

Association of Body Mass Index and  
Gastroesophageal Reflux Disease and its  
Complications.

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By

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#### **IV. ABSTRACT IN MALAY**

Pengenalan: Obesiti adalah penyakit yang semakin epidemik di rantau Asia Pasifik terutamanya di Malaysia. Menurut Kajian Kesihatan dan Morbiditi Kebangsaan 2015, obesiti di Malaysia membentuk 17.7 peratus daripada penduduk manakala mereka yang dikategorikan sebagai berat badan berlebihan adalah sebanyak 30 per cent. Landskap penyakit usus di Asia telah berubah secara drastik disebabkan oleh obesiti, terutamanya penyakit gastroesophageal reflux (GERD) dan komplikasi berkaitan seperti hernia hiatus, refluks esophagitis dan esofagus Barrett. Objektif kajian ini adalah untuk menentukan sama ada wujudnya hubungan antara GERDs komplikasi seperti hernia hiatus, refluks esophagitis dan esofagus Barrett dengan indeks jisim badan melalui esophagogastroduodenoscopy (OGDS) di Hospital Universiti Sains Malaysia (HUSM)

Kaedah: Pesakit GERD dan sistem soal selidik GerdQ yang menjalani Ujian Endoskopi Esofagus (OGDS) di Hospital Universiti Sains Malaysia dari Januari 2014 hingga Mei 2017 telah dikaji semula secara retrospektif. Pesakit telah dibahagikan kepada 2 kumpulan mengikut indeks mereka jisim badan (BMI) berdasarkan WHO (klasifikasi penduduk ASIAN): 1) kumpulan Normal BMI dengan BMI kurang daripada 22.9 kg / (m<sup>2</sup>) (54 pesakit) dan 2) kumpulan Gemuk dengan BMI lebih daripada 23 kg / (m<sup>2</sup>) (73 patients). Faktor-faktor klinikal (umur, jantina, ethnicity, berat badan, ketinggian, BMI dan GerdQ soal pemarkahan) dan penemuan OGDS (hiatus hernia, refluks esophagitis dan esofagus Barrett) telah dianalisis. Kami menggunakan pakar perubatan gastroenterologist untuk menjadi interobserver untuk menganalisis gambar penemuan semasa ujian OGDS. Beliau mengredkan penemuan tersebut berdasarkan darjah keterukan. Hiatus hernia dengan menggunakan Hill Grading, refluks esophagitis menurut klasifikasi Los Angeles dan esofagus Barrett mengikut Prague Classification (C dan M).

Keputusan: Seramai sampel 127 pesakit telah dimasukkan ke dalam kajian ini di mana lelaki penduduk terutamanya ditawan dengan 57,48% berbanding dengan penduduk wanita yang merupakan 42.52%. Umur min sampel berumur 43,91 tahun. Obesiti seperti dalam BMI > 30 kg / m<sup>2</sup> secara statistik signifikan ( $p = 0.028$ ) dengan hernia Hiatus berdasarkan Hill Grading dan persatuan statistik yang signifikan ( $p = 0.015$ ) dengan esophagitis refluks berdasarkan klasifikasi LA. Walau bagaimanapun, obesiti adalah persatuan secara statistik tidak signifikan ( $p = 0,704$ ) dengan Barrett esofagus histologi. pesakit obes juga menunjukkan persatuan secara statistik tidak signifikan dengan esofagus Barrett endoscopically berdasarkan klasifikasi Prague daripada lilitan daripada metaplasia (C) ( $p = 0,660$ ) dan maksimum sejauh mana metaplasia (M) ( $p = 0,524$ ). Ramalan risiko menunjukkan statistik hubungan yang signifikan ( $p = 0.002$ ) antara Indeks Jisim Badan (BMI) dengan esophagitis refluks berdasarkan (LA Classification). Mereka dalam kumpulan obes mempunyai Odds 3.6 kali lebih tinggi untuk mendapatkan gejala esophagitis refluks berbanding mereka dalam kumpulan BMI normal.

Kesimpulan: Pesakit obes mempunyai kaitan lansung dengan hernia hiatus dan refluks esophagitis, tetapi tidak untuk esofagus Barrett. Kemungkinan risiko antara Indeks Jisim Badan (BMI) adalah dengan esophagitis refluks berdasarkan (Pengelasan LA) dalam kumpulan obes mempunyai 3.6 kali gejala berbanding mereka dalam kumpulan BMI normal. Dalam pesakit obes yang mempunyai simptom GERD yang teruk dan berterusan seperti memuntahkan dan pedih ulu hati walaupun pada rawatan perubatan (Proton pam perencat) perlu menjalani pembedahan pembetulan bariatric. Kami mencadangkan bahawa, laparoscopi Roux En Y Gastrik prosedur bypass telah ditunjukkan untuk menjadi kaedah yang lebih berkesan untuk mengurangkan gejala GERD kerana ia memainkan peranan dalam penurunan berat badan yang ketara berbanding dengan laparoscopi gastrectomy.

