, T. Mizote, K. Okita, and T. Nakazawa. 1998. Urease plays an important role in the chemotactic motility of *Helicobacter pylori* in a viscous environment. Infect. Immun. 66:4832-4837.

73. Nedenskov, P. 1994. Nutritional requirements for growth of *Helicobacter pylori*. Appl. Environ. Microbiol. 60:3450-3453.

74. Nilsson, H. O., J. Blom, W. Abu Al-Soud, A. Ljungh, L. P. Andersen, and T. Wadstrom. 2002. Effect of cold starvation, acid stress, and nutrients on metabolic activity of *Helicobacter pylori*. Appl. Environ. Microbiol. 68:11-19.

75. Pan, Z. J., R. W. M. van der Hulst, G. N. J. Tytgat, J. Dankert, and A. van der Ende. 1999. Relation between vacA subtypes, cytotoxin activity, and disease in *Helicobacter pylori*-infected patients from the Netherlands. Amer. J. Gastroenterol. 94:1517-1521.

76. Patel SK, Pratap CB, Jain AK, Gulati AK, Nath G. Diagnosis of Helicobacter pylori: what should be the gold standard? World J Gastroenterol. 2014 Sep;20(36):12847–59.

77.Wang Y-K, Kuo F-C, Liu C-J, Wu M-C, Shih H-Y, Wang SSW, et al. Diagnosis of Helicobacter pylori infection: Current options and developments. World J Gastroenterol. 2015 Oct;21(40):11221–35.

78.Reynders MBML, Deyi VYM, Dahma H, Scheper T, Hanke M, Decolvenaer M, et al.

Performance of individual Helicobacter pylori antigens in the immunoblot-based detection of H.pylori infection. FEMS Immunol Med Microbiol [Internet]. 2012 Apr 1;64(3):352–63. Available from: https://doi.org/10.1111/j.1574-695X.2011.00920.x

79.Kosunen TU, Seppäla K, Sarna S, Sipponen P. Diagnostic value of decreasing IgG, IgA, and IgM antibody titres after eradication of Helicobacter pylori. Lancet. 1992;339(8798):893–5.

80.Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, Bazzoli F, et al. Management of Helicobacter pylori infection—the Maastricht IV/Florence consensus report. Gut. 2012;61(5):646–64.

81.Chey WD, Wong BCY, Gastroenterology PPC of the AC of. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Off J Am Coll Gastroenterol ACG. 2007;102(8):1808–25.

82.Reddy BS, Venkateswarlu P, Jyothi BN, Devi AR. Role of H. pylori in Gastroduodenal Diseases. J Evol Med Dent Sci. 2015;4(4):581–7.

83.Jalalypour F, Farajnia S, Somi MH, Hojabri Z, Yousefzadeh R, Saeedi N. Comparative Evaluation of RUT, PCR and ELISA Tests for Detection of Infection with Cytotoxigenic H. pylori. Adv Pharm Bull. 2016;6(2):261.

85.Pourakbari B, Ghazi M, Mahmoudi S, Mamishi S, Azhdarkosh H, Najafi M, et al. Diagnosis of Helicobacter pylori infection by invasive and noninvasive tests. Brazilian J Microbiol. 2013;44(3):795–8.

86.Maimbilly KD, Kundoly VS. Utility of Anti-Helicobacter pylori IgG Estimation in the Diagnosis of Acid Peptic Diseases: A Comparison of Serum IgG Level with Rapid Urease Test. 2019;

87.Rastogi I, Madan SQM, Asthana AK, Thakuria B, Singhal S. Role of ELISA in Diagnosis of Helicobacter Pylori. Exec Ed. 2013;4(4):188.

88.Shetty V, Lamichhane B, Tay CY, Pai GC, Lingadakai R, Balaraju G, et al. High primary resistance to metronidazole and levofloxacin, and a moderate resistance to clarithromycin in Helicobacter pylori isolated from Karnataka patients. Gut Pathog [Internet]. 2019;11(1):21. Available from: https://doi.org/10.1186/s13099-019-0305-x

89.Loghmari H, Bdioui F, Bouhlel W, Melki W, Hellara O, Ben Chaabane N, et al. Clarithromycin versus metronidazole in first-line Helicobacter pylori eradication. Prospective randomized study of 85 Tunisian adults. Tunis Med [Internet]. 2012;90(1):31–5. Available from: http://europepmc.org/abstract/MED/22311445

90.Nishizawa T, Suzuki H, Suzuki M, Takahashi M, Hibi T. Proton pump inhibitor-amoxicillin-clarithromycin versus proton pump inhibitor-amoxicillin-metronidazole as first-line Helicobacter pylori eradication therapy. J Clin Biochem Nutr. 2011;1203270151.

