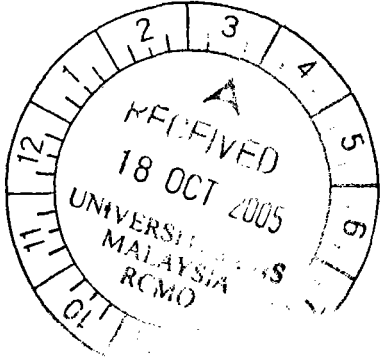**BAHAGIAN PENYELIDIKAN & PEMBANGUNAN
CANSELORI
UNIVERSITI SAINS MALAYSIA**

Laporan Akhir Projek Penyelidikan Jangka Pendek

1)   Nama Penyelidik: Dr. Amir Hakim Basri

Nama Penyelidik-Penyelidik
Lain (Jika berkaitan)   :   ....

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2)   Pusat Pengajian/Pusat/Unit   : Jabatan Perubatan, Pusat Pengajian Sains
Perubatan

3)   Tajuk Projek: The Risk Factors of *Helicobacter pylori* Infection and it's Prevelence
in Adult Orang Asli Population in Gua Musang Area of Kelantan.

No. Geran 304/PPSP/6131251

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4)   (a)   Penemuan Projek/Abstrak
(Perlu disediakan makluman di antara 100 – 200 perkataan di dalam Bahasa Malaysia dan Bahasa Inggeris. Ini kemudiannya akan dimuatkan ke dalam Laporan Tahunan Bahagian Penyelidikan & Pembangunan sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti).

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Bahasa Malaysia – Lampiran A

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Bahasa Inggeris – Lampiran B

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(b) Senaraikan Kata Kunci yang digunakan di dalam abstrak:

Bahasa Malaysia	Bahasa Inggeris
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5) Output Dan Faedah Projek

(a) Penerbitan   (termasuk laporan/kertas seminar)
(Sila nyatakan jenis, tajuk, pengarang, tahun terbitan dan di mana telah diterbit/dibentangkan).   29855

1- Malaysian Medical Journal Volume 59 June 2004 (Supplement).

2- Gastroenterology Tnternational Journal Volume 19 (2004) (Supplement).   29856

3- Journal of Chinese Gastroenterology September 2004.   29857

4- Presentation at 2 Events (1 National & International).

   i – National Gastroenterology Penang Congress Malaysian Society   29858
       Gastroenterology /Hepotology Scientific Meeting June 2004, Young
       Investigator Award 3rd Place.

   Ii – Asia Pacific Digestive Gastroenterology Week Beijing, China   29859
        September 2004. Congress of Gastroenterology.

(b)   Faedah-Faedah Lain Seperti Perkembangan Produk, Prospek Komersialisasi
       Dan Pendaftaran Paten.
       (Jika ada dan jika perlu, sila guna kertas berasingan)

              Tiada
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(c)   Latihan Gunatenaga Manusia

       i)   Pelajar Siswazah: Dr. Amry Abdul Rahim (M. Med)
                                     graduated tahun 2004

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       ii)   Pelajar Prasiswazah: ....

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       iii)   Lain-Lain :   ....

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6. Peralatan Yang Telah Dibeli:

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UNTUK KEGUNAAN JAWATANKUASA PENYELIDIKAN UNIVERSITI

Hasil penyelidikan baik — beberapa prestasi telah dapat dihasilkan

T/TANGAN PENGERUSI
J/K PENYELIDIKAN
PUSAT PENGAJIAN

PROFESSOR ABDUL AZIZ BABA
Chairman of Research & Ethics Committee
School of Medical Sciences
Health Campus
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

USM J/P-06 - 5

ABSTRAK

KAJIAN INFEKSI *H. PYLORI* DI KALANGAN ORANG ASLI DEWASA DI KAWASAN GUA MUSANG, KELANTAN DAN ANALISA FAKTOR RISIKO YANG MEMBAWA KEPADA JANGKITAN.

