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"PREVALENCE OF H.PYLORI INFECTION IN PEPTIC ULCER DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL, KURNOOL, ANDHRA PRADESH."

Gastroenterology

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ABSTRACT

BACKGROUND: With the outstanding & revolutionary discovery of Helicobacter Pylori(H.Pylori) organism as a causative agent in Peptic Ulcer Disease (PUD), Gastric carcinoma and Malt Lymphoma, there has been a lot of interest generated about H.Pylori in modern times. The role of Non-Steroidal Anti-Inflammatory Drugs(NSAIDs) in the causation of Gastric Ulcer (GU) & Duodenal Ulcer (DU) is also an important point of study now-a-days.

AIM & OBJECTIVES: To assess the prevalence of H.Pylori in patients of PUD diagnosed with Upper Gastro-Intestinal Endoscopic (UGIE) examination.

MATERIALS & METHODS: Total 100 patients of the study underwent UGIE examination. Rapid Urease Test of gastric biopsy specimens of all patients was done for the presence of H.Pylori.

RESULTS: Out of 100 PUD patients, 74 were males & 26 were females. Out of 54 H.Pylori associated PUD patients, 41(76%) were males and 13(24%) were females. About 47% patients had GU, 43% had DU and 10% had both GU & DU. About 34(79%) DU patients were associated with H.Pylori infection. Out of 47 GU patients, 11(23%) are associated with NSAID usage, 7(15%) are associated with H.Pylori & other 53% had associated co-morbidities like HTN, DM, CAD and CLD. Descriptive analysis in percentage was done by using MS Excel.

CONCLUSION: The findings of this study reveal that H.Pylori infection is more common in males than females. High prevalence of H.Pylori infection is seen in DU patients. NSAID abuse was high in GU patients. This study highlights the significance of H.Pylori & NSAID usage in PUD patients.

KEYWORDS

PUD, UGIE, NSAID, H.Pylori, GU, DU

INTRODUCTION

Peptic ulcer disease (PUD) is a mucosal defect that extends to or beyond muscularis mucosa with mucosal damage due to pepsin and gastric acid secretion. The annual prevalence of peptic ulcer disease worldwide based on physician's diagnosis ranged from 0.12%-1.5% and that based on hospitalization data 0.10%- 0.19%.[1]

The complications of this disease include haemorrhage (73%), perforation (9%) and obstruction (3%)[2] which increases the morbidity and mortality and also increases the economic burden.

The most important etiological agents include H.Pylori which colonizes gastric epithelial cells & NSAIDs intake. Annual incidence of H.Pylori in developing nations is about 4-5%. In India, Prevalence of H.Pylori infection ranges from 56- 87%.[3]Prevalence of H.Pylori worldwide is 44.3%[4].

H.Pylori is a Gram negative, micro-aerophilic bacteria which have greater implications in causing many diseases like Peptic ulcer disease, Gastric adenocarcinoma and Gastric MALToma, peptic ulcer disease being the most common among them. Risk of infection is related to poor hygienic conditions and contaminated water is the primary source of infection.

Early diagnosis of H.Pylori by using a high sensitive and specific test like rapid urease test, urea breath test helps in diagnosing and treating patients reducing the risk of complications associated with peptic ulcer disease.

REVIEW OF LITERATURE

Peptic Ulcers are acid and pepsin -induced lesions found in the stomach and duodenum characterized by denuded mucosa with defect extending into the sub-mucosa or muscularis propria.[5]

Prevalence of peptic ulcer increased with age, with a peak prevalence of 28.8% in the fifth decade of life. The life time prevalence of Peptic Ulcer disease was 11.22%.[6]The annual prevalence of PUD based on physician's diagnosis ranged from 0.12%-1.5% and that based on hospitalization data ranged from 0.10%-0.19%.