91.Cheha KM, Dib SOA, Alhalabi MM. Pilot study: Comparing efficacy of 14-day triple therapy Clarithromycin versus levofloxacin on eradication of Helicobacter pylori infection in Syrian population single-center experience. Avicenna J Med [Internet]. 2018;8(1):14–7. Available from: https://pubmed.ncbi.nlm.nih.gov/29404268

92. Kasmi H, Doukani K, Ali A, Tabak S, Bouhenni H. Epidemiological Profile of *Helicobacter pylori* Infection in Patients with Digestive Symptoms in Algeria. J Epidemiol Glob Health. 2020 Dec;10(4):293-297. doi: 10.2991/jegh.k.200527.001. Epub 2020 Jun 19. PMID: 32959615; PMCID: PMC7758841.

PATIENT INFORMATION SHEET

STUDYTITLE:"COMPARATIVE STUDY OF ENDOSCOPIC RAPID URI ASE TEST AND SEROLOGY OF HELICOBACTERPYLORI INFECTION IN ACID PEPTIC DISEASE'

Study location:R L Jalappa Hospital and Research Centre attached to Sri Deva rajUrs Medical College, Tamaka, Kolar

•Details of the study – All Patients presenting with acidpeptic disease both OPD and inpatients will Be included in this study. Patients in this study will have to undergo routine investigations Complete hemogram, HIV, HIbsAg. Under strict aseptic precautions endoscopicbiopsy of mucosa of stomach will be obtained and subjected to rapid urease test. Routine blood samples will be drawn and serology demonstration of lmmunoglobulin G antibody will be done by ELISA method. The study expenses will be paid by Dr.Deepthi.

•Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (asperproforma)from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

RUT is one of the sensitive and specific test to detect Hpylori. ELISA is non-invasive method of detecting antibody against Hpylori. All information collected from you will be kept confidential and will not be disclosed to any outsider.Your identity will not be revealed.This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee.

•There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/provide thumb impression only if you voluntarily agree to participate in this study.

•For further information contact:

•Dr DEEPTHI PRADEEP PATIL KULKARNI.

•JUNIOR RESIDENT

•Department Of General Surgery SDUMC,Kolar

•CONTACT NO. : 7411170554

INFORMED CONSENT FORM

•IMr./Mrs have been explained in our own Language about "COMPARATIVESTUDYOF ENDOSCOPICRAPIDUREASETESTAND SEROLOGY OF HELICOBACTER PYLORI INFECTION IN ACID PEPTIC DISEASE"

- •Disease,investigation,duringpre-procedure finding, post-procedure course will be assessed and documented for study purpose
- •I have been explained that my participation in this study is entirelyVoluntary and I can withdraw from the study anytime and this will not affect my relation with my doctor or the treatment for my ailment.
- •I have been explained about the following details and possible benefits i.e early detection and intervention and adversities i.e iatrogenic oesophageal perforation, upperGIbleed, retching and vomiting due to the investigation in my own understandable language
- •I have understood that all my details taken during the study are kept Confidential and while publishing or sharing of the findings my identify will be masked.
- •I have principal investigator mobile number for enquiries.
- •I in my sound mind give full consent to be included in this study.

Signature of patient

NAME:

Signature of witness

NAME:

Left Thumb impression of the patient Left Thumb impression of the witness

ಒಪ್ಪಿಗೆ ಸೂಚಿಸುವ ಪತ್ರ

ಶ್ರೀ/ಶ್ರೀಮತಿ ಆದ ನಾನು "ಕಂಪೆರೇಟಿವ್ ಸ್ಟಡಿ ಬಿಟ್ವೀನ್ ರಾಪಿಡ್ ಯುರೇಸ್" ಪರೀಕ್ಷೆ ಮತ್ತು 'ಸಿರೊಲಜಿ ಆಫ್ ಹೆಲಿಕೊಬ್ಯಾಕ್ಟರ್ ಪೈಲೊರಿ ಇನ್‌ಫೆಕ್ಷನ್ ಇನ್ ಎಸಿಡ್ ಪೆಪ್ಟೆ' ಕಾಯಿಲೆ ಕುರಿತು ಪರೀಕ್ಷೆಗಳನ್ನು ಆರ್.ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ನನ್ನ ಮೇಲೆ ನಡೆಸುವದಕ್ಕೆ ನಾನು ಸ್ವಂತ ತಿಳುವಳಿಕೆಯಿಂದ ಒಪ್ಪಿರುತ್ತೇನೆ.