1. Latar Belakang

Jangkitan bakteria *H. pylori* adalah merupakan jangkitan yang paling biasa dijumpai di kalangan penduduk negara membangun[1]. Bakteria *H. pylori* ini telah pertama kali dijumpai oleh Warren dan Marshall di Australia[2] pada tahun 1982 melalui kajian endoskopi, dan ia dianggap suatu penemuan yang mengubah cara pemikiran terhadap penyakit ulser peptik kerana bakteria ini telah dijumpai di dalam hampir kesemua kajian tisu mukosa gastric penghidap penyakit ulser peptik[3].

Hasil kajian yang dijalankan kemudiannya membuktikan bakteria *H. pylori* adalah punca kepada penyakit ulser peptik[3]. Bagi negara yang membangun seperti Malaysia, jangkitan kuman *H. pylori* didapati di kalangan kesemua kumpulan etnik utama iaitu Melayu, Cina dan India, kadar jangkitan juga berbeza-beza bergantung kepada kumpulan etnik dan lokasi geografi kumpulan etnik berkenaan[7]. Kajian yang telah dilakukan sebelum ini membuktikan bahawa kadar jangkitan bakteria *H. pylori* adalah tinggi di kalangan etnik Cina dan India tetapi rendah di kalangan etnik Melayu[7].

Walaubagaimanapun tiada data yang menguraikan kadar jangkitan bakteria *H. pylori* di kalangan etnik Orang Asli di Semenanjung Malaysia . Juga tiada sebarang maklumat tentang faktor risiko yang boleh menyumbangkan kepada peningkatan kadar jangkitan pada kumpulan dewasa etnik Orang Asli .

2. Objektif

Tujuan utama kajian adalah untuk mengetahui kadar jangkitan bakteria *H. pylori* di kalangan populasi dewasa etnik Orang Asli di kawasan Gua Musang , Kelantan .

Tujuan kedua adalah untuk menganalisa faktor-faktor risiko yang boleh membawa kepada peningkatan kadar jangkitan kuman *H. pylori* .
Objektif sampingan adalah untuk membandingkan kadar jangkitan kuman *H. pylori* pada etnik Orang Asli terhadap kadar jangkitan kuman *H. pylori* pada etnik Melayu , Cina dan India di Semenanjung Malaysia .

3. Methodologi Dan Subjek

Kajian ini dijalankan di kalangan dewasa etnik Orang Asli yang menetap di Jajahan Gua Musang , Kelantan . Jumlah subjek yang diperlukan adalah ditetapkan menggunakan analisa komputer menerusi "Windows Power And Sampling (PS) Software " iaitu dengan ketepatan kajian ditetapkan pada tahap 80.0 % (Power of study) , di mana bilangan subjek adalah 480 . Setelah subjek dikenalpasti mereka akan menjalani proses pemilihan secara

rawak (Randomisation methods) . Subjek yang terpilih diberi penerangan yang menyeluruh berkenaan kajian yang akan dijalankan dan setiap subjek diwajibkan memberi persetujuan secara tandatangan atau cap jari untuk diambilkira dalam kajian ini.

Subjek yang terpilih akan diambil darah untuk tujuan diagnosis secara serologi untuk menentukan jangkitan *H. pylori* . Mereka juga akan ditemuramah berdasarkan borang kaji selidik yang telah disediakan . Sampel darah yang diambil akan dikaji secara ELISA untuk mengesan kehadiran antibodi IgG terhadap infeksi *H. pylori*. Kertas cadangan untuk kajian yang akan dijalankan telah dibentangkan dan diluluskan pada Mesyuarat Majlis Etika Penyelidikan Universiti Sains Malaysia . Disamping itu kelulusan daripada jabatan kerajaan yang berkenaan diperolehi iaitu Jabatan Hal Ehwal Orang Asli (JHEOA) .

4. Keputusan

Sebanyak 480 subjek telah menjalani kajian ini dan didapati bahawa 91 subjek dijangkiti oleh bakteria *H. pylori* (19.0 %) di mana daripada jumlah ini 52 subjek (57.1 %) adalah lelaki dan 39 subjek (42.9 %) adalah perempuan . Daripada jumlah yang mengalami jangkitan *H. pylori* ini , majoritinya iaitu 64 subjek (70.3 %) tidak mempunyai sebarang latar belakang persekolahan , disamping 77 subjek (84.6 %) berkenaan adalah perokok . Walaubagaimanapun kebanyakan subjek berkenaan iaitu 77 subjek (84.6 %) tidak pernah mengambil sebarang minuman keras .