## V. ABSTRACT IN ENGLISH

**Introduction:** Obesity is a fast-emerging epidemic in the Asia-Pacific region especially in Malaysia. According to National Health and Morbidity Survey of 2015, obesity in Malaysians make up 17.7 per cent of the population while those who are categorised as overweight make up 30 per cent..The landscape of gut diseases in Asia has been drastically changed by obesity, especially the gastroesophageal reflux disease (GERD) and its complication such as hiatus hernia, reflux esophagitis and Barrett's esophagus. The objectives of this study are to determine the association between GERDs complications such as hiatus hernia, reflux esophagitis and Barrett's esophagus with body mass index via esophagogastroduodenoscopy (OGDS) in Hospital Universiti Sains Malaysia (HUSM).

**Methods:** GERD patients with GerdQ questionnaire scoring system who had underwent OGDS in Hospital Universiti Sains Malaysia from January 2014 to Mei 2017 were reviewed retrospectively. The patients were divided into 2 groups according to their body mass index (BMI) based on WHO (ASIAN population classification) : 1) Normal BMI group with BMI less than 22.9 kg / (m<sup>2</sup>) (54 patients) and 2) Obese group with the BMI more than 23 kg / (m<sup>2</sup>) (73 patients). The clinical factors (age, gender, ethnicity, weight, height, BMI and GerdQ questionnaire scoring) and OGDS findings (hiatus hernia, reflux esophagitis and Barrett's esophagus) were analyzed. We used a gastroenterologist to be the interobserver to analyse the OGDS films.He graded the findings based to it severity. Hiatus hernia by using Hill's Grading, reflux esophagitis according to Los Angeles classification and Barrett's esophagus according to Prague Classification (C and M).

**Results:** A total sample of 127 patients were included in this study where male population predominantly conquered with 57.48% compared to female population which is 42.52% . The

mean age of the samples were 43.91 years old. Obesity as in BMI > 30 kg/m<sup>2</sup> were statistically significant association (p = 0.028) with Hiatus hernia based on Hill's Grading and statistically significant association (p = 0.015) with reflux esophagitis based on LA classification. However, obesity was statistically insignificant association (p = 0.704) with Barrett's esophagus histologically. Obese patient also showed statistically insignificant association with Barrett's esophagus endoscopically based on Prague classification of Circumferential of metaplasia (C) (p = 0.660) and Maximum extend of metaplasia (M) (p = 0.524). The risk prediction shows statistically significant association (p = 0.002) between Body Mass Index (BMI) with reflux esophagitis based (LA Classification). Those in obese group have 3.6 times higher Odds to get reflux esophagitis symptoms compared to those in normal BMI group.

Conclusion: Obese patient has association with hiatus hernia and reflux esophagitis, but not for the Barrett's esophagus. The risk prediction association between Body Mass Index (BMI) is with Reflux Esophagitis based (LA Classification) in obese group have 3.6 times symptoms compared to those in normal BMI group. In obese patient with severe and persistent GERD symptoms such as regurgitation and heartburn despite on medical treatment (Proton pump inhibitor) should undergo bariatric surgical correction. We suggest that, Laparoscopic Roux En Y Gastric bypass procedure have shown to be more effective procedure for alleviating the symptoms of GERD as it plays a role in significant weight loss compare with laparoscopic sleeve gastrectomy patient.

## **1-INTRODUCTION**

### **1.1- INTRODUCTION**

Obesity is a fast-emerging epidemic in the Asia-Pacific region, with numbers paralleling the rising global prevalence within the past 30 years. The landscape of gut diseases in Asia has been drastically changed by obesity, especially the gastroesophageal reflux disease (GERD) (Lee et al., 2015). It is a common digestive disorder that affects the lower esophageal sphincter (LES), that has been linked to obesity. The symptoms are heartburn and regurgitation which causes the mucosal damage. Oesophagogastroduodenoscopy (OGDS) procedure is one of common procedure in Malaysia usually done by surgeons or gastroenterologist. It is normally done as an outpatient procedure in patient with GERD symptoms.

Malaysia, known as Asia's fattest country, recorded an increase in its obesity rate in year 2015, with the latest statistics showing that the overweight and the obese make up nearly half of its 30 million population. According to the National Health and Morbidity Survey of 2015, obese Malaysians make up 17.7 per cent of the population while those who are categorised as overweight make up 30 per cent. The obesity prevalence have increased drastically from 4.4 per cent in 1996 to 17.7 per cent in 2015.

