RESEARCH ARTICLE

PREVALENCE, ENDOSCOPIC AND HISTOPATHOLOGICAL FEATURES OF HELICOBACTER PYLORI (H. PYLORI) INFECTION IN CHRONIC KIDNEY DISEASE (CKD) / END STAGE RENAL DISEASE (ESRD) VERSUS NORMAL POPULATION AT A TERTIARY CARE CENTER IN NORTH INDIA: A CASE CONTROL HOSPITAL BASED STUDY.

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Manuscript Info

Objective: To determine the prevalence of H.Pylori infection, esophagogastroduodenoscopy (EGD) and pathological findings among patients of chronic kidney disease (CKD) versus normal population.

METHODS: This study was carried out from October 2012 to November 2014. Seventy (70) patients of CKD (Cases) underwent upper GI endoscopy (EGD). Endoscopic changes were described and antral gastric biopsies were taken one for Histopathological examination and another for detection of H.Pylori by Rapid urease test (RUT). These findings were compared to findings in 50 consecutive patients (controls) with normal renal function undergoing endoscopy (EGD) for assessment of dyspepsia.

RESULTS: The Endoscopic findings were abnormal in 63 (90%) among cases with antral gastritis as most common finding in 29 (42%) and among controls. EGD findings were abnormal in 39 (78%) patients with antral gastritis in 16(32%)( p-value=0.436). Among 70 cases; RUT was positive in 57(81.4%), Negative in 10(14.3%) and among 50 Controls; RUT was positive in 42 (84%), Negative in 8 (16%) patients (p-value=0.445). On HPE for H.Pylori detection among cases H.Pylori was positive in 52(74.3%), Negative in 15 (21.4%) and among controls H.Pylori was positive in 40(80%), Negative in 9(18%) (P-value=0.698). The HPE findings on microscopy among cases reveals chronic active gastritis as most common finding seen in 51(72.9%) and among controls chronic active gastritis was seen in 34(68%)(p value=0.166).

Conclusion: The prevalence of H.Pylori infection, Endoscopic and pathological findings are same among patients of CKD and Normal population with GI Symptoms with antral gastritis as most common finding on endoscopy. Chronic active gastritis as most common Histopathological diagnosis.

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Introduction:-
Helicobacter Pylori (H. pylori) is a gram negative spiral flagellate bacillus that resides usually in the gastric mucosa and can cause chronic active gastritis, peptic ulcer disease (1). In addition, chronic H. Pylori infection has close associations with gastric hyper-plastic polyps, gastric adenoma, gastric cancer, and gastric mucosa associated lymphoid tissue lymphoma (2, 3, 4, 5, 6). Extra gastrointestinal disorders including chronic idiopathic urticaria, iron deficiency anemia and idiopathic thrombocytopenic purpura (ITP) are also related to H. pylori infection. (7, 8, 9) H. pylori infection is the most common chronic bacterial infection in humans. Estimates indicate that approximately 60% of the world population is colonized with this agent. (10) H. pylori is regarded as an alternating agent, capable to both directly cause a local inflammatory reaction in the gastric and duodenal mucous membranes, and indirectly influence upon the processes of systemic inflammation by way of its effect upon the biochemical components of metabolism (11). With underlying H. pylori infection, apart from direct damage of the stomach, there occurs an abatement of the immune protective properties of the body and a multitude of systemic effects develop that cause adequate reactions on the part of other organs and systems, one of them being the urinary system. There is an evidence of a close interrelation between the development of erosive ulcerous lesions of the gastro duodenal zone and CKD progression. It is necessary to note that the progression of both pathologic processes is mutually dependent. On the one hand, H. pylori infection causes a number of systemic effects (an activation of LPO, pro-inflammatory cytokines, apoptosis; the secretion of biologically active substances that result in an enhancement of ischemia, tissue hypoxia, of affected organs and an activation of the thrombocyctic component of homeostasis) that pathologically affect the kidneys and add to CKD progression. On the other hand, with kidney disease, especially with reduced renal function, COX-1 activation processes also reduce, thus leading to a decrease of the production of prostaglandins which are essential for sustaining both local and systemic hemodynamic in health and, in particular, they take part in the stomach protection from the factors of aggression (an enhancement of the mucus secretion, bicarbonate excretion, etc.). The epidemiological data concerning H. pylori infection in ESRD patients are controversial. The reported frequency of anti H. pylori antibody in patients with renal failure ranges from 21-64% (12, 13, 14). These conflicting results may be related to various factors including the methods of detecting H. pylori infection, the size of the study population, the local prevalence of the organism in the general population, and the various features of the study population. Several studies of the epidemiological features of H. pylori infection have revealed similar findings in end stage renal disease (ESRD) (10). However, higher or lower prevalence rates of H. pylori infection in ESRD patients than the general population has been reported by many other investigators (15). There are different explanations for the variable prevalence; Some investigators focused on the higher concentration of urea in the gastric juice of renal failure patients raising the local gastric pH and providing abundant substrate for H. pylori (16). Some investigators concluded that the higher levels of urea in the mucus of stomach in ESRD patients may result in a lower prevalence of H. pylori colonization in these patients (17). Furthermore, fluctuations in the gastric blood supply, low gastric motility, and hypo as well as hyperchlorhydria have also been proposed for the higher prevalence of H. pylori infection in uremic patients (18). Leffeld et al (14), Lanza et al (13), Fabrizi et al (10) and Hosseini et al (20) found no difference of prevalence of H. pylori infection between patients on Hemodialysis (HD) and healthy controls.