Suatu perkara yang menarik perhatian terhadap subjek yang dijangkiti *H. pylori* adalah kesemua subjek memasak air yang mereka minum dan kebanyakan mereka iaitu 60 subjek (65.9 %) tidak pernah menggunakan ubat penahan sakit bukan steroid (non steroidal anti inflammatory drug) .

Subjek yang dikenalpasti mengalami jangkitan *H. pylori* juga didapati mengamalkan pemakanan makanan eksotik seperti landak dan tapir iaitu seramai 84 (92.3 %) daripada 91 subjek . Mereka juga mempunyai sejarah keluarga menghidapi penyakit ulser peptik iaitu 63 subjek (69.2 %). Majoriti di kalangan mereka menerima bantuan air paip bersih daripada kerajaan iaitu 68 subjek (74.7 %) daripada 91 subjek yang positif terhadap jangkitan *H. pylori* .

5. Kesimpulan

Kadar jangkitan *H. pylori* di kalangan dewasa etnik Orang Asli di Jajahan Gua Musang , Kelantan adalah 19.0 % iaitu suatu kadar yang rendah yang hampir menyamai kadar jangkitan etnik Melayu 22.0 %[10] .

ABSTRACT

STUDY ON RISK FACTORS OF *H. PYLORI* INFECTION AND IT'S PREVALENCE AMONG ADULT ORANG ASLI POPULATION IN GUA MUSANG, KELANTAN .

1. Background

Helicobacter pylori (*H. pylori*) , a bacteria consistently found in the gastric mucosa biopsy of patients suffering dyspeptic symptoms and subsequent investigation by endoscopic biopsy confirmed its presence[1].
H. pylori was first discovered by Warren and Marshall in Australia[2] in 1982 . The discovery was considered a landmark[1] because it changed the way the medical fraternity view and treat peptic ulcer disease particularly since *H. pylori* was subsequently isolated in almost all gastric mocosa biopsies in patients suffering from peptic ulcer disease[3] . Subsequent studies confirmed *H. pylori* as the main contributing factor in the development of peptic ulcer disease[8] .

H. pylori infection was not uncommon in developing country like Malaysia[6]. *H. pylori* infection prevalence among various ethnic communities in Malaysia were well known with variation to the prevalence of infection depending on the ethnicity and geographical location of the affected communities, a high prevalence rate was seen in the Indian and Chinese community but a consistently low prevalence was seen among ethnic Malays[7].

However there was no report regarding the prevalence rate of *H. pylori* infection among the indigenous Orang Asli population as they were not well established. There was also lack of data regarding risk factors that may have important clinical consequences towards the rate of *H. pylori* infection rate in the indigenous Orang Asli community.

2. Objective

The objective of this study was to determine the prevalence rate of *H. pylori* infection among adult indigenous Orang Asli population in the area of Gua Musang, Kelantan.

The second major objective was to determine the various risk factors that contribute to the prevalence of *H. pylori* infection in the Orang Asli community which has important health and socioeconomic impact.

3. Methodology And Subjects

The study involved adult indigenous Orang Asli population in Gua Musang, Kelantan. The initial study proposal was reviewed and approved by the University Sains Malaysia Ethical Committee for research and the consent from the relevant government agency ie. Jabatan Hal Ehwal Orang Asli (JHEOA) was taken.

The study population was calculated using Windows Power And Sampling (PS) software, with the power of the study 80.0%, which calculated the sample size as 480 subjects. The study involved data and blood samples collection upon visits to the indigenous Orang Asli community. The identified adult Orang Asli will undergo a randomisation process and the selected subjects were 'given lengthy information and any queries about the study were fully explained. Each subject was required to give their consent by signature or thumbprint by filling the prepared consent forms.

