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ERADICATION FAILURE OF HELICOBACTER PYLORI IS RELATED TO THE NATIONALITY OF THE UNITED ARAB EMIRATES RESIDENTS IN AL AIN

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ABSTRACT

Helicobacter pylori (H. pylori) infection is the main cause of gastritis, peptic ulcer, gastric cancer and MALT-lymphoma. *H. pylori* eradication has been shown to have a prophylactic effect against gastric cancer. However, the most challenging point in eradicating *H. pylori* is the antibiotic resistance. In the United Arab Emirates, eradication of *H. pylori* is based on a triple therapy regimen comprising a proton pump inhibitor and two antibiotic drugs. The aim of our study is to evaluate the eradication rate of *H. pylori* using this therapy regimen in infected patients (n=1000) from Hospitals and Medical centers in al Ain, United Arab Emirates during 2012. Analysis of the results using the Urea Breath Test shows a 15% eradication failure. Interestingly, Sudanese resident patients in al Ain seem to have the highest eradication failure while Filipino residents patients have a 100 % eradication success. Further studies are needed to explore the antibiotic resistance of *H. pylori* in the United Arab Emirates in order to cure the peptic ulcer and to avoid the progression of the infection to severe carcinogenic disease such as gastric cancer and MALT lymphoma.

Keywords: Helicobacter pylori, United Arab Emirates, Urea Breath test, Eradication, Antibiotic resistance, Peptic ulcer, Gastric cancer.

INTRODUCTION

Helicobacter pylori (H. pylori) was first discovered nearly 30 years ago by Dr. Barry J. Marshall and Dr. J. Robin Warren in 1982. In recognition of their very important discovery, they were awarded the 2005 Nobel Prize for Medicine & Physiology [1]. *H. pylori* is a gram-negative microaerophilic spiral bacterium that colonizes and persists in the human gastric mucosa despite its high acidity. It chronically infects more than half of the world`s population, with a prevalence ranging from 25% in developed countries to more than 90% in developing areas [2,3,4,5,6]. It is the causative agent of chronic gastritis, peptic ulcer, gastric cancer and MALT-lymphoma [7,8]. For this reason, the World Health Organization (WHO) and International Agency for Research on Cancer (IARC) has classified *H. pylori* as a "Class- I-Carcinogen".

Despite declining incidence rates in Western countries, gastric cancer remains the second most common cause of cancer deaths worldwide and *H. pylori* is one of the strongest risk factor for this malignancy [9,10,11,12]. Based on the pattern of cancer in the United Arab Emirates (UAE) referred to Al Ain Hospital since 1997, the incidence of gastric cancer in UAE is unusually high and ranks second in both sexes after breast cancer [13]. Moreover, a former study in the UAE has demonstrated that gastric atrophy, a gastric precancerous lesion, was observed in 54 % of *H. pylori* infected patients [14]. Since the role of *H. pylori* infection in causing gastric cancer was established, the management of *H. pylori* infected patients has become a mandatory.

To date, there is no single standardized treatment regimen for *H. pylori*. Currently, available eradication regimens for *H. pylori* are triple therapy regimens, comprising a proton pump inhibitor (PPI) and two antibiotic drugs for 1 week or 10 days. Clarithromycin, Metronidazole and Amoxicilin are

the most commonly used antibiotics. As a second line therapy, the quadruple therapy which includes additional bismuth salts is prescribed [15,16,17,18].

