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Prevalence of *Helicobacter pylori* Infection in Patients with Type 2 Diabetes Mellitus in Hyderabad, Pakistan

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ABSTRACT

Type 2 diabetes mellitus occurs due to high blood glucose levels owing to insulin resistance or insufficiency. The uncontrolled glycemic levels could impact gastrointestinal inflammation indicating a potential link between T2DM and *Helicobacter pylori* infection. **Objective:** To study the risk factors and prevalence related to *Helicobacter pylori* in T2DM and non-diabetic mellitus patients in Hyderabad Pakistan. **Methods:** A case-control study with a cross-sectional design was done by including 146 participants from Hyderabad, divided into two groups, one with type 2 diabetes mellitus and the other healthy individuals. A 5 mL blood sample was taken to analyze HbA1C levels and *Helicobacter pylori* infection. A questionnaire was used to collect other demographic and clinical information. The significance of differences in the data were evaluated using t-test and chi-square. **Results:** Out of 146 participants, *Helicobacter pylori* was detected in 39.7% (29) of diabetic patients and 45.2% (33) of non-diabetic participants with no statistical significance (p-value > 0.05). *Helicobacter pylori* positive diabetic patients had higher BMI values and were found to be obese as compared to Non-DM *Helicobacter pylori* positive participants. In *Helicobacter pylori* positive non-diabetic patients, it was found statistically significant differences (p-value <0.05) among fast food consumption. Diabetic patients on prolonged use of medications were found to have significant incidence of *Helicobacter pylori* as compared to non-diabetics. **Conclusions:** This study revealed that *Helicobacter pylori* infection was significantly higher in non-diabetic control group than in diabetic patients.

INTRODUCTION

T2DM is specifically a metabolic disorder resulting from high concentration of blood sugar levels because of inadequate amounts of insulin and insulin sensitivity [1]. Over the period of 2016 to 2022, there has been a significant increase in diabetes prevalence in Pakistani adults, escalating from 11.7% to 26.7% which makes up about 33 million cases. It ranks Pakistan third worldwide in prevalence after China and India [2]. *Helicobacter pylori*, commonly referred to as *Helicobacter pylori*, is a gram-negative bacterium, associated with a variety of gastric conditions that range from simple gastritis, through peptic ulcers to malignant gastric disorders [3]. It is a prevalent human bacterial pathogen, especially in low-resource countries and is identified as a global health problem [4]. The presence of *Helicobacter pylori*-induced infection in the intestinal tract can interfere with the lipid and glucose absorption, processes that are already disrupted in diabetes mellitus [5]. *Helicobacter pylori* Infection triggers severe inflammatory response in the stomach, followed by a chronic infiltration of mononuclear cells [6]. Nevertheless, the occurrence of *Helicobacter pylori* is associated with low-grade inflammation and induces molecular mimicry mechanisms. It interrupts the absorption process of drugs and nutrients, potentially affecting the emergence and evolution of several ailments including T2DM [7]. The association between T2DM and *Helicobacter pylori* in this population has been discussed in the previous investigations [8, 9]. Whereas, others show no variation between *Helicobacter pylori* infection and T2DM [10]. It is evident that diabetic patients may be more susceptible to infections due to impaired immunity, reduced gut motility, altered glucose metabolism, and frequent hospital visits [11]. Further, the infection by *Helicobacter pylori* in the intestinal mucosa causes

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inflammation and may interfere with the secretion of gastrin, somatostatin, ghrelin, leptin that may raise the instance of diabetes [12]. Furthermore, some research studies suggest that obesity might be linked to a higher likelihood of Helicobacter pylori colonization, potentially due to decreased stomach movement [10]. More than 58% of people in Pakistan are infected with Helicobacter pylori, and it is common for these individuals to be asymptomatic [13]. Research studies suggest a correlation among diabetes and *Helicobacter pylori* infection, as diabetic individuals demonstrate a higher incidence of *Helicobacter pylori* infection contrary to non-diabetic individuals [14]. The last case control study in the Hyderabad region conducted in the year 2010 explained the positive correlation of *Helicobacter pylori* with the type 2 diabetes [8].