Aims and objectives:-
- To study the prevalence of H. Pylori infection in ESRD patients.
- Endoscopic (EGD) and pathological findings in ESRD patients.
- Compare the prevalence of H.Pylori infection, endoscopic and pathological findings between patients of CKD/ESRD and normal patients with GI symptoms.

Materials and methods:-
The study was conducted in the Department of Nephrology, Gastroenterology and Pathology, Sheri-Kashmir Institute of Medical Sciences (J & K India), over period of two years from October 2012 to November 2014. This study was cleared by Ethical committee as a Case-control study, total of 130 patients were enrolled in this study. Seventy patients of CKD/ESRD with Gastrointestinal symptoms were taken as Cases, Fifty (50) patients with normal kidney function and dyspeptic symptoms were taken as controls. All patients (cases and controls) underwent Esophagogastroduodenoscopy (EGD). EGD findings were noted and two antral biopsies were taken one for Rapid Urease test and another for Histopathological examination (HPE).
Inclusion criteria:-
- All diagnosed cases of CKD/ESRD with upper gastrointestinal tract symptoms like GERD, dyspepsia, belching and APD.

Exclusion criteria:-
- Insufficient mental capacity of patients making him unable to give consent.
- Smoking and alcohol abuse.
- Peptic ulcer disease, upper GI bleed.
- Prior H.Pylori eradication therapy.
- Patients who had received antibiotic, antacid, PPI, Histamine receptor inhibitor therapy during past two months.
- Lack of consent or patient not willing to go for EGD.

Results:-

Demographic profile and other baseline characteristics of the two groups

| Characteristics | Cases (n=70) | Controls (n=50) |
|-----------------|-------------|----------------|
| Mean Age        | 49.9±12.04  | 46.46±10.60    |
| Male            | 44          | 33             |
| Female          | 26          | 17             |
| HYPERTENSION    | 39          | 12             |
| DIABETES        | 11          | 4              |
| ADPKD           | 5           | 0              |
| HTN + DIABETES  | 15          | 2              |
| NORMAL          | 0           | 32             |

Graphic Representation of Mean age between cases and controls.

Endoscopic findings in cases and controls.

| EGD FINDINGS       | Group | Total |
|--------------------|-------|-------|
|                    | Cases | Control |
| Antral Gastritis   | 29    | 45     |
|                    | 42%   | 37.5%  |
| Duodenitis         | 17    | 27     |
|                    | 24%   | 22.5%  |
| Duodenal ulcer     | 10    | 18     |
|                    | 14%   | 15%    |
| ERYTHEMA           | 7     | 12     |
|                    | 10%   | 10%    |
| Normal             | 7     | 18     |
|                    | 10%   | 22%    |
| **Total**          | 70    | 50     | 120   |
Results of H. Pylori detection by Rapid urease test.

| Groups   | Rapid urease Test | Total |
|----------|-------------------|-------|
|          | +ve   | -ve   | Inconclusive |       |
| Cases    | 57    | 10    | 3            | 70    |
|          | 81.4% | 14.3% | 4.3%         | 100.0%|
| Control  | 42    | 8     | 0            | 50    |
|          | 84.0% | 16.0% | 0.0%         | 100.0%|
| Total    | 99    | 18    | 3            | 120   |
|          | 82.5% | 15.0% | 2.5%         | 100.0%|

H. Pylori detection between cases and controls on Histopathology

| H. PYLORI on HPE | Total |
|------------------|-------|
|                  |       |
| Inconclusive     | +ve   | -ve   |
| Group            |       |       |
| Cases            | 3     | 52    | 15    | 70    |
|                  | 4.3%  | 74.3% | 21.4% | 100.0%|
| Control          | 1     | 40    | 9     | 50    |
|                  | 2.0%  | 80.0% | 18.0% | 100.0%|
| Total            | 4     | 92    | 24    | 120   |
|                  | 3.3%  | 76.7% | 20.0% | 100.0%|