(Lee et al.,2013, Lee et al.,2015), suggested that central obesity is an important factor in the aetiology of reflux and does this by the increased abdomino-thoracic pressure gradient inducing hiatus hernia and increasing the rate of flow of reflux when sphincter opens. Central obesity also induces short segment intrasphincteric reflux and thereby columnar metaplasia of the most distal oesophagus resulting severe erosive oesophagitis and Barrett's oesophagus



(Lee et al., 2013). Many studies including population based studies in the United States, United Kingdom, Norwegian, and Spanish populations have found that there were associations between body mass index with GERD symptoms .

An Asian based systemic review was conducted by (Hye et al., 2011), to see the epidemiology features of GERD. They review the GERD symptoms and its complication such as endoscopic reflux esophagitis and Barrett's esophagus. The prevalence of GERD symptoms in Eastern Asia was found to be increasing in it trend from 5% before 2005 to 10 % from 2005 to 2010. In Southeast and Western Asia, it was 6.3%-18.3% after 2005, which was much higher compared to Eastern Asia. The prevalence of endoscopic reflux.

Barrett's esophagus is histologically confirmed by specialized intestinal metaplasia. It is considered to be one of the most important complications of GERD due to its strong association with adenocarcinoma. The relative risk of GEJAC among patients with BE is high compared with the general population of 11% to 42% . The overall risk of cancer developing in BE patients is estimated to be approximately 0.12-0.5% per year (Lee et al., 2013, Hye et al., 2011, Seiji et al., 2015).

## 1.2- LITERATURE REVIEW

In asian based literature review , (Seiji et al., 2015), did a systematic meta analysis involving 47 Asian countries. They divided them into 4 contingents. Eastern Asia, South Central Asia, Western Asia and South Eastern Asia which includes Malaysia. A total of 51 studies was done in asian country. South east asian only 4 studies. This study evaluate the prevalence of BE in Asian countries and its temporal trends and risk factors. They conclude that GERD was the main risk factor for BE in Asian countries. Obesity and H pylori infection have no histologic BE. There was no clear trend of increasing BE prevalence among studies conducted between 1991 and 2014 (Seiji et al., 2015, Lee et al., 2011).

Meanwhile in a Swedish study was conducted by (Shao et al.,2016), Cancer Incidence in Five Continents (CI5) series volumes VII–X. They included seven Asian countries which were China, Japan, India, Israel, Philippines, Thailand and Singapore. Data was analysed from year 1988–2007. They concluded that Singapore and Israel have increasing prevalence of obesity and GERD symptoms.

(Hampel et al., 2005), conducted a meta analysis between obesity and the risk for gastroesophageal reflux disease, erosive esophagitis, Barrett's esophagus and esophagus adenocarcinoma between 1966 to October 2004. A total of 9 studies was included in this study. They analysed the association of body mass index (BMI) with GERD symptoms. GERD symptoms among overweight and obese persons were 1.5 and 2.0 fold higher compare to normal weight respectively. 6/7 studies found significant associations of BMI with erosive esophagitis and 6/7 found significant associations with esophageal adenocarcinoma. They concluded that obese patient has statistically significant increase risk for GERD

symptoms and its complications such as erosive esophagitis, Barrett esophagus and esophageal adenocarcinoma.

(Watari et al., 2013), conducted a multicentric pilot study in 1581 Japanese population from November 2011 to June 2012. They analysed the adiposity by measuring the BMI, waist circumference and waist-to-hip ratio. They concluded that visceral obesity in terms of waist circumference is associated with severe gastroesophageal acid reflux and causes BE.

(Michael et al., 2008), conducted a systematic meta-analysis regarding the risk of increasing adiposity in Barrett's Esophagus. They analysed using Search strategies were conducted in MEDLINE (U.S. National Library of Medicine, Bethesda, MD) from year 1966 till 2005 and EMBASE (Reed Elsevier PLC, Amsterdam, The Netherlands) from year 1980 to 2005. A total of 10 studies was included. They concluded that increasing adiposity is only an indirect risk factor of Barrett's esophagus through the precursor lesion of GERD. Hence, BMI status has no predictive value with respect to GERD patients and their risk of progression to Barrett's esophagus.

(Hashem et al.,2005), conducted a retrospective case control study on abdominal obesity and the risk of Barrett's Esophagus. It was a single center study done between 2000 till 2003.They examined the effect of obesity as measured by BMI and the amount and distribution of abdominal fat as measured by CT scan.They concluded that obesity seems to be associated with an increased risk of BE. Abdominal visceral adiposity might mediate most of this risk.