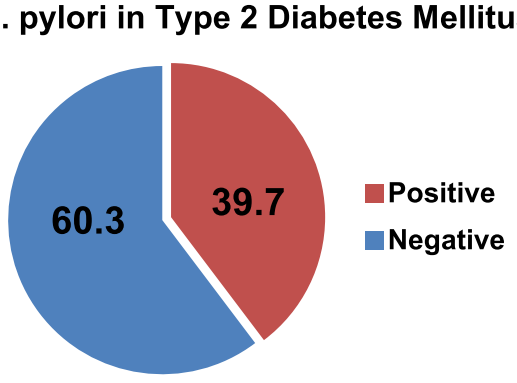
This research aimed to compare the pervasiveness of *Helicobacter pylori* infection among individuals with T2DM and non-diabetic in the Hyderabad region and examine potential risk factors and dietary habits.

METHODS

This research was done among diabetic patients who were admitted at the Liaquat University of Medical Health and Sciences (LUMHS) Hospital Hyderabad during September 2019 to January 2020. The study was started following ethical approval of the ethical committee at the Institute of Biochemistry, University of Sindh (Jamshoro) with a reference number IOB/371/2019. It was a case control study comprising of 146 patients from LUMHS, Civil Hospital Hyderabad. It was utilized that a probability sampling method with a simple random sampling strategy to gather samples at random from 69 men and 77 female patients admitted to LUMHS hospital with diabetes. Two groups were selected in this study, those with T2DM termed as cases and others without diabetes (healthy individuals) referred as controls. It was included those patients who provided consent, had type 2 diabetes since last 3 years, and were between 20 to 60 age group. Whereas, patients who did not provide consent and were on regular long-term Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) were excluded from this study. All the participants of both groups were thoroughly told about the study and sampling procedure. In total, it was enrolled that 73 cases in T2DM group and 73 controls in Non-DM group who belonged to Hyderabad and its adjoining areas representing different socioeconomic and demographic backgrounds. Their demographic and clinical data were collected using a questionnaire. A 5 mL blood sample was withdrawn in EDTA-purple top vacutainers for both HbA1C test and Helicobacter pylori detection. The HbA1C test was performed to diagnose diabetes and values of HbA1C equal to or greater than 6.5% were considered indicative of diabetes. Patients with these values were classified into T2DM group. Whereas in the healthy individuals group (Non-DM), it was also made sure that they were not pre-diabetic or diabetic their HbA1C values were below 5.7%. Moreover, for *Helicobacter pylori* detection, the samples were centrifuged for at least 10 minutes at 3,000 rpm speed to obtain the serum. *Helicobacter pylori* was detected by the use of *Helicobacter pylori* antibody rapid test kit (Sun Diagnostics, USA) according to the manufacturer's instructions. The data were analyzed using Microsoft Excel 2016 and Graph Pad Prism software. Version 8.0. Microsoft Excel was used primarily for the organization of initial demographic data, including age, gender, and other clinical information, along with generating graphs and tables. However, Graph Pad Prism was employed for t-test and chi square test calculations with 0.05 level of statistical significance. The collected sample size was calculated using the Social Science Statistics online tool with an 85% confidence level, 6% error margin, 50% population proportion, and a population size of 1 million.

RESULTS

146 participants were employed in this research with 73 Individuals in each group. In the T2DM group, 45.2% were males and 54.8% were females while, in the non-diabetic group, there were 49.3 were males and 50.7% were females. The statistical data analysis shows no significant difference between the genders of both groups (p-value > 0.05). The participants were divided into three age groups, covering 21-30, 31-40, and 41-50 years. In the T2DM group, 64.4% of patients were 41-50 years old. While, in Non-DM group, highest percentage (37%) was from same 41-50 age group. The participants belonged to mixed socioeconomic status majority belonged to Hyderabad City, and some were from the adjoining areas of Hyderabad. These detailed demographic properties were shown in the supplementary data table S1. As far as Helicobacter pylori infection was concerned, it was found out that the Non-DM group had a higher proportion of infected patients (45. 2%) compared to T2DM patients (39. 7%), but the difference was not statistically significant ($p<0.05$) (Figure 1).