The mortality risk and need for hospitalization due to PUD has decreased worldwide. This is most likely secondary to decline in H.Pylori infections because of effective treatment and improved hygiene. This trend of decreasing PUD incidence is also attributed to increased availability of over-the-counter acid suppressing medications and caution with NSAID usage.[7,8,9]

Peptic ulcer disease includes Gastric ulcer and Duodenal ulcer of which duodenal ulcer is the pre- dominant lesion. Males are most commonly affected and age distribution is shifting towards the senior citizens.[10,11]

The major etiological factors responsible for peptic ulceration are infection by gram negative pathogen i.e., H.Pylori and the usage of NSAID's. Rarer causes include Gastric ischemia (responsible for stress ulcers that occur in patients with multiple organ failure in ICU's), ZE Syndrome (syndrome of gastric acid hypersecretion caused by gastrin secreting neuro-endocrine tumor), Certain medications (E.g.: Potassium chloride, Bisphosphonates), Infections (CMV, HIV) and Crohn's disease.[12]

Patients with Peptic Ulcers and particularly pyloric channel ulcers may have food-provoked symptoms due to visceral sensitization and gastro duodenal motility. These symptoms include Epigastric pain, Epigastric burning, Bloating, Fullness, Heart burn.[13] Complications of PUD include Haemorrhage (73%) being the most common complication of PUD followed by perforation (9%) and obstruction (3%).

H.Pylori is a spiral shaped, micro- aerophilic, Gram negative bacterium measuring approximately 3.5 microns in length and 0.5 microns in width. High power microscopy reveals that the organism has 2-7 unipolar sheathed flagella which enhances its motility through viscous solutions. In vitro, it is a slow growing organism that can be cultured on blood agar or selective media such as skirrow's media with standard micro-aerobic conditions of 85% N_2, 10% CO_2, 5% O_2 for its growth which occurs at 34^{0}C-40^{0}C with an optimum of 37^{0}C for 3-7 days. H.Pylori grows between pH6-8 with optimal growth at pH6 and has urease activity between pH2.7-7.4 as evidenced by pH rises in bicarbonate buffered solutions of urea.[14]

H.Pylori adhesion protein Bab_2 (BLOOD GROUP antigen binding adhesin) plays a crucial role in bacterial colonisation and in induction of severe gastric infection particularly in combination with the expression of CagA (Cytotoxic associated gene Antigen) and VacA (Vacuolatingcytotoxin Antigen). Genes in Cag pathogenicity island

also contribute to the inflammatory response by initiating a signal transduction cascade, resulting in IL-8 production & Th1 cytokines. Vac causes cytoplasmic vacuolisation in gastric epithelial cells. Vac include $VacAs_1$ which is more virulent and $VacAs_2$ which is lesser virulent (non-toxic).[15]

Triple Positive Strains – Lacks CagA, $BabA_2$, $VacAs_1$.
Expresses $VacAs_2$.
Triple Negative Strains – Lacks $VacAs_2$.
Expresses CagA, $BabA_2$, $VacAs_1$.
Positive strains occur in higher frequency in patients with DU, Atrophic gastritis and Gastric carcinoma**.**

Duodenal ulcer promoting Antigen (DupA) pathogenesis appears to involve the induction of IL-8 production in antrum leading to antrum predominant gastritis, which is well recognized characterstic of DU and it also induces IL-2 production of monocytes.[16]

H.Pylori is a urease producing organism which protects acid sensitive bacterium against gastric juice and provides ammonia for bacterial protein synthesis necessary for colonisation.[17,18]

H.Pylori infection represents key factor in the etiology of various gastrointestinal diseases ranging from chronic active gastritis without clinical symptoms to peptic ulceration, gastric adenocarcinoma and gastric MALToma.[19]

Currently there are various diagnostic methods used for diagnosis of H.Pylori infection. According to traditional classification H.Pylori infection can be diagnosed by non-invasive tests such as H.Pylori antigen in stool specimen, Urease Breath test, serology and invasive tests such as histological examination, culture, RUT, PCR.[20]

RUT is a rapid, inexpensive, simple test with high sensitivity and specificity which provides the indirect evidence of an active infection by identifying the presence of urease in the gastric mucosa. As RUT is an invasive test, it requires a sample of gastric mucosa that is added to the kit containing urea in a well which brings the sample into the contact with urea and 2 drops of saline water is added and the hydrolysis products are NH_3 and Co_2.