(Matthew et al.,2013), conducted an epidemiological study in United States from year 1973 till 2008. They analysed the data from the National Cancer Institute's. They have created a registry called as Surveillance, Epidemiology, and End Results (SEER) cancer registry program. They concluded that more than half of the esophageal adenocarcinoma

disease burden is attributable to smoking and elevated BMI. (1) Combinations of smoking, elevated BMI, and GERD may account for almost 70% of total cases.(2) They have suggested that endoscopic surveillance programs and chemoprevention agents should be used as a prevention strategy.

(Rusch et al.,2004), conducted a retrospective study and noted that there were a drastic increase in the incidence of esophageal adenocarcinoma in the Western world, especially in middle-aged Caucasian males. They concluded that the incidence of esophageal adenocarcinoma was related to the prevalence of obesity, smoking, and gastroesophageal reflux.

(Kamat et al.,2009), conducted a study to see the association between elevated body mass index (BMI) with Barrett's esophagus (BE).They analysed 11 meta-analysis studies which was published through 2008. They concluded that there were a statistically significant association between elevated BMI and BE. The prevalence of obesity and increasing incidence rates for esophageal adenocarcinoma was associated with symptomatic GERD symptoms.

(Hardikar et al., 2013), did a prospective cohort study on 411 BE patients. They investigated whether smoking, obesity or alcohol intake could predict progression of BE to EA. Data were collected during personal interview. They concluded that EA risk significantly increased with increasing age and cigarette exposure. However they found that measures of central (abdominal) obesity, but not BMI was associated with a modestly increase EA risk.

(Yates et al., 2014), conducted an EPIC-Norfolk Study prospective cohort study involving 24,068 men and women, aged from 39 years old till 79 years old, recruited between year 1993 to 1997. They analyses data on anthropometry, smoking and alcohol intake. The cohort was monitored until December 2008.They concluded that smoking and

alcohol intake were not associated with the development of BE but obesity may be involved in early carcinogenesis and the association with EAC .

### **1.3 - RATIONALE FOR THE STUDY**

Incidence of GERD symptoms and its complications are increasing today. Surgeons and physicians having the difficulties to treat this disease. Hampel H et al.(2005), conducted a meta analysis between obesity and the risk for gastroesophageal reflux disease, erosive esophagitis, Barrett esophagus, esophagus adenocarcinoma and GEJAC between 1966 to October 2004. They concluded that obesity patient has statistically significant increase risk for GERD symptoms and its complications such as erosive esophagitis, Barrett esophagus and esophageal adenocarcinoma. The epidemiology of GERD in Malaysia are not well documented maybe because it is variable in its nature. So far in Kelantan, there is no paper or article about the epidemiology or demographic study which associates body mass index with GERD and its complications in this region. By performing this study, we can obtain the epidemiology / demographic for our own institution/region. This study will determine the association between body mass index with GerdQ questionnaire scoring system and its endoscopic findings such as reflux esophagitis, hiatus hernia and Barrett's esophagus. From this study, we can help to stratify patient and help in term of treatment and follow up. Hopefully, this study will also help the bariatric surgeons in deciding their managements in weight reduction surgeries including laparoscopic fundoplication, laparoscopic sleeve gastrectomy and Laparoscopic Roux En Y Gastric bypass procedure.

**2-STUDY PROTOCOL**

**2.1- DOCUMENT SUBMITTED FOR ETHICAL APPROVAL**

**Association of Body Mass Index and  
Gastroesophageal Reflux Disease and its  
Complications.**

**JEPeM Code: USM/JEPeM/17060294**

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**DEPARTMENT OF SURGERY, HUSM.**

**CO-SUPERVISOR 2:**

**PROF. DR. LEE YEONG YEH**

**DEPARTMENT OF INTERNAL MEDICINE , HUSM.**

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**1-TITLE:**

1-a-Association of Body Mass Index and Gastroesophageal Reflux Disease and its complications.

1-b-This study is a retrospective study to see the association between body mass index and gastroesophageal reflux disease (GERD) and its complications such as hiatus hernia, reflux esophagitis and Barret's esophagus. This study involves all patients who are diagnosed with GERD in Hospital Universiti Sains Malaysia. The patients involving in this study are screened with our inclusion and exclusion criterias. List of patients diagnosed with GERD based on GerdQ tool questionnaire which were translated into Malay language and validated from year January 2014 to Mei 2017 is obtained from endoscopic room records. The medical records of patients that recruited in the study will be reviewed and the data will be entered into the data collection form. The data will be analyzed. The study will analyze the association between body mass index with GerdQ questionnaire scoring and its endoscopic findings such as reflux esophagitis, hiatus hernia and Barret's esophagus. The literature review of studies done before relating to this topic have produced similar results. However in Malaysia we do not have such demographic data available.