In UAE, a 2 week triple therapy (omeprazole + clarotromycin + amoxicillin) and a 1 week triple therapy (pantoprazole + claritromycin + amoxicillin) yielded a great rate of eradication in a region of high risk to metronidazole [19,20,21]. However, the emerging resistance of *H. pylori* all over the world to the most commonly used antibiotics (claritromycin + amoxicillin) became the most challenging point in treating *H. pylori* [17,18,22,23,24]. Hopelessly, in UAE, there is limited data regarding the pattern of *H. pylori* antibiotic resistance prevalence. Only two studies conducted by Alfaresi have mentioned the emergence of resistant *H. pylori* to clarithromycin, one of the most common used antibiotics in the course treatment of *H. pylori* [25]. Moreover, they found that the acquired resistance to clarithromycin was correlated to a point mutation (A2143)[26,27]. Even though the finding of these two studies was interesting, however the pattern of *H. pylori* antibiotic resistance is still not well explored in UAE and this can affect significantly the eradication rate of *H. pylori.* In order to highlight more on the *H. pylori* antibiotic resistance in UAE and to urge additional future studies in this domain, we tried in this study to evaluate the eradication rate of *H. pylori* from the antibiotic therapy followed by gastroenterologists from different hospitals and medical centers in UAE. Besides, since UAE is a country harboring multinational resident's patients, and since *H. pylori* exhibit a high level of genetic diversity in the same patients and between patients from different or same geographic repartition [28,29,30,31], we tried also in this study to find if there is any correlation between the nationality, age, gender of patients and eradication failure of *H. pylori.*

MATERIALS AND METHODS

Sample: The clinical data of 1000 patients (474 males and 526 females) residents in Al Ain, UAE from 43 different nationalities (mostly from Egypt, UAE, Sudan, Maroc, Bangladesh, Pakistan Oman, Yemen and Jordan) during 2012 were collected and were enrolled in this study. The age of the patients ranged from 5 to 94 years old. All the patients submitted to the Urea Breath Test (UBT) four weeks after finishing the treatment were already diagnosed infected by *H. pylori*. Moreover, antibiotics and Proton Pump Inhibitor or bismuth preparations were not administered to the patients within 2 weeks prior to the UBT. The study protocol was approved by the Ethics Committee at all hospitals and medical centers enrolled in this study. Written inform consent was obtained from all patients before enrolment.

Urea Breath test: The urea breath test is a rapid non-invasive diagnostic procedure used to identify before and after *H. pylori* treatment. It is based up-on the ability of *H. pylori* to convert urea to ammonia and carbon dioxide. Patients swallow the urea labeled with an uncommon isotope non-radioactive carbon – 13. In the subsequent 10–30 minutes, the detection of isotope-labelled CO2 in exhaled breath indicates that the urea was split; this indicates that urease is present in the stomach and hence that *H. pylori* bacteria are present. In this study, the Tau Kit from Isomed® was applied on the 1000 patients. Patients were considered infected if the percentage of *H. pylori* density is above 50 % based on the indication of the spectrophotometer.

RESULTS AND DISCUSSION

The analysis of the UBT of the 1000 patients treated from the *H. pylori* infection show those 145 patients (59 males and 86 females/ 1000) residents in UAE were still infected by *H. pylori* even after antibiotic treatment. Thus, the eradication failure was estimated 15% (Figure 1). Since

Since *H. pylori* exhibits pronounced genetic diversity between strains isolated from different geographic repartition, and since UAE is a multinational country, we tried in parallel to find if the eradication failure is correlated to the nationality, age and gender of patients.

Correlation between H. pylori eradication failure and patient nationality: Among the 1000 infected patients from 43 nationalities, only 10 nationalities (mostly Egyptian, Sudanese, Pakistani, Bengladeshi, Filipino) in addition to the Emiratie nationality were analyzed in this study because the remaining 32 nationalities were not representatives for the data analysis and not even a frequent resident nationality in UAE (Figure 2). The analysis of the UBT results showed that the *H. pylori* eradication failure range from 0 % to 23 % based on the patient nationality. The highest eradication failure was observed in Sudanese and Bangladeshi patients resident in UAE (23%, 20%, respectively). However, Filipino patient's residents in UAE seem to be the best nationality that responds to the *H. pylori* treatment of UAE since the eradication rate failure for this nationality was 0%**.** Interestingly, we have noticed that patients from Gulf area (Oman, UAE, and Yemen) share almost the same *H. pylori* eradication failure rate (14 %, 13%, 10%) (Figure 3).

2. Correlation between H. pylori eradication failure and age of the patients.

The data analysis shows no correlation between the *H. pylori* eradication failure and the age of the patients.