$(NH_2)_2CO + 2H_2O \dashrightarrow CO_2 + H_2O + 2NH_3$.
Ammonia alkalizes the medium and change in PH is detected by color change to pink or red at PH 8.4 within 2 hours then the test is considered as positive**.**

Initially, mainstay of therapy included histamine H_2 receptor blockers with an antibiotic. The rate of successful eradication was 73%-84%. With time, this therapy was used less frequently as newer regimens with better outcomes emerged. Bismuth based triple therapy and PPI based triple therapy was introduced which became the most widely used therapies worldwide.

PPI based triple therapy- Omeprazole 20mg twice daily + Amoxicillin 1gm twice daily + Clarithromycin 500 mg, twice daily.

Quadruple therapy - Omeprazole 20 mg once daily + Bismuth subsalicylate 120mg four times daily+ Metronidazole 400 mg thrice daily + Tetracycline 500 mg four times daily.

Non-Bismuth Based Quadruple therapy (Concomitant)- PPI bid + Amoxicillin 1 g bid + Clarithromycin 500 mg bid + Metronidazole 500 mg bid.

Sequential - PPI bid and Amoxicillin 1gm bid, then PPI bid + Clarithromycin 500 mg bid+ Metronidazole 500 mg bid.

LOAD therapy – Levofloxacin 250 mg, QD Omeprazole double dose, QD
Nitrazoxanide(Alinia)500mg bid Doxycycline 100 mgqd.[21,22]

AIMS AND OBJECTIVES

1. To assess or estimate the prevalence of H.Pylori in patients with peptic ulcer disease (Gastric and Duodenal ulcer).
2. To compare the prevalence rates of H.Pylori with that of World wide data.

MATERIALS AND METHODS

This is a cross sectional study with a sample size of 100 patients conducted in a Tertiary Care Hospital, Kurnool, Andhra Pradesh with the study duration of two months from 15/08/2019 to 15/10/2019 after getting Institutional Ethics Committee approval.

All the patients presented to Gastro enterology department with symptoms of dyspepsia were evaluated and detailed history was taken to rule out alarm symptoms like GI bleed, recurrent vomiting, dysphasia, weight loss. Any history of drug intake like aspirin , non steroidal anti inflammatory drugs , steroids and history of addiction to smoking , alcohol were enquired .Presence of any co- morbid illness like coronary artery disease ,chronic liver disease, Diabetes mellitus, Hypertension were noted. An informed consent was taken from all the participants of the study by explaining the procedure before it was done**.**

Patients with Gastric ulcer and duodenal ulcer were included in this study. Exclusion Criteria includes those who are already on Proton Pump Inhibitors/antibiotics within one month, gastrointestinal bleeding and gastrointestinal malignancy. As it is an invasive technique, children below the age of 15 are also excluded from the study.

All the patients were instructed to be overnight fasting for at least 8 hours and they are subjected to upper GI endoscopy (Olympus 150CV scope). Biopsy was taken from antrum and body of stomach (2 each from antrum and stomach) in PUD patient and the sample was placed on Standard Rapid Urease kit.

Later, 2 drops of saline solution is added to kit and then color change to pink/red indicates presence of H.Pylori i.e, positive test. As the H.Pylori is the source of Urease production, it hydrolysis the urea present in the well of standard Rapid Urease kit and give rise to ammonia which changes the pH of medium to alkalinity and this change in pH is detected by an indicator already present in the well. The descriptive analysis in percentage was done by using MS Excel.

OBSERVATIONS AND RESULTS

TABLE 1: The Proportion Of Peptic Ulcer Disease In Study Population (N=100)

Gastric ulcer	47
Duodenal ulcer	43
Gastric and Duodenal ulcer	10

In our study of 100 patients with Peptic Ulcer Disease, 47 patients had Gastric Ulcer, 43 patients had Duodenal Ulcer and 10 had a combination of both Gastric and Duodenal Ulcer.

Graph 1: The Proportion Of Peptic Ulcer Disease In Study Population (N=100)

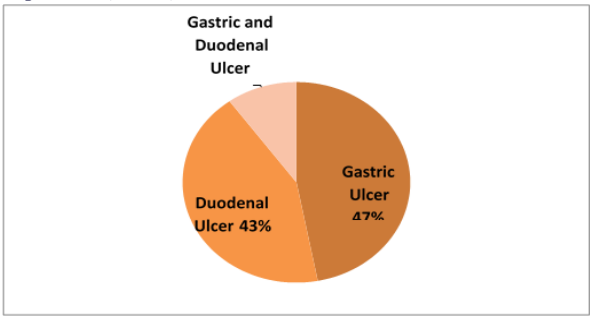

TABLE 2: Associated Factors And Suspected Causes For Each Type Of Peptic Ulcer Disease.