## **2-a-Introduction**

Obesity is a fast-emerging epidemic in the Asia-Pacific region, with numbers paralleling the rising global prevalence within the past 30 years. The landscape of gut diseases in Asia has been drastically changed by obesity, especially the gastroesophageal reflux disease (GERD) (Lee et al., 2015). It is a common digestive disorder that affects the lower esophageal sphincter (LES), that has been linked to obesity. The symptoms are heartburn and regurgitation which causes the mucosal damage. Oesophagogastroduodenoscopy (OGDS) procedure is one of common procedure in Malaysia usually done by surgeons or gastroenterologist. It is normally done as an outpatient procedure in patient with GERD symptoms.

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Barrett's esophagus is histologically confirmed by specialized intestinal metaplasia. It is considered to be one of the most important complications of GERD due to its strong association with adenocarcinoma. The relative risk of GEJAC among patients with BE is high compared with the general population of 11% to 42% . The overall risk of cancer developing in BE patients is

estimated to be approximately 0.12-0.5% per year (Lee et al.,2013, Hye et al.,2011,Seiji et al.,2015).

Keyword: Obesity, Gastroesophageal reflux disease, reflux esophagitis, Barrett's esophagus, Hiatus hernia, Gastroesophageal Junction Adenocarcinoma, Oesophagogastroduodenoscopy

## **2-b-Literature review**

In asian based literature review , (Seiji et al.,2015), did a systematic meta analysis involving 47 Asian countries. They divided them into 4 contingents. Eastern Asia, South Central Asia, Western Asia and South Eastern Asia which includes Malaysia. A total of 51 studies was done in asian country. South east asian only 4 studies. This study evaluate the prevalence of BE in Asian countries and its temporal trends and risk factors. They conclude that GERD was the main risk factor for BE in Asian countries. Obesity and H pylori infection have no histologic BE. There was no clear trend of increasing BE prevalence among studies conducted between 1991 and 2014 (Seiji et al.,2015, Lee et al.,2011).

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(El-Serag et al.,2005), conducted a retrospective case control study on abdominal obesity and the risk of Barrett's Esophagus. It was a single center study done between 2000 till 2003.They examined the effect of obesity as measured by BMI and the amount and distribution of abdominal fat as measured by CT scan.They concluded that Obesity seems to be associated with an increased risk of BE. Abdominal visceral adiposity might mediate most of this risk.

(Matthew et al.,2013),conducted an epidemiological study in United States from year 1973 till 2008. They analysed the data from the National Cancer Institute's. They have created a registry called as Surveillance, Epidemiology, and End Results (SEER) cancer registry program. They concluded that more than half of the GEJAC disease burden is attributable to smoking and elevated BMI. 1) Combinations of smoking, elevated BMI, and GERD may account for almost 70% of total cases. 2)They have suggested that

endoscopic surveillance programs and chemoprevention agents should be used as a prevention strategy.

(Rusch et al.,2004), conducted a retrospective study and noted that there were a dramatic increase in the incidence of GEJAC in the Western world, especially in middle-aged Caucasian males. They concluded that the incidence of GEJAC was related to the prevalence of obesity,smoking, and gastroesophageal reflux.

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(Hardikar et al.,2013), conducted a prospective cohort study on 411 BE patients. They investigated whether smoking, obesity or alcohol intake could predict progression of BE to EA. Data were collected during personal interview. They concluded that EA risk significantly increased with increasing age and cigarette exposure. However they found that measures of central (abdominal) obesity, but not BMI was associated with a modestly increase EA risk.

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smoking and alcohol intake. The cohort was monitored until December 2008. They concluded that smoking and alcohol intake were not associated with the development of BE but obesity may be involved in early carcinogenesis and the association with EAC.