ಈ ವೈದ್ಯಕೀಯ ಪರೀಕ್ಷೆಗಳನ್ನು ನಿರ್ವಹಿಸಿದಾಗ ಕಂಡು ಬರುವ ಫಲಿತಾಂಶಗಳನ್ನು ಕೇವಲ ಅಭ್ಯಾಸಕ್ಕೋಸ್ಕರ ನಿರ್ವಹಿಸುವುದಾಗಿ ನನಗೆ ಮನವರಿಕೆ ಮಾಡಿ ಕೊಟ್ಟಿರುತ್ತಾರೆ.

ಈ ವೈದ್ಯಕೀಯ ಪರೀಕ್ಷೆಯಲ್ಲಿ ನನ್ನ ಪಾಲುಗೊಳ್ಳುವಿಕೆ ನನ್ನ ಸ್ವಇಚ್ಛೆಯಿಂದ ಇರುತ್ತದೆ. ನಾನು ಈ ಪರೀಕ್ಷೆಯಿಂದ ಯಾವಾಗ ಬೇಕಾದರೂ ಹೊರಬರಹುದು ಮತ್ತು ಹಾಗೆ ಮಾಡುವದರಿಂದ ನನಗೂ ಹಾಗೂ ವೈದ್ಯರಿಗೂ ಇರುವ ಸಂಬಂಧದಲ್ಲಿ ಕಂದು ಉಂಟಾಗುವುದಿಲ್ಲ ಮತ್ತು ನನ್ನ ಶುಶ್ರೂಷೆ ಯಾವುದೇ ಭಾದೆ ಇಲ್ಲದೇ ಮುಂದುವರೆಯುತ್ತದೆ ಎಂದು ನನಗೆ ಮನವರಿಕೆ ಮಾಡಿರುತ್ತಾರೆ.

ಈ ಪರೀಕ್ಷೆಗಳಿಂದ ಆಗುವ ಲಾಭಗಳನ್ನು ಮತ್ತು ಹೊಸ ಆವಿಷ್ಕಾರಗಳನ್ನು ನನಗೆ ತಿಳಿಹೆಳುವುದಾಗಿ ತಿಳಿಸಿರುತ್ತಾರೆ. ಮತ್ತು ಅಭ್ಯಾಸದ ಕುರಿತು ನನ್ನ ಮೇಲೆ ನಡೆಸುವ ಈ ಎಲ್ಲಾ ಪರೀಕ್ಷೆಗಳನ್ನು ನಡೆಸಿರುವುದಕ್ಕೆ ಹಾಗೂ ಪ್ರಚುರಪಡಿಸುವುದರಲ್ಲಿ ನನ್ನ ಹೆಸರು ಮತ್ತು ಗುರುತನ್ನು ಗುಪ್ತವಾಗಿಡುವುದಾಗಿ ನನಗೆ ತಿಳುವಳಿಕೆ ನೀಡಿರುತ್ತಾರೆ.

ನಾನು ಮುಖ್ಯ ಪರೀಕ್ಷಕನಾಗಿದ್ದು, ಯಾವುದೇ ವಿಚಾರಣೆಗೆ ನನ್ನ ಮೊಬೈಲ್ ಸಂಖ್ಯೆ ಇರುತ್ತದೆ.

ನಾನು ನನ್ನ ಪೂರ್ಣ ಪ್ರಜ್ಞೆ ಮತ್ತು ತಿಳುವಳಿಕೆಯಿಂದ ಈ ಮೇಲಿನ ಪರೀಕ್ಷೆಗಳನ್ನು ನಡೆಸಲು ಈ ಒಪ್ಪಿಗೆ ಪತ್ರವನ್ನು ನೀಡಿರುತ್ತೇನೆ.

ರೋಗಿಯ ಸಹಿ:–

ರೋಗಿಯ ಎಡಗೈ ಹೆಬ್ಬೆರಳಿನ ಗುರುತು

ಹೆಸರು:–

ಸಾಕ್ಷಿದಾರರ ಸಹಿ:–

ಸಾಕ್ಷಿದಾರನ ಎಡಗೈ ಹೆಬ್ಬೆರಳಿನ ಗುರುತು

ಹೆಸರು:–

KEY TO MASTER CHART

p	Positive
n	Negative
DM	Diabetes mellitus
HTN	Hypertension
IHD	Ischemic heart disease
N	Normal
D	Days
M	Months
W	Weeks
m	Male
f	Femal
HP kit	Helicobacter pylori kit
CMO kit	Clarithromycin, metronidazole, omeprazole