Type of Ulcer	H.Pylori associated	%	NSAID's associated	%	Others	%	H.Pylori + NSAID's associated	%	Total	%
Gastric Ulcer	7	15%	11	23%	25	53 %	4	9%	47	100 %
Duodenal Ulcer	34	79%	8	19%	0	0%	1	2%	43	100 %
Gastric and Duodenal Ulcer	7	70%	2	20%	0	0%	1	10%	10	100 %

The above table shows 79% of duodenal ulcer were associated with H.Pylori and higher incidence of Gastric Ulcer with NSAID's abuse. 7 out of 10 patients with the combination of Gastric and Duodenal Ulcer had H.Pylori infection as the risk factor.

GRAPH 2: Bar Graph Showing Associated Factors and Suspected Causes For Each Type Of Peptic Ulcer Disease

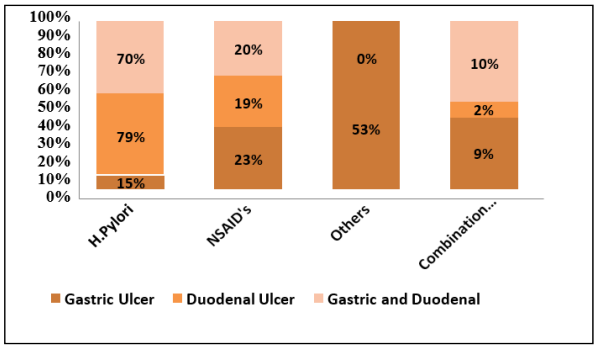

TABLE 3: Gender Distribution of Study Participants

Male	74	74	41	76
Female	26	26	13	24

In our study of 100 peptic ulcer disease patients 74 % were males and 26 % were females. A total of 41 males among 74 were having H pylori associated PUD.

Graph 3: Gender Distribution of Study Participant

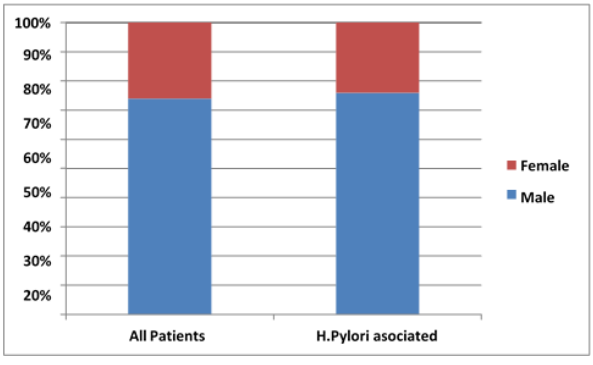

Table 4: Associated Risk Factors Amongst H.Pylori Associated Peptic Ulcer Disease Cases

Smoking	8	15%
Alcohol	1	2%
Smoking + Alcohol	18	33%
None	27	50%
Total	54	100%

15 % of H.pylori patients had associated smoking and 33 % had both smoking and alcohol addiction.

Graph 4: Associated Risk Factors amongst H.Pylori Associated Peptic Ulcer Disease Cases

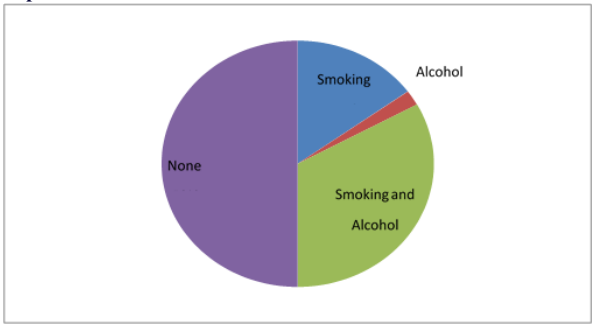

Table 5: Co-Morbidities Associated With Peptic Ulcer Disease

Type of ulcer	Coronary Artery Disease	Hypertension	Diabetes Mellitus	Chronic Liver Disease	Total number of patients
Gastric Ulcer	5	11	7	2	47
Duodenal Ulcer	1	4	3	4	43
Gastric Ulcer +Duodenal Ulcer	0	3	1	0	10

Out of 47 Gastric ulcer patients, 25 of them were associated with co-morbidity illness like Coronary Artery Disease, Hypertension, Diabetes Mellitus and Chronic Liver Disease.