## **2-c-Problem statement & rationale of studies.**

Incidence of GERD symptoms and its complications are increasing today. Surgeons and physicians having the difficulties to treat this disease. (Hampel et al., 2005), conducted a Meta-Analysis between obesity and the risk for gastroesophageal reflux disease, erosive esophagitis, Barrett esophagus, esophagus adenocarcinoma and GEJAC between 1966 to October 2004. They concluded that obesity patient has statistically significant increase risk for GERD symptoms and its complications such as erosive esophagitis, Barrett esophagus and esophageal adenocarcinoma. The epidemiology of GERD in Malaysia are not well documented maybe because it is variable in its nature. So far in Kelantan, there is no paper or article about the epidemiology or demographic study which associates body mass index with GERD and its complications in this region. By performing this study, we can obtain the epidemiology / demographic for our own institution/region. This study will determine the association between body mass index with GerdQ questionnaire scoring system and its endoscopic findings such as reflux esophagitis, hiatus hernia and Barrett's esophagus. From this study, we can help to stratify patient

and help in term of treatment and follow up. Hopefully, this study will also help the bariatric surgeons in deciding their managements in weight reduction surgeries including Laparoscopic fundoplication, Laparoscopic Sleeve gastrectomy and Laparoscopic Gastric bypass.

## **2-d-Objectives**

General objective:

To determine the association between GERD complications such as reflux esophagitis, hiatus hernia and Barrett esophagus with body mass index via esophagogastroduodenoscopy (OGDS) in Hospital University Sains Malaysia (HUSM).

Specific objectives:

- 1) To determine the association of body mass index with reflux esophagitis severity based on Los Angeles classification.
- 2) To determine the association of body mass index with hiatus hernia severity based on Hill grading.
- 3) To determine the association of body mass index with Barrett's esophagus.

## **Hypothesis**



Null hypothesis

- There is no association between BMI with GERD complications endoscopically.

Alternative Hypothesis

- There is correlation between BMI with GERD complications endoscopically.

### **3-Research Methodology**

#### **3-a Study Design**

- This is a retrospective record review involving patient diagnosed with gastroesophageal reflux disease in HUSM.

#### **4-a Study population**

##### **4-a-i Reference population**

- All patient in Hospital University Sains Malaysia (HUSM) KubangKerian

##### **4-a-ii Source population**

- All patients that meet the inclusion criteria and diagnosed to have gastroesophageal reflux disease in Hospital University Sains Malaysia (HUSM) Kubang Kerian

#### **4-a-iii Inclusion criteria**

- All patients who have been diagnosed gastroesophageal reflux disease with GerdQ questionnaire scoring system and an esophagogastroduodenoscopy (OGDS) was done in Hospital University Sains Malaysia.
- All BMI patient is taken into account

#### **4-a-iv Exclusion criteria**

- All patients who have been diagnosed gastroesophageal reflux disease but without having GerdQ questionnaire scoring system
- Incomplete documentation of patient's case note
- Patient without esophagogastroduodenoscopy (OGDS)

#### **4-b Study settings**

##### **4-b-i Study Location**

- Hospital University Sains Malaysia (HUSM) Kubang Kerian.

#### **4-b-ii Study Duration**

- The study includes all patients who diagnosed with gastroesophageal reflux disease with GerdQ questionnaire scoring system from January 2014 to Mei 2017. The data collection will be started after ethical approval.

#### **4-c Sampling Method**

Due to limited time of data collections and available sample during this study period therefore Non probability sampling method will be applied (convenient sampling).

### **5-Sampling size.**

#### **5-a-i Sample size determination**

Two proportions formula is used to obtain the appropriate sample size. The calculation of sample size is done by using Power and Sample Size Calculation (PS) Software.

The parameters used are:

Objective 1: To determine the association between body mass index with reflux esophagitis.

Outcome variable: reflux esophagitis

Exposure: obese

$$\alpha = 0.05$$

$$\text{Power} = 80\%$$

$P_0$  = Is the probability of obesity among patients without reflux esophagitis: 0.18

Reported in previous study (El-Serag et al., 2008).

$P_1$  = Is the probability of obesity among patients with reflux esophagitis based on expert opinion: 0.4

Ratio = 1 (with reflux esophagitis: without reflux esophagitis)

Total sample size = 132 patients (66 per group)

Objective 2: To determine the association between body mass index with Hiatus hernia.

Sample size cannot be calculated because there is no published report on hiatus hernia

Objective 3: To determine the association between body mass index with Barrett's esophagus.

Outcome variable: Barrett's esophagitis

Exposure: obese

$$\alpha = 0.05$$

$$\text{Power} = 80\%$$

$P_0$  = Is the probability of obesity among patients without Barrett's esophagus:

$$0.08$$

Reported in previous study (Stein et al, 2005).

$P_1$  = Is the probability of obesity among patients with Barrett's esophagus based on expert opinion: 0.4

Ratio = 1 (with Barrett's esophagus: without Barrett's esophagus)

Total sample size = 54 (27 per group)

Therefore, the largest sample size from the objectives was 132, after adding 10% of unusable patients' data, a total of 146 Gerd patients are needed.