The selected subjects were then interviewed by the researcher using a set of prepared questionnaire and blood sample were taken for the purposes of detecting the presence of antibody IgG against *H. pylori*. These tests were done using ELISA method of detection[13].

Validation tests for the ELISA serological tests was done based on gastric mucosal histopathological diagnosis by Pathologist from tissue samples taken during gastroscopy examination in University Sains Malaysia. Relevant data were then statistically analysed and the risk factors were reviewed to find any relationship and correlation with the end result of the prevalence study.

4. Results

480 adult subjects from the indigenous Orang Asli population in Gua Musang area were selected through a randomization process.

We found *H. pylori* infection among 19.0 % of subjects , of which males made up 57.1 % and females 42.9 % . 70.3 % of those infected with *H. pylori* had no background of formal education at all with 84.6 % were cigarette smokers . However , the majority of those infected , which was 84.6 % had never consumed alcoholic drinks .

An interesting finding in the study was that all the subjects who tested positive for *H. pylori* boil their drinking water and a further 65.9 % had never taken any non steroidal anti inflammatory drugs in their lifetime .

The subjects positive for *H. pylori* also practiced eating exotic food items which include tapir and porcupine making up 92.3 % .
These subjects also had a positive family history of dyspeptic symptoms which was seen in 69.2 % . 74.7 % of these subjects also received clean piped water supplied by the government .

5. Conclusion

The prevalence rate of *H. pylori* infection among adult indigenous Orang Asli population in Gua Musang , Kelantan was 19.0 % , a low rate of infection comparable with the ethnic Malays of 22.0 % infection rate[10] .

Another epidemiological study confirmed a high prevalence of *H. pylori* infection among children of poor socioeconomic background in poor peri urban area in Bangladesh[33] . This was supported by the high prevalence of *H. pylori* infection in children of West African countries[34] . In China , epidemiological data proved a high rate of *H. pylori* infection among adults with 65.0 % prevalence rate in periurban area of Mainland China[35] .

Most of these data reported utilized serology methods which was the most widely used methods for the diagnosis of *H. pylori* infection in epidemiological studies worldwide[14] . The population tested varied from blood donors , healthy volunteers and patients presented in health centres .

It was assumed that once *H. pylori* infection is acquired , it persisted until old age , then the progressive increase in seroprevalence might be considered as a surrogate for incidence[31]. If these figures were considered among adults in developed countries , the annual incidence of infection appears only to be 1.0 % to 2.0 % only[75] . Results from many of these studies suggested that although the prevalence of infection among adults of developed countries were high , but the incidence is low with rates between 0.5 % to 5.0 % per year[75] .

Eradication of *H. pylori* infection cures peptic ulcer disease and it's complications[3] . Recurrences of *H. pylori* infection after apparently successful eradication may occur but the reinfection rates were low , if it occured at all[2] . The reported recurrence rate varies according to trials reported[2,3].

A similar study in Singapore among the three main ethnic group also showed a comparable results as reported by Kang J Y *et al*[8] in 1990 which proved *H. pylori* infection and gastritis in patients with peptic ulcer and non ulcer dyspepsia showed ethnic differences in Singapore[8] . It was found that the prevalence rate among ethnic Malay was 15.0 % as compared to 38.0 % in Chinese and 35.0 % in Indians[9] .

Goh K L *et al*[11] published a paper in 1996 on the *Helicobacter pylori* infectior among indigenous Kadazan Dusun population in Sabah, East Malaysia which gave evidence for a high prevalence of 75.0 % among the indigenous population[11] . Internationally , epidemiological studies showed evidence of a high prevalence of 85.0 % among indigenous Indian population in Andean mountain of Chile living in a poor socioeconomics condition as compared to 55.0 % infection rate in adult population living in the urban area of the capital Santiago[32] .

These evidence were further supported by international data which describes an overwhelming prevalence of infection among the low socia. economic status and a low level of educational level in the community as these were directly associated with the poor hygiene status of the community[31] .

The infection was more prevalent in the lower socioeconomic groups with risks factors which include poor living standards such as crowded living condition[76] . In the more developed westernised countries , the prevalence is low in children but rises with increasing age paralleling the age related prevalence of chronic gastritis with 20.0 % of those aged 20 years old and 60.0 % among those aged 60 years old[75] .