DISCUSSION

In our study of 100 Peptic Ulcer Disease patients, 47% had Gastric Ulcer and 43%had Duodenal Ulcer and 10% had both the combination of Gastric Ulcer and Duodenal Ulcer. This is in concordance with the study done by OP Dhakal, Mona Dhakal et al[23]where they found 50-65% of Duodenal Ulcer and 38-62% of Gastric Ulcer.

Out of 100 Peptic Ulcer Disease patients, 54% of patients were associated with Helicobacter Pylori infection and in comparision with Zamani M et al[4] whose study showed the worldwide prevalence of H. Pylori infection which is about 44.3%.

Our study has 34 Duodenal Ulcer patients associated with H.Pylori infection (79%) out of 43. In Comparision with S.Prasad et al[24] who have done retrospective study on H.Pylori associated Duodenal Ulcers which accounts for 80%-90%.

K.L. Goh et al,[25]in their study showed H.Pylori associated Duodenal Ulcers accounts for 70%-85%.

Around 11(23%), out of 47 patients with Gastric Ulcers are associated with NSAID's usage in our study. Only 15% is associated with H.Pylori and the other 53% may be due to risk of association with other risk factors like Hypertension, Coronary Artery Disease, Diabetes Mellitus, Chronic Liver Disease. In concordance with Allison MC et al[26]whohad done study on Peptic Ulcer showed an association with the NSAID's usage which accounts for 21.7%.

Out of total, 74 were males. Out of 54 H. Pylori associated Peptic Ulcer Disease, 41 were males (76%) in our study. Similar results were shown by MS Khuroo et al[27]where Peptic Ulcer Disease is 2-4 times more commonly seen in males compared to females.

Alcohol and smoking were associated with H. Pylori related Peptic Ulcer Disease in 33% of cases in our study. Li Zhang et al[28] also found that 34.8% of H. Pylori ulcer patients had smoking and alcohol history. Gastric Ulcer patients in our study were associated with Co-morbid illness like Diabetes Mellitus, Hypertension, Chronic Liver Disease, and Coronary Artery Disease which accounts to 53%. Kazuko L. Shem et al[29] also found that there is a positive association between H. Pylori infection and Hypertension, Coronary Artery Disease, Diabetes Mellitus, high serum lipid concentration and stroke.

CONCLUSION

The findings of the study reveal that H.Pylori infections are more common in males than females. Our study demonstrates the high prevalence of H.Pylori infection in patients with Duodenal Ulcer and NSAID's abuse was higher with Gastric Ulcer among the Peptic Ulcer Disease. This study can be extended by comparing the PUD patients with NSAIDs and without NSAIDs. The study duration and sample size can also be increased.

SUMMARY

H.Pylori associated Peptic Ulcer Disease has a tremendous effect on morbidity and mortality in unhygienic conditions, low socio-economic areas especially in developing countries which has a huge cost-burden. Despite substantial advances in diagnosis and treatment, this disease still remains an important clinical problem, largely because of increased prescription, over the counter availability of NSAID's, Aspirin and risk factors like Smoking, Alcohol, co-morbid illness like Chronic Liver Disease, Coronary Artery Disease, Hypertension, Diabetes mellitus. Early diagnosis of H.Pylori using RUT helps in starting the treatment early and prevent the morbidity, mortality and complications.

Conflict of Interest: None declared.