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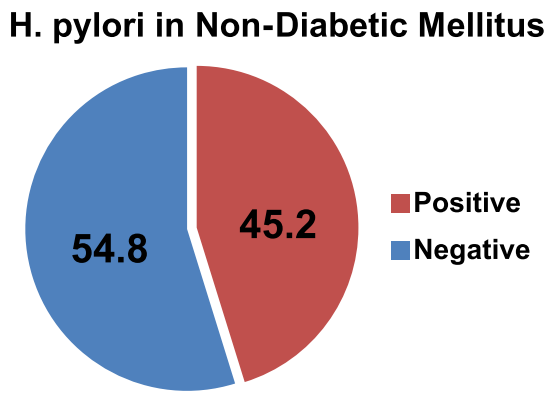

Figure 1: Helicobacter pylori Incidence in T2DM and Non-DM Groups

Gender-wise data analysis shows that *Helicobacter Pylori* infection was higher in females (69% and 51%) both in case of diabetics as well as non-diabetics (as shown in table 1) with no statistical significance. Age wise comparison reveals that *Helicobacter Pylori* infection was predominant in 41-50 age group in case of diabetic patients and 31-40 age group in case of non-diabetics with no statistical difference (Table 1). The diabetic patients enrolled in this research exhibited the mean HbA1C levels of 8.6 ± 1.9%. Conversely, the non-diabetic participants had normal HbA1C levels measuring at 5.11 ± 0.3. Furthermore, The HbA1C levels of diabetic patients were compared between those who tested positive and negative for *Helicobacter Pylori*, with no significant association found (Table 1).

Table 1: Age, Gender and HBA1C Association with *Helicobacter Pylori* Incidence in T2DM and Non-DM

Variables	T2DM N (%) / Mean ± SD		Non-DM N (%) / Mean ± SD		p-value
	Helicobacter Pylori Positive	*Helicobacter Pylori* Negative	*Helicobacter Pylori* Positive	*Helicobacter Pylori* Negative	
Gender					
Male	9 (31%)	24 (54.5%)	16 (48.5%)	42.5% (17)	0.21
Female	20 (69%)	20 (45.5%)	17 (51.5%)	57.5% (23)	
Age					
21-30	2 (6.9%)	4 (9.1%)	7 (21.2%)	19 (47.5%)	0.17
31-40	11 (37.9%)	9 (20.5%)	14 (42.4%)	7 (17.5%)	
41-50	16 (55.2%)	31 (70.4%)	12 (36.4%)	14 (35%)	
HbA1C					
Mean ± SD	8.3 ± 1.8	8.9 ± 2.0	5.2 ± 0.3	5.0 ± 0.3	0.89

All participating individuals had a physical assessment, which involved accessing their height, weight, and waist circumference. The mean weight and waist circumference of T2DM patients was found to be higher than that of non-DM participants, resulting in a complex BMI for the T2DM group (29.6 ± 5 kg/m^2) compared to non-DM participants (23.2 ± 3.6 kg/m^2). Moreover, we found a higher BMI values in *Helicobacter pylori* -negative in both DM and non-DM participants and this was found to be statistically non-significant (p-value > 0.05). Furthermore, these findings indicate a significantly higher (43.8%) incidence of obesity among diabetic patients, with none of the non-diabetic patients being obese (with a statistical significance (p-value < 0.05). These results were shown in supplementary data, Table 2. In the present study, we examined the fast-food intake, smoking, and betel nut chewing history among the participants. We found that fast food intake was higher (93.9%) in Helicobacter pylori positive non-diabetic participants than diabetic patients (58.6%). Additionally, smoking and betel nut chewing habits were also observed and we found no statistical significance (p-value > 0.05) in Non-DM Helicobacter pylori positive group vs DM Helicobacter pylori positive group (Table 2).

Table 2: Fast Food Consumption, Smoking and Betel Nut Chewing History in T2DM and Non-DM with and without *Helicobacter pylori* Infection

T2DM	N (%)	Non-DM	N (%)	p-value
***Helicobacter pylori* Positive**				
Fast Food Consumption	17 (58.6%)	Fast Food Consumption	31 (93.9%)	<0.001
No Fast Food	12 (41.4%)	No Fast Food	2 (6.1%)	
***Helicobacter pylori* Negative**				
Fast Food Consumption	18 (40.9%)	Fast Food Consumption	38 (95%)	<0.001
No Fast Food	26 (59.1%)	No Fast Food	2 (5%)	
***Helicobacter pylori* Positive**				
Smoking	3 (75%)	Smoking	7 (77.8%)	0.9
Betel Nut Chewing	1 (25%)	Betel Nut Chewing	2 (22.2%)	
***Helicobacter pylori* Negative**				
Smoking	4 (66.7%)	Smoking	2 (50%)	0.59
Betel Nut Chewing	2 (33.3%)	Betel Nut Chewing	2 (50%)	