## **Statistical Analyses**

Data analysis will be conducted Using SPSS 24. Numerical Variable will be described using mean and Standard Deviation.Categorical variable will be described using frequency and percentage.Numerical variables will be check for normal distribution by using histogramgraph.

For Objective 1 to 3, Pearson Chi-Square will be used to examine the association between obesity with GERD complications such as Reflux esophagitis ,Hiatus hernia ad Barret's Esophagus.If the assumption of Chi-Square is not met,Fisher Exact test result will be reported.

## **Expected Result:**

### **Objective 1:**

Exposure	Reflux esophagitis		X <sup>2</sup> (df)	p-value
	yes	No		
Obese				
Non-obese				

### **Objective 2:**

Exposure	Hiatus Hernia		X <sup>2</sup> (df)	p-value
	yes	No		
Obese				
Non-obese				

### **Objective 3:**

Exposure	Barret's Esophagus		X <sup>2</sup> (df)	p-value
	yes	No		
Obese				
Non-obese				

	Obesity		Non Obesity	
	Mean (SD)	N (%)	Mean (SD)	N (%)
Gender				
1) Male				
2) Female				
Age				
weight				
height				
BMI				



Gerd Q				
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## **6-Research Tool**

- After ethical approval, a list of patients who diagnosed with gastroesophageal reflux disease with Gerd Q questionnaire scoring system from January 2014 to Mei 2017 will be obtained from the medical record in the record office. Patients who fulfill the inclusion and exclusion criteria will be recruited in the study. The data of patients will be obtained by retrospective review of patient's medical records. The data will be entered in a data collection form.

### **1) GERDQ Questionnaire**

- Patient question on symptoms of gastroesophageal reflux disease based on GerdQ tool questionnaire by (Jones et al., 2009), which have been translated and validated in Bahasa Malaysia by Lee et al in our institution .

- GerdQ is a useful complementary tool for the diagnosis for gastroesophageal reflux disease in primary care.

## 2) Esophagogastroduodenoscopy (OGDS)

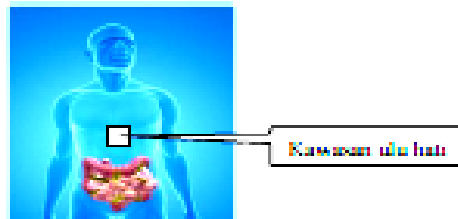
- Recent guidelines from GI societies such as American College of Gastroenterology (ACG), American Society for GI Endoscopy (ASGE), and American College of Physicians (ACP) have discuss regarding role of esophagogastroduodenoscopy (OGDS) in GERD.
- OGDS is the most important diagnostic tool for evaluation and management of patients with GERD.
- OGDS to evaluate esophageal mucosa for evidence of reflux esophagitis, Barrett's esophagus and hiatus hernia.

**Unit Fungsi GI dan Motiliti,  
Hospital USM, Kubang Kerian  
Soal Selidik GERD (Gastro-Esophageal Reflux Disease)**

Nama \_\_\_\_\_ Jantina Lelaki / Perempuan Tinggi \_\_\_\_\_ cm  
No. Pendaftaran \_\_\_\_\_ Umur \_\_\_\_\_ Berat \_\_\_\_\_ kg  
Nombor K/P \_\_\_\_\_ BMI \_\_\_\_\_

(A) Sila jawab soalan yang tertera di bahagian ini. Jawapan anda dapat membantu doktor anda memberi rawatan yang sewajarnya bagi mengatasi masalah kesihatan anda supaya anda dapat menikmati kehidupan anda dengan sempurna.

Tanda-tanda gejala yang dialami oleh setiap individu berkemungkinan berlainan. Jawab soalan tersebut mengikut tanda-tanda gejala yang dialami oleh anda sendiri berdasarkan dalam tempoh 7 hari yang lepas.



No.	Soalan (berdasarkan tempoh 7 hari yang lepas)	Kekerapan (hari)			
		0 hari	1 hari	2-3 hari	4-7 hari
A1	Berapa kerap anda berasa seperti panas dan / atau pedih di kawasan ultra hati?				
A2	Berapa kerap anda berasa seperti cecair atau makanan bergerak ke arah atas menuju ke tekak atau mulut?				
B1	Berapa kerap anda mengalami kesakitan di kawasan ultra hati?				
B2	Berapa kerap anda berasa loya atau peristaltik hendak muntah?				
C1	Berapa kerap anda mengalami kesukaran tidur jika disebabkan pedih ultra hati dan/atau rasa hendak muntah?				
C2	Berapa kerap anda mengambil ubat-ubatan tambahan ( seperti Gaviscon, Zantac, Omexoc) untuk mengatasi masalah pedih ultra hati atau rasa hendak muntah?				