Histopathological findings between Cases and control

| HPE FINDINGS      | Group       | Control     | Total |
|-------------------|-------------|-------------|-------|
|                   | Cases       |            |       |
| Chronic active Gastritis | 51          | 34          | 85    |
|                    | 72.9%       | 68.0%       | 70.8% |
| Chronic Inactive Gastritis | 14          | 6           | 20    |
|                    | 20%         | 12%         | 16.7% |
| Acute Gastritis    | 3           | 5           | 8     |
|                    | 4.3%        | 10.0%       | 6.7%  |
| Normal             | 2           | 5           | 7     |
|                    | 2.9%        | 10.0%       | 5.9%  |
| **TOTAL**          | 70          | 50          | 120   |
|                   | 100%        | 100%        | 100%  |

Discussion:-
Endoscopic findings were abnormal in 63 (90%) of Cases (CKD/ESRD) with antral gastritis in 29 (42%), duodenitis in 17 (24%), duodenal ulcer in 10 (14%) and antral erythema in 7 (10%) while as EGD findings were abnormal in 39 (78%) of controls (Normal kidney functions) with Antral gastritis in 16 (32%), duodenitis in 10 (20%), duodenal ulcer 8 (16%) and antral erythema 5 (10%). Although EGD findings are more common in cases than controls, but statistically there was no significant difference with (p-value > 0.05) which is in agreement with published data (22, 24, 26). Detection of H. Pylori by RUT and HPE. Our study demonstrated that among cases Rapid urease test (RUT) was positive in 57 (81.4%), negative in 10 (14.3%) and inconclusive in 3 (4.3%) while as among controls RUT was positive in 42 (84%), negative in 8 (16%) with (p-value=0.329). Histopathological examination (HPE) among cases H. Pylori was positive in 52 (74.3%), negative in 15 (21.4%) and inconclusive in 3 (4.3%) while as among controls H. Pylori was positive in 40 (80%), negative in 9 (18%) and inconclusive in 1 (2%) with (p-value=0.686). From these results we observe that there is no significant difference in prevalence of H. Pylori between cases and controls with (p-value > 0.05) which is consistent with published data (16, 21, 22, 25, 26, 27). Chronic active gastritis was seen in 51 (72.9%), Chronic Inactive Gastritis 14 (20%), Acute Gastritis in 3 (4.3%) and normal findings in 2 (2.9%), while among Controls Chronic active gastritis was present in 34 (68%), Chronic Inactive Gastritis in 6 (12%), Acute gastritis in 5 (10%) and Normal in 5 (10%). From these observations we found that there is no
statistically significant differences in HPE findings between cases and controls with (p-value=0.08) which goes in agreement with published data(16).

In a study Conducted by Shen-Shong Chang, Hsiao-Yun Hu etal (29); stratified the one million study population according to CKD or ESRD. They retrospectively investigated the incidence of H. pylori infection in PUD patients with or without CKD or ESRD between 2000 and 2008 in a nationwide, population-based cohort using data from the Taiwan National Health Insurance Research Database. The comparison cohort consisted of PUD patients without CKD. A logistic regression model was used to calculate the odds ratios (ORs) and 95% confidence intervals, to determine whether the occurrence of H. pylori infection in CKD or ESRD patients with PUD differed from that of PUD patients without CKD. Among the CKD patients, 261 patients had H. pylori-positive and 185 H. pylori-negative peptic ulcers. Among the ESRD patients, 81 had H. pylori-positive and 63 H. pylori-negative peptic ulcers. Among the non-CKD control patients, 1658 patients had H. pylori-positive and 702 H. pylori-negative peptic ulcers. The results revealed a lower H. pylori infection rate in CKD (OR ¼ 0.64, p < 0.001) and ESRD (or ¼ 0.54, p ¼ 0.001) patients with peptic ulcer disease (PUD) than in PUD patients without CKD. (Journal of the Chinese Medical Association 77 -2014). Our study the prevalence of H.Pylori in CKD/ESRD patients was less than the controls but was not statistically significant (p-value=>0.05); reason could be the very less size of our Cohort.

Conclusion:-
The prevalence of H.pylori infection, Endoscopic and pathological findings are same among patients of CKD and Normal population with GI Symptoms with antral gastritis as most common finding on Endoscopy. Chronic active gastritis as most common Histopathological diagnosis.

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