3. Correlation between H. pylori eradication failure and gender of the patients.

The data analysis shows no correlation between the *H. pylori* eradication failure and the gender of the patients.

The obtained results suggest a clear fact that the *H. pylori* treatment followed in UAE should be updated because it is not effective enough. This may due to many reasons:

1. *H. pylori* strains have developed a resistance to the common antibiotics used in the treatment of *H. pylori* in UAE such as the clarithromycin and this was observed previously by Alfaresi research [14,15,16].
2. *H. pylori* strains have already acquired the resistance to antibiotic in their original country (Sudan and Bangladesh) due to the uncommon use of antibiotic in their country, than they have transmitted this resistance for other strains when they emigrate to UAE.
3. The negligence of patients in completing the course treatment of *H. pylori* has emerged resistant strains to antibiotics.
4. *H. pylori* can revert to a coccoid form under antibacterial agents such as amoxicillin coccoid form meets the necessary criteria for survival. This may explain why in some patients, *H. pylori* were observed even after the antibiotic treatment. Thus, to be successful, treatment must aim not only at eliminating the vegetative form, but also at preventing the development of the coccoid form.

The fact that Sudanese and Bangladeshi patients resist more the eradication of *H. pylori* can be explained by the resistant strains of *H. pylori* emigrating from Sudan and Bangladesh where the use of antibiotic is more common and uncontrolled than in UAE. Moreover, the low socioeconomic levels of these two nationalities in UAE plus their life style could explain why they are resistant to the eradication and why they are infected by more virulent strains.

Further studies are needed to investigate whether the Sudanese and Bangladeshi patients who fail in eradicating *H. pylori* are residents from long time in UAE in order to know whether *H. pylori* have acquired the resistance in UAE or these patients were already harboring resistant strains from their original country. Moreover, we have noticed that patients from UAE, Oman and Yemen share the same eradication failure rate which can be explained by the common geographic environment and life style traditions of these three countries**.** The Filipino patients do not show any *H. pylori* eradication failure even though the Filipino community is wide spread in UAE. Further studies are really needed to compare genetically the *H. pylori* strains of these two nationalities in order to understand the different eradication therapy outcome. The results of this study suggest strongly the establishment of a huge *H. pylori* antibiotic resistance prevalence study in all the country. The study should include strains from the most common nationality resident in UAE. This type of study will give clear answers on *H. pylori* antibiotic resistance prevalence not done yet in UAE at a statistical level. All these data will provide a clear pattern for *H. pylori* treatment in order to cure from peptic ulcer and prevent the progression of the disease toward severs gastrointestinal diseases such as gastric cancer and MALT lymphoma.

CONCLUSION

The data analysis of the Urea Breath Test results performed in hospitals and medical centers in Al Ain, shows that among the 1000 patients treated for *H. pylori*, 15 % presented an eradication failure. Interestingly, the Sudanese resident's patients in UAE were more resistant to *H. pylori* eradication while Filipino resident`s patients in UAE respond better to the *H. pylori* treatment. However, there was no correlation between *H. pylori* eradication failure and the age and gender of the infected treated patients.

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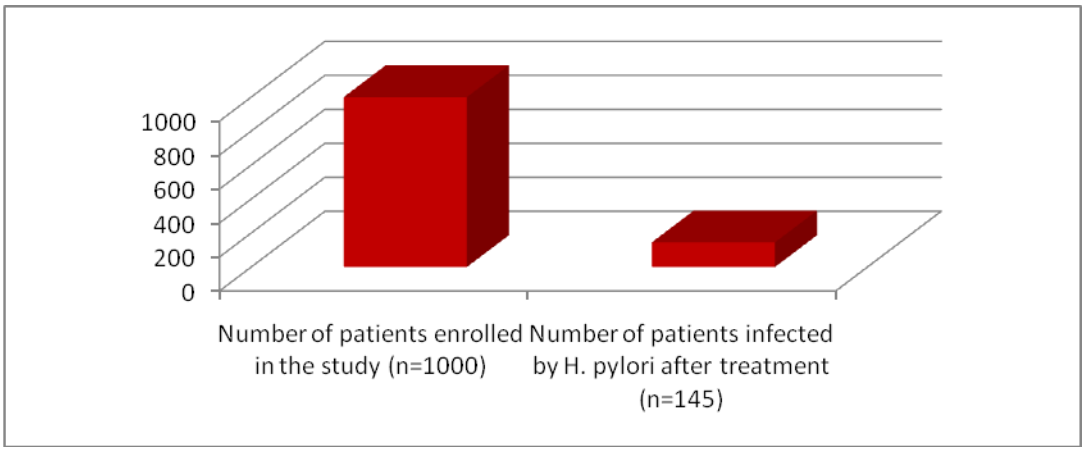