(B) Bahagian pengiraan skor ini akan diisi oleh staf kesihatan yang bertugas. Merujuk kepada jawapan yang diberikan oleh pesakit, tandakan '✓' pada ruang yang berkenaan.

No.	Skor				Jumlah mata
	0 hari ( 0 mata )	1 hari ( 1 mata )	2-3 hari ( 2 mata )	4-7 hari ( 3 mata )	
A1					mata
A2					mata
B1					mata
B2					mata
C1					mata
C2					mata
<b>Jumlah Skor</b>					mata

Keputusan	
Jumlah skor 0-8 mata	Less likely GERD
Jumlah skor 9-16 mata	Highly suggestive of GERD

Tarikh \_\_\_\_\_ Nama & Tandatangan Staf \_\_\_\_\_

TOTAL SCORE:

0 to 2 points = 0 % likelihood of GERD

3 to 7 points = 50 % likelihood of GERD

8 to 10 points = 79 % likelihood of GERD

11 to 18 points = 89 % likelihood of GERD

### 3) BMI classification based on WHO (ASIAN population)

Defination: It is defined as the weight in kilograms divided by the square of the height in metres (kg/m<sup>2</sup>).

- $BMI = \text{kg} / (\text{m}^2)$

(James et al., 2002), interpreted the WHO BMI cut-offs in Asian and pacific populations (WHO/IASO/IOTF 2000). A proposal has been made to redefine the classification of obesity using BMI for Asian population as there are now evidence that the increased risks of co-morbidities with obesity occurs at a lower BMIs in Asians (WHO/IASO/IOTF 2000).

**Table 1: Classification based on ASIAN of according to BMI (WHO/IASO/IOTF 2000)**

<b>Classification</b>	<b>BMI (kg/m<sup>2</sup>)</b>
Underweight	< 18.5
Normal range	18.5 – 22.9
Overweight:	> 23.0
At Risk	23.0 – 24.9

Obese class I	25.0 – 29.9
Obese class II	> 30.0

## **7- Data collection**

Data collection will be recorded in a data collection form. The following information will be recorded: patient's demographic, Body mass index value, GerdQ questionnaire scoring, endoscopic informations and findings.

## **8-Proposed data analysis**

Data entry and analysis will be done by using SPSS version 22. Descriptive analysis will be done using mean and standard deviation for numerical variables and frequency and proportion for categorical variables. For objective 1, 2, and 3, I will use Pearson Chi-square to determine the association between the study variables stated in the objectives. If the assumption of Chi-square is not met, Fisher exact test will be used.

## **9-Ethical Issue**

### **9.1 Declaration of Conflict of Interest**

I hereby declare there is no conflict of interest

### **9.2 Handling Privacy and Confidentiality Issues**

The study will be conducted in compliance with MGCP and Declaration of Helsinki. The personal information and data will not be disclosed unless required by law. Subject's confidentiality will be protected; no name or identifiable information will be collected. The data collection form will have serial numbers instead of names of the subjects to prevent recognition. Data will be protected through password setting to access the database and securely locked. The data is only accessible by researchers involve in this study. The data will be used and remain directly available up to completion of the study. Thereafter, the data will be compressed with encryption and archived in a flash drive after proper documentation. This is to destroy by formatting the flash drive after a 5-years maintenance period determined by the date of its formal closure. We define the formal closure as the submission of a closure report to the National Medical Research Registry of Malaysia.

Subject's data and information will be kept confidential and will be known by research team only. The subject study will be not given access

to the personal information and study data. Only aggregated (grouped) results will be presented and submitted to local or international peer-reviewed medical journals and relevant government ministries.

### **9.3 Publications And Presentation**

The data and results will be presented either in poster format or published in any upcoming conference without revealing any subject's private information

### **9.4 Community Benefit**

Hopefully the information and the result from this study can be beneficial for the researcher to evaluate regarding management of gastroesophageal reflux disease and will enable us to formulate steps that can enhance the quality of service given by healthfacilities in the future.

## **10-Expected Result**

### **Research outcome**

Our research outcome suggests that overweight and obesity patients tend to have more severe GERD complications such as reflux esophagus, hiatus hernia and Barrett's oesophagus (BE).

## **Conclusion**

This study will provide the correlation of overweight and obesity are relative risk factors for GERD complications. Weight loss exercise and weight loss surgery (Bariatric surgery) will be able to improve the GERD symptoms and its complications. Subsequently this research should also clarify the role of risk factors such as BE causing esophageal carcinoma development and progression. Endoscopic surveillance with biopsy sampling can probably be carried out in high risk BE patients.