However in poorer countries like Zaire in Africa , the prevalence of infection is as high as between 70.0 % to 90.0 % in all age groups[30] .
In the developing countries it was found that infection rate was higher in children , 85.0 % of the children below the age of 15 years old were infected and these chronic infection continued until adult life[31] .

Several landmark epidemiological studies were done in Malaysia regarding *H . pylori* infection . Goh K L *et al*[7] reported on the prevalence and risk factors for *H . pylori* infection in a multiracial Malaysian population undergoing endoscopy which had shown a higher prevalence of *H . pylori* infection which was 56.4 % in ethnic Chinese and 51.9 % in Indians , however consistent data had shown a lower prevalence of 31.4 % in ethnic Malays living in Kuala Lumpur area[7] .

This was further supported by the studies done by Uyub A M *et al*[10] in 1994 on *H . pylori* infection in North Eastern Malaysia which showed evidence for an unusually low prevalence of 22.0 % among ethnic Malays as compared to 48.0 % in ethnic Chinese and 57.0 % in Indians[10] .

The specific feature of this organism that allows them to survive and adapt in a highly acidic environment of the stomach is their ability to generate local alkali ammonia by enzymatic cleavage of urea by the enzyme urease[21] . This outstanding adaptation of enzyme urease catalyses urea into ammonia and carbon dioxide . Ammonia production is an important survival mechanism for *H. pylori* due to its hostile acidic gastric environment[21] . Eventhough fastidious , *H. pylori* can be isolated fro gastric mucosa specimen if appropriate methods were used[19].

This is the basis of the diagnostic tests to diagnose the presence of the organisms ie. using urea breath tests . Diagnostic techniques that do not require endoscopy methods include urea breath tests and serological tests using ELISA methods to detect antibody IgG against the organism[13] . All of these diagnostic tests - culture , histopathology , urea breath test and serology if performed appropriately have more than 95.0 % accuracy rate[13-16].

1.3. Epidemiology Of *H. pylori*

H. pylori is considered the most common bacterial infection in the world with an estimated 75.0 % of the population in the developing world infected by the organism even at an early age[2] . However, it must be noted that in the majority of these people , for several decades they were asymptomatic due to the symbiotic nature of the organism which caused nothing more than minor gastritis and inflammation[21] .

The importance of *H. pylori* as a causal agent in the development of peptic ulcer disease is now recognized worldwide and its eradication was considered as an utmost importance in the management of peptic ulcer disease[3]. It has revolusionised the understanding of upper gastrointestinal disease and approach to its management.

In 1975 Howard Steer of Southampton, England first published electronmicrographs of spiral bacteria related to gastritis but he was unable to culture the organism. This started the hypothesis that this bacteria played a significant role in the development of peptic ulcer disease.
In April 1982 the first culture grew the bacteria which was initially known as *Compylobacter pyloridis*, however a genus was created in 1989 naming it *Helicobacter pylori (H. pylori)*[3,4]. It was interesting to note that 18 species of *H. pylori* had been isolated but only one species is seen in humans and the rest were isolated from animals such as birds[21].

1.2. Description Of The Organism

Helicobacter pylori are gram negative curved or spiral, flagellated organism that can be found living in the mucus layer that acts as the protective layer overlying the gastric epithelium. Due to their microaerophilic nature, they survive quite well in the semipermeable mucus layer.
The organism are actively motile with the help of multiple flagella at one pole of its structure[21].

1. INTRODUCTION

1.1. Historical Perspective

Helicobacter pylori (H. pylori) was the commonest bacterial infection in the developing country like Malaysia. It was first discovered in 1982 by Warren and Marshall in Australia[6] and was considered as a landmark discovery because *H. pylori* was consistently found in the biopsy of gastric mucosa of patients with peptic ulcer disease[8]. Subsequently it was proven that *H. pylori* played a direct active role in the pathogenesis of peptic ulcer disease and thus markedly changed the way we manage and treat peptic ulcer disease[3].