Figure 1. Number of patients still infected by *H. pylori* after treatment.

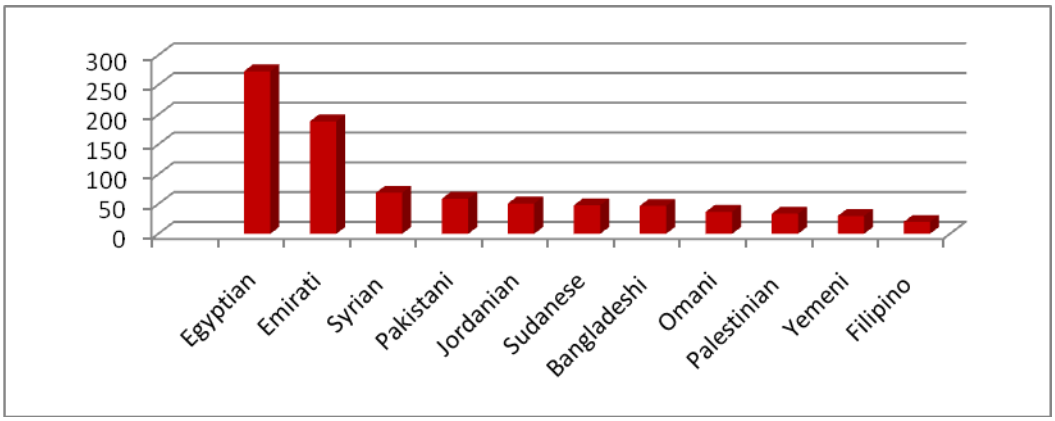

Figure 2. Number of patients enrolled in the study per nationality.

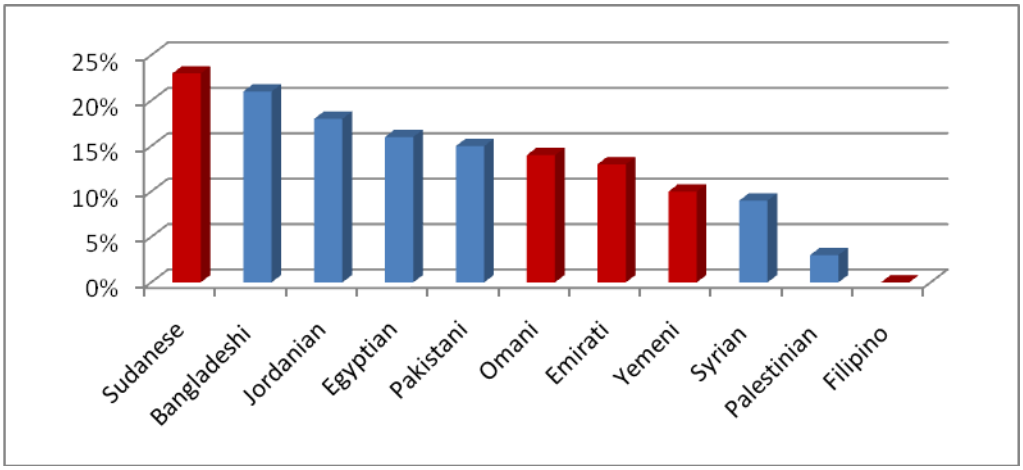

Figure 3. Number of patients infected by *H. pylori* after treatment (per nationality).

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