It was categorized patient responses into four (sedentary, active, somewhat active, and low active) groups to assess physical activity. These findings revealed that *Helicobacter pylori* positive diabetic patients led sedentary lifestyle than *Helicobacter pylori* negative. However, it did not find any significant difference between *Helicobacter pylori* infected diabetic and non-diabetic patients' life styles (p-value > 0.05). Further details were provided in supplementary data, Table 3. During this study, it was examined that the patients who were taking medicines for diabetes in DM group, and in non-DM group who used any medication in last 1 month. This study showed that DM patients had a higher prevalence of *Helicobacter pylori* infection who were on prolonged medication (p-value < 0.05). However, in non-DM group did not find any significant difference (p-value > 0.05) (Table 3).

Table 3: Medication History in T2DM and non-DM Participants.

T2DM	*Helicobacter pylori* Positive N (%)	*Helicobacter pylori* Negative N (%)	p-value
Medication Users	51.1% (22)	48.9% (21)	0.03
Non-Users	26.7% (8)	73.3% (22)	
Non-DM	*Helicobacter pylori* Positive	*Helicobacter pylori* Negative	-
Medication Users	55.6% (10)	44.4% (8)	0.3
Non-Users	41.8% (23)	58.2% (32)	

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DISCUSSION

A study was conducted, it included eighty-four diabetes patients (41 males, 43 females) and 92 healthy controls. *H. pylori* status was assessed in serum samples by using ELISA test. Out of the 84 patients, 65 patients (77.4%) were H. pylori positive (+ve) and 19 (22.6%) were *H. pylori* negative (-ve), with the difference being statistically significant. And it was found that diabetes is significantly associated with the infection of *H. pylori* in the studied sample of Iraqi patients [14]. Other studies also reported similar results with no significant link among T2DM and *Helicobacter pylori* infection [15, 16]. However, these results contradict those that report a positive relation between *Helicobacter pylori* infection and T2DM [17]. There was a significant disparity in the prevalence of *Helicobacter pylori* between diabetic and non-diabetic individuals, and can be explained by methodological differences, study population and lifestyle changes [8]. The findings of the study showed a positive significantly higher antibody titer for *H. pylori* infection (IgA > 250) in diabetic patients (50.7%) compared to controls (38.2%) ($P < 0.001$), thus it was concluded that *H. pylori* infections were significantly higher in diabetic patients compared to controls [18]. According to the meta-analysis, it was hypothesized that *Helicobacter pylori* infection might have an association with type 2 diabetes [19]. Given the fact that genetic factors were widely confirmed to affect diabetes development, thus, one must consider the role of family history to assess the strength of the relationship between *Helicobacter pylori* infection and diabetes. As per these results, age and gender did not depict any statistical association with *Helicobacter pylori* incidence. According to several investigations, elevated HbA1C concentrations were directly connected to *Helicobacter pylori* infection [20]. It was compared that mean HbA1C levels among *Helicobacter pylori* positive and *Helicobacter pylori* negative diabetic patients and no significant association was reported. These results were similar to an earlier study that found no relationship between HbA1C levels and *Helicobacter pylori* infection [21]. In a study it was observed that the participants who were Hp-positive and ≥60 years old (OR = 9.16, 95% CI: 3.29–25.52), Hp-positive and obese (OR = 3.35, 95% CI: 1.57–7.14) or Hp-positive and hypertensive (OR = 6.10, 95% CI: 3.10–12.01) had a significantly higher risk for T2DM than those who were Hp-negative and ≤50 years old, Hp-negative and nonobese or Hp-negative and nonhypertensive. Hence it was concluded that Hp infection is associated with an increased risk of T2DM in the middle-aged and elderly Chinese population [22]. The positive association of BMI with *Helicobacter pylori* infection might be attributed to obesity. Metabolic disorders and obesity were correlated with T2DM and *Helicobacter pylori* infection individually, contributing to an increased risk of infection and insulin resistance [23]. These observations revealed that more cases of *Helicobacter pylori* infection were found in patients taking medicines in DM group compared to Non-DM group who took any medicines in last 1 month. This was in concordance with previous findings by other researchers who revealed that incidence of gastrointestinal side effects from metformin was higher in diabetic patients with *Helicobacter pylori* infection compared to those without the infection [24].