H. pylori infection was not uncommon in the Malaysian population, with different rates of infection among the different ethnic groups[6]. The consistent low prevalence of *H. pylori* infection among ethnic Malays and the higher prevalence among ethnic Chinese and Indian are well known[7]. However, there was lack of data on the risk factors and prevalence among adult indigenous Orang Asli population in Malaysia.

Several landmark studies over the past few years had proven the importance of *H. pylori* infection in the development of peptic ulcer disease[1,8]. Warren and Marshall[6] has paved the way in proving the presence of *H. pylori* in the gastric mucosa of patients suffering from chronic active gastritis[1].

We found *H. pylori* infection among 19.0 % of subjects , of which males made up 57.1 % and females 42.9 % . 70.3 % of those infected with *H. pylori* had no background of formal education at all with 84.6 % were cigarette smokers . However , the majority of those infected , which was 84.6 % had never consumed alcoholic drinks .

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Sebanyak 480 subjek telah menjalani kajian ini dan didapati bahawa 91 subjek dijangkiti oleh bakteria *H. pylori* (19.0 %) di mana daripada jumlah ini 52 subjek (57.1 %) adalah lelaki dan 39 subjek (42.9 %) adalah perempuan . Daripada jumlah yang mengalami jangkitan *H. pylori* ini , majoritinya iaitu 64 subjek (70.3 %) tidak mempunyai sebarang latar belakang persekolahan , disamping 77 subjek (84.6 %) berkenaan adalah perokok . Walaubagaimanapun kebanyakan subjek berkenaan iaitu 77 subjek (84.6 %) tidak pernah mengambil sebarang minuman keras .

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Tujuan kedua adalah untuk menganalisa faktor-faktor risiko yang boleh membawa kepada peningkatan kadar jangkitan kuman *H. pylori* . Objektif sampingan adalah untuk membandingkan kadar jangkitan kuman *H. pylori* pada etnik Orang Asli terhadap kadar jangkitan kuman *H. pylori* pada etnik Melayu , Cina dan India di Semenanjung Malaysia .

3. Methodologi Dan Subjek

Kajian ini dijalankan di kalangan dewasa etnik Orang Asli yang menetap di Jajahan Gua Musang , Kelantan . Jumlah subjek yang diperlukan adalah ditetapkan menggunakan analisa komputer menerusi "Windows Power And Sampling (PS) Software " iaitu dengan ketepatan kajian ditetapkan pada tahap 80.0 % (Power of study) , di mana bilangan subjek adalah 480 . Setelah subjek dikenalpasti mereka akan menjalani proses pemilihan secara

ABSTRAK

KAJIAN INFEKSI *H. PYLORI* DI KALANGAN ORANG ASLI DEWASA DI KAWASAN GUA MUSANG, KELANTAN DAN ANALISA FAKTOR RISIKO YANG MEMBAWA KEPADA JANGKITAN.

1. Latar Belakang

Jangkitan bakteria *H. pylori* adalah merupakan jangkitan yang paling biasa dijumpai di kalangan penduduk negara membangun[1]. Bakteria *H. pylori* ini telah pertama kali dijumpai oleh Warren dan Marshall di Australia[2] pada tahun 1982 melalui kajian endoskopi, dan ia dianggap suatu penemuan yang mengubah cara pemikiran terhadap penyakit ulser peptik kerana bakteria ini telah dijumpai di dalam hampir kesemua kajian tisu mukosa gastric penghidap penyakit ulser peptik[3].

Hasil kajian yang dijalankan kemudiannya membuktikan bakteria *H. pylori* adalah punca kepada penyakit ulser peptik[3] . Bagi negara yang membangun seperti Malaysia , jangkitan kuman *H. pylori* didapati di kalangan kesemua kumpulan etnik utama iaitu Melayu, Cina dan India , kadar jangkitan juga berbeza-beza bergantung kepada kumpulan etnik dan lokasi geografi kumpulan etnik berkenaan[7] . Kajian yang telah dilakukan sebelum ini membuktikan bahawa kadar jangkitan bakteria *H. pylori* adalah tinggi di kalangan etnik Cina dan India tetapi rendah di kalangan etnik Melayu[7].

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