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REFERENCES

1. Ehlin, A. (2003). Prevalence of gastrointestinal diseases in two British national birth cohorts. *Gut*, *52*(8), 1117-1121. https://doi.org/10.1136/gut.52.8.1117
2. Lau, J., Sung, J., Hill, C., Henderson, C., Howden, C., & Metz, D. (2011). Systematic Review of the Epidemiology of Complicated Peptic Ulcer Disease: Incidence, Recurrence, Risk Factors and Mortality. *Digestion*, *84*(2), 102-113. https://doi.org/10.1159/000323958
3. Chey, W., & Wong, B. (2007). American College of Gastroenterology Guideline on the Management of Helicobacter pylori Infection. *The American Journal Of Gastroenterology*, *102*(8), 1808-1825. https://doi.org/10.1111/j.1572-0241.2007.01393.x
4. Zamani, M., Ebrahimtabar, F., Zamani, V., Miller, W., Alizadeh-Navaei, R., Shokri-Shirvani, J., & Derakhshan, M. (2018). Systematic review with meta-analysis: the worldwide prevalence of Helicobacter pylori infection. *Alimentary Pharmacology & Therapeutics*, *47*(7), 868-876. https://doi.org/10.1111/apt.14561
5. CONWAY, J., & MORGAN, D. (2003). Sleisenger and Fordtran s gastrointestinal and liver disease. pathophysiology/diagnosis/management7th ed. vol. 1 and 2 edited by Mark Feldman, Lawrence S. Friedman, and Marvin H. Sleisenger. 1192 pp. (volume 1); 1187 pp. (volume 2). $229.00. Saunders, Philadelphia, Pennsylvania, 2002. ISBN 0-7216-8973-6. Web address for ordering: www.us.elsevierhealth.com. *Gastroenterology*, *125*(5), 1549-1550. https://doi.org/10.1016/s0016-5085(03)01391-x
6. Araki, S., & Goto, Y. (1985). Peptic ulcer in male factory workers: a survey of prevalence, incidence, and aetiological factors. *Journal Of Epidemiology & Community Health*, *39*(1), 82-85. https://doi.org/10.1136/jech.39.1.82
7. Sonnenberg, A. (2013). Review article: historic changes ofHelicobacter pylori-associated diseases. *Alimentary Pharmacology & Therapeutics*, *38*(4), 329-342. https://doi.org/10.1111/apt.12380
8. Lanas, A., & Chan, F. (2017). Peptic ulcer disease. *The Lancet*, *390*(10094), 613-624. https://doi.org/10.1016/s0140-6736(16)32404-7
9. Lanas-Gimeno, A., & Lanas, A. (2017). Risk of gastrointestinal bleeding during anticoagulant treatment. *Expert Opinion On Drug Safety*, *16*(6), 673-685. https://doi.org/10.1080/14740338.2017.1325870
10. Kiær, T., Roin, J., Djurhuus, J., Niclassen, S., & Bonnevie, O. (1985). Epidemiological Aspects of Peptic Ulcer Disease on the Faroe Islands: An Interim Report. *Scandinavian Journal Of Gastroenterology*, *20*(9), 1157-1162. https://doi.org/10.3109/00365528509088888
11. Weil, J., Colin Jones, D., Langman, M., Lawson, D., Logan, R., & Murphy, M. et al. (1995). Prophylactic aspirin and peptic ulcer bleeding. *Gastroenterology*, *108*(4), A256. https://doi.org/10.1016/0016-5085(95)23683-x
12. Hung, L., Ching, J., Sung, J., To, K., Hui, A., & Wong, V. et al. (2005). Long-term Outcome of Helicobacter pylori–Negative Idiopathic Bleeding Ulcers: A Prospective Cohort Study. *Gastroenterology*, *128*(7), 1845-1850. https://doi.org/10.1053/j.gastro.2005.03.026
13. Gururatsakul, M., Holloway, R., Talley, N., & Holtmann, G. (2010). Association between clinical manifestations of complicated and uncomplicated peptic ulcer and visceral sensory dysfunction. *Journal Of Gastroenterology And Hepatology*, *25*(6), 1162-1169. https://doi.org/10.1111/j.1440-1746.2010.06269.x
14. Goodwin, C., & Worsley, B. (1993). MICROBIOLOGY OF HELICOBACTER PYLORI. *Gastroenterology Clinics Of North America*, *22*(1), 5-19. https://doi.org/10.1016/s0889-8553(21)00260-0