CONCLUSIONS

Conclusively, it was found that Helicobacter pylori infection was higher in non-diabetic participants than in diabetic without any significant difference. Higher BMI values in *Helicobacter pylori*-negative in both DM and Non-DM participants were noted with no statistical significance. Whereas higher ratio of obese participants was seen in diabetic group with (p-value < 0.05). Non-diabetic *Helicobacter pylori* positive participants were consuming fast food more frequently compared to diabetic patients and this found to be statistically significant factor contributing to infection (p-value < 0.05). It was also found a greater incidence of *Helicobacter pylori* infection in diabetic patients who were taking medicines which often cause gastrointestinal problems as side effects. It was recommended that diabetic patients regularly monitor their blood glucose levels, exercise regularly to prevent obesity and get tested for infectious diseases including *Helicobacter pylori*.

Authors Contribution

Conceptualization: SA, KM, AA
Methodology: WA, BK
Formal analysis: RZ, KM, AHM, AA
Writing, review and editing: WA, SA, KM

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB *et al.* Pathophysiology of type 2 diabetes mellitus. International Journal of Molecular Sciences. 2020 Aug; 21(17): 6275. doi: 10.3390/ijms21176275.

[2] Azeem S, Khan U, Liaquat A. The increasing rate of diabetes in Pakistan: A silent killer. Annals of

DOI: https://doi.org/10.54393/pbmj.v7i08.1124

Medicine and Surgery. 2022 Jul; 79. doi: 10.1016/j.amsu.2022.103901.

[3] Senchukova MA, Tomchuk O, Shurygina EI. *Helicobacter pylori* in gastric cancer: features of infection and their correlations with long-term results of treatment. World Journal of Gastroenterology. 2021 Oct 10; 27(37): 6290. doi: 10.3748/wjg.v27.i37.6290.

[4] Hassan MN, Arif A, Shahzad MS, Ibrahim M, Rahman HA, Razaq MA *et al*. Global prevalence of *Helicobacter pylori* and its effect on human health. Pure and Applied Biology (PAB). 2020 Feb; 9(1): 936-48. doi: 10.19045/bspab.2020.90098.

[5] Mohammadi SO, Yadegar A, Kargar M, Mirjalali H, Kafilzadeh F. The impact of Helicobacter pylori infection on gut microbiota-endocrine system axis; modulation of metabolic hormone levels and energy homeostasis. Journal of Diabetes & Metabolic Disorders. 2020 Dec; 19(2): 1855-61. doi: 10.1007/s40200-020-00608-y.

[6] Eisa SY, Ahmed KY, El Sayed WE. The relationship between *Helicobacter pylori* infection and control of type 2 diabetes mellitus. The Scientific Journal of Al-Azhar Medical Faculty, Girls. 2020 Jul; 4(3): 388-93. doi: 10.4103/sjamf.sjamf_50_20.

[7] Tsay FW and Hsu PI. *Helicobacter pylori* infection and extra-gastroduodenal diseases. Journal of Biomedical Science. 2018 Dec; 25: 1-8. doi: 10.1186/s12929-018-0469-6.

[8] Devrajani BR, Shah SZ, Soomro AA, Devrajani T. Type 2 diabetes mellitus: A risk factor for *Helicobacter pylori* infection: A hospital based case-control study. International Journal of Diabetes in Developing Countries. 2010 Jan; 30(1): 22. doi: 10.4103/0973-3930.60008.

[9] Memon IA and Ali AA. Prevalence of *Helicobacter Pylori* in Type II Diabetes Mellitus. Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University. 2020 Nov; 16(2): 58-62. doi: 10.48036/apims.v16i2.321.

[10] He C, Yang Z, Lu NH. Helicobacter pylori infection and diabetes: is it a myth or fact?. World Journal of Gastroenterology. 2014 Apr; 20(16): 4607. doi: 10.3748/wjg.v20.i16.4607.

[11] Khanam A, Hithamani G, Naveen J, Pradeep SR, Barman S, Srinivasan K. Management of invasive infections in diabetes mellitus: A comprehensive review. Biologics. 2023 Mar; 3(1): 40-71. doi: 10.3390/biologics3010004.