15. Kusters, J., van Vliet, A., & Kuipers, E. (2006). Pathogenesis of Helicobacter pylori Infection. *Clinical Microbiology Reviews*, *19*(3), 449-490. https://doi.org/10.1128/cmr.00054-05
16. Hussein, N., Argent, R., Marx, C., Patel, S., Robinson, K., & Atherton, J. (2010). Helicobacter pylori dupAIs Polymorphic, and Its Active Form Induces Proinflammatory Cytokine Secretion by Mononuclear Cells. *The Journal Of Infectious Diseases*, *202*(2), 261-269. https://doi.org/10.1086/653587
17. Labigne, A., Cussac, V., & Courcoux, P. (1991). Shuttle cloning and nucleotide sequences of Helicobacter pylori genes responsible for urease activity. *Journal Of Bacteriology*, *173*(6), 1920-1931. https://doi.org/10.1128/jb.173.6.1920-1931.1991
18. Eaton, K., Brooks, C., Morgan, D., & Krakowka, S. (1991). Essential role of urease in pathogenesis of gastritis induced by Helicobacter pylori in gnotobiotic piglets. *Infection And Immunity*, *59*(7), 2470-2475. https://doi.org/10.1128/iai.59.7.2470-2475.1991
19. Fock, K., Graham, D., & Malfertheiner, P. (2013). Helicobacter pylori research: historical insights and future directions. *Nature Reviews Gastroenterology & Hepatology*, *10*(8), 495-500. https://doi.org/10.1038/nrgastro.2013.96
20. Wang, Y. (2015). Diagnosis ofHelicobacter pyloriinfection: Current options and developments. *World Journal Of Gastroenterology*, *21*(40), 11221. https://doi.org/10.3748/wjg.v21.i40.11221
21. Peura, D. (1998). Helicobacter pylori: rational management options. *The American Journal Of Medicine*, *105*(5), 424-430. https://doi.org/10.1016/s0002-9343(98)00297-6
22. Malfertheiner, P., Megraud, F., O'Morain, C., Bazzoli, F., El-Omar, E., & Graham, D. et al. (2007). Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. *Gut*, *56*(6), 772-781. https://doi.org/10.1136/gut.2006.101634
23. Dhakal, M., & Dhakal, O. (2018). Prevalence of Helicobacter pylori infection & pattern of gastrointestinal involvement in patients undergoing upper gastrointestinal endoscopy in Sikkim. *Indian Journal Of Medical Research*, *147*(5), 517. https://doi.org/10.4103/ijmr.ijmr_1482_16
24. PRASAD, S., MATHAN, M., CHANDY, G., RAJAN, D., VENKATESWARAN, S., RAMAKRISHNA, B., & MATHAN, V. (1994). Prevalence of Helicobacter pylori in southern Indian controls and patients with gastroduodenal disease. *Journal Of Gastroenterology And Hepatology*, *9*(5), 501-506. https://doi.org/10.1111/j.1440-1746.1994.tb01281.x
25. GOH, K. (1997). Prevalence of and risk factors for Helicobacter pylori infection in a multi-racial dyspeptic Malaysian population undergoing endoscopy. *Journal Of Gastroenterology And Hepatology*, *12*(6), S29-S35. https://doi.org/10.1111/j.1440-1746.1997.tb00455.x
26. Allison, M., Howatson, A., Torrance, C., Lee, F., & Russell, R. (1992). Gastrointestinal Damage Associated with the Use of Nonsteroidal Antiinflammatory Drugs. *New England Journal Of Medicine*, *327*(11), 749-754. https://doi.org/10.1056/nejm199209103271101
27. Khuroo, M., Mahajan, R., Zargar, S., Javid, G., & Munshi, S. (1989). Prevalence of peptic ulcer in India: an endoscopic and epidemiological study in urban Kashmir. *Gut*, *30*(7), 930-934. https://doi.org/10.1136/gut.30.7.930
28. Zhang, L., Eslick, G., Xia, H., Wu, C., Phung, N., & Talley, N. (2009). Relationship between Alcohol Consumption and Active Helicobacter pylori Infection. *Alcohol And Alcoholism*, *45*(1), 89-94. https://doi.org/10.1093/alcalc/agp068.
29. Shem, K., & Englander, J. (1998). Symptomatic Helicobacter pylori infection in a neurorehabilitation population. *Archives Of Physical Medicine And Rehabilitation*, *79*(10), 1297-1300. https://doi.org/10.1016/s0003-9993(98)90278-7