[12] Okikiade A, Browne-Caesar R, Ogunesan D, Afolayan-Oloye O, Oshobu I, Okundaye D. Conceptualization of Endocrine Function of the Gastrointestinal Tract. Asian Journal of Research and Reports in Gastroenterology. 2022 Jun; 6(2): 16-28.

[13] Hafiz QM, Ikram O, Zia MT, Theba FK, Ikram N, Tariq A. *Helicobacter pylori* infection among type 2 diabetics: A case control study. International Journal of Research in Medical Sciences. 2020 Mar; 8: 1047-50. doi: 10.18203/2320-6012.ijrms20200779.

[14] Al-Rawi NF, Al-Khafaf AH, Ibrahem HA, Hussein NR. Association of *Helicobacter pylori* Infection with type 2 diabetic patients in Dohuk governorate, Iraq. Iraqi Journal of Science. 2022 Jan, 63(1): 62-69. doi: 10.24996/ijs.2022.63.1.7.

[15] Man S, Ma Y, Jin C, Lv J, Tong M, Wang B *et al*. Association between *Helicobacter pylori* Infection and Diabetes: A Cross-Sectional Study in China. Journal of Diabetes Research. 2020 Sep; 2020(1): 7201379. doi: 10.1155/2020/7201379.

[16] Wawro N, Amann U, Butt J, Meisinger C, Akmatov MK, Pessler F *et al. Helicobacter pylori* seropositivity: prevalence, associations, and the impact on incident metabolic diseases/risk factors in the population-based KORA study. Frontiers in Public Health. 2019 Apr; 7: 96. doi: 10.3389/fpubh.2019.00096.

[17] Wan Z, Song L, Hu L, Hu M, Lei X, Huang Y *et al. Helicobacter pylori* infection is associated with diabetes among Chinese adults. Journal of Diabetes Investigation. 2020 Jan; 11(1): 199-205. doi: 10.1111/jdi.13102.

[18] Bener A, Ağan AF, Al-Hamaq AO, Barisik CC, Öztürk M, Ömer A. Prevalence of *Helicobacter pylori* Infection among Type 2 Diabetes Mellitus. Advanced Biomedical Research. 2020 Jan; 9(1): 1-6. doi 10.4103/abr.abr_248_19.

[19] Mansori K, Moradi Y, Naderpour S, Rashti R, Moghaddam AB, Saed L *et al. Helicobacter pylori* infection as a risk factor for diabetes: a meta-analysis of case-control studies. BioMed Central Gastroenterology. 2020 Dec; 20: 1-4. doi: 10.1186/s12876-020-01223-0.

[20] Chen Y, Yang C, You N, Zhang J. Relationship between *Helicobacter pylori* and glycated hemoglobin: a cohort study. Frontiers in Cellular and Infection Microbiology. 2023 Jun; 13: 1196338. doi: 10.3389/fcimb.2023.1196338.

[21] Boyuk B, Kilicaslan G, Celebi A, Atalay H, Mavis O, Ekizoglu I. Dyspeptic symptoms in patients with type 2 diabetes mellitus: *Helicobacter pylori* infection and its associations with metabolic control. Journal of Gastrointestinal and Digestive System. 2017; 7(6): 542. doi: 10.4172/2161-069X.1000542.

[22] Zhou J, Wang X, Liu K, Chen K. Association between *Helicobacter pylori* Infection and the Risk of Type 2 Diabetes Mellitus based on a Middle-Aged and Elderly Chinese Population. Endocrine Journal. 2022; 69(7): 839-46. doi: 10.1507/endocrj.EJ21-0591.

DOI: https://doi.org/10.54393/pbmj.v7i08.1124

[23] Azami M, Baradaran HR, Dehghanbanadaki H, Kohnepoushi P, Saed L, Moradkhani A *et al.* Association of *Helicobacter pylori* infection with the risk of metabolic syndrome and insulin resistance: an updated systematic review and meta-analysis. Diabetology & Metabolic Syndrome. 2021 Dec; 13(1): 145. doi: 10.1186/s13098-021-00765-x.

[24] Huang Y, Sun J, Wang X, Tao X, Wang H, Tan W. *Helicobacter pylori* infection decreases metformin tolerance in patients with type 2 diabetes mellitus. Diabetes Technology & Therapeutics. 2015 Feb; 17(2): 128-33. doi: 10.1089/dia.2014.0203.