A 2 YEAR RETROSPECTIVE EVALUATION OF MANNHEIM PERITONITIS INDEX IN PATIENTS WITH SECONDARY PERITONITIS IN HOSPITAL UNIVERSITI SAINS MALAYSIA (FROM JANUARY 2013 TO OCTOBER 2014)

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DEDICATION

To my beloved wife, Sangeta and our son Haarshaan

My beloved parents

My ever encouraging teachers who believed in me

Dr Mehboob Alam Pasha, Dr Zaidi Zakaria, Dr Ikhwan Sani,

My fellow friends with all their help

The patients in HUSM who made this a possibility

My surgical idol whom I look up to, Dato RR Naidu

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LIST OF ABBREVIATIONS

- MPI- Mannheim peritonitis index
- HUSM- Hospital Universiti Sains Malaysia
- SLE- Systemic Lupus Erythematosis

ABSTRAK

Tajuk: Penilaian retrospektif dua tahun indeks peritonitis Mannheim di Hospital Universiti Sains Malaysia dari bulan Januari 2013 hingga Oktober 2014.

Latar belakang: Semenjak beberapa abad yang lalu, masalah keradangan peritoneum adalah satu masalah yang amat mencabar bagi pelbagai bidang kepakaran perubatan terutamanya, dalam bidang pembedahan. Satu kaedah berkesan diperlukan untuk memberi skala dan faktor-faktor indivividu bagi meramalkan prognosis pesakit daripada segi kadar kematian dan morbiditi. Objektif disertasi ini adalah untuk menilai kesesuaian menggunakan indeks peritonitis Mannheim di Hospital Universiti Sains Malaysia bagi masalah perubatan keradangan peritoneum sekunder yang menjalani pembedahan.

Kaedah disertasi dilakukan: Populasi pesakit yang telah menjalani pembedahan bagi masalah keradangan peritoneum sekunder di Hospital Universiti Sains Malaysia daripada bulan Januari 2013 hingga Oktober 2014 diterima sebagai sampel. Jumlah sampel yang diperolehi adalah 113. Rekod pesakit ini telah di rujuk setelah menerima kebenaran daripada Tuan Pengarah Hospital Universiti Sains Malaysia. Semua data pesakit dari segi sosioekonomi, klinikal, dan status hidup atau mati diisikan ke dalam borang proforma. Data yang dikumpul, dimasukkan ke dalam perisian komputer SPSS versi 21 dan analisis

dilakukan secara terperinci menggunakan ujian 'Pearson chi-square' dan 'independent t-test'. Perbezaan antara data yang diperolehi dianggap jitu hanya jika kebarangkalian atau 'p value' adalah sama atau kurang daripada 0.05.

Keputusan: Min bagi indeks peritonitis Mannheim dalam disertasi ini adalah 25.22 (*-.8.03). Nilai indeks peritonitis Mannheim yang terendah ialah 10 and nilai yang tertinggi ialah 43. Nilai indeks peritonitis Mannheim yang terunggul (threshold) ialah 26.5 dan hanya 1 kematian yang berlaku dibawah nilai ini. Tiada kematian yang berlaku bagi nilai indeks peritonitis Mannheim dibawah 21 mata. Faktor-faktor yang menentukan kadar kematian dalam indeks peritonitis Mannheim adalah umur lebih dari 50 tahun, jantina, kegagalan organ dan kesebaran radang peritonium yang meluas. Manakala bila analisis dilakukan bagi faktor-faktor nilai indeks peritonitis Mannheim, kesemua faktor kecuali punca radang peritoneum yang bukan dari usus besar yang memberikan kesan jitu kepada nilai yang lebih tinggi. Bila analisis dilakukan dengan lengkokkan "receiver operating characteristics" bagi menilai kadar ramalan kematian, nilai sensitiviti ialah 94.7% dan nilai spesifisiti ialah 70.2%, pada nilai mata keunggulan indeks peritonitis Mannheim 26.5.

Kesimpulan: Indeks peritonitis Mannheim adalah satu penilaian yang mudah dan effisien bagi membezakan pesakit radang peritonium sekunder yang tenat daripada yang kurang tenat, dan juga prognosis. Kekuatan indeks peritonitis Mannheim boleh dibaiki dengan penambahan faktor fisiologi seperti yang dilakukan dalam APACHE 2. Jika applikasi indeks peritonitis Mannheim diamalkan di Malaysia, parameter punca keradangan peritonium bukan dari usus besar perlu ditukarkan ke punca keradangan peritonium dari usus besar mendapat nilai mata yang lebih tinggi.

ABSTRACT

Topic: A 2 year retrospective evaluation of Mannheim peritonitis index in patients with secondary peritonitis in Hospital Universiti Sains Malaysia (January 2013 - October 2014).

Backgound: For decades, peritonitis has presented surgeons a challenge despite newer advances in various facets of medicine. The risk stratification of patients is important to appropriately study the individual risk factors to predict possible outcome in terms of morbidity and mortality. The objective of this study is to evaluate the Mannheim peritonitis index in determining the outcome in patients operated for secondary peritonitis in HUSM.

Method: The study population consisted of patients who underwent any form of intraabdominal operations for secondary peritonitis during the period of study. The total
number of patients were 113. The patient's medical records was traced from the hospital
records department after permission was granted from the Hospital Director. The relevant
socio demographic, clinical, operative notes and survival status was entered into a
proforma form. All the data recorded was entered into SPSS software version 21 and
analyzed. Pearson chi-square and independent t-test were used as statistical tests.

Significant difference was taken into account if the probability or 'p' value is equal or less than 0.05.

Results: The mean MPI score was 25.22 (*1.8.03) with the lowest score of 10 and highest score of 43. The threshold MPI score was 26.5 and there was only 1 death which occurred below this score. No deaths occurred below score of 21. The significant predictive factors for mortality was age more than 50 years, gender, organ failure and diffuse generalized peritonitis. Meanwhile, all parameters for MPI affected the MPI scoring except for source of sepsis not from colon. The ROC curve for mortality showed a sensitivity of 94.7% and specificity of 70.2% at a threshold MPI of 26.5.

Conclusion: For patients with secondary peritonitis undergoing operation, MPI scoring would be the best for grading severity and prognosis due to its simplicity and cost efficiency. Further increase in its prognostic power is desirable with some physiological data such as from APACHE 2. Application of MPI in the Malaysian population would be appropriate by changing the source of sepsis parameter to a higher score for those who have colonic source instead of non colonic which is the current MPI scoring system.

CHAPTER 1

INTRODUCTION

1.1 Introduction and history

contained viscera. Despite newer advances in various facets of medicine with ICU care and antibiotics, mortality rate is still high up to 14% in the best tertiary centre as demonstrated in University of Bern Hospital Switzerland (Seiler CA, 2000). It has presented surgeons a challenge in management ever since surgery was practiced. The surgical treatment of peritonitis started with the first laparotomy for an infected ovarian cyst by McDowell in the beginning of the 19th century. As advancement in abdominal surgery was achieved, towards the end of 19th century, Mikulicz felt that laparotomy was indicated in all patients with purulent peritonitis. In the beginning of the 20th century, Körte and Kirschner defined the principles of surgery for peritonitis that are valid up to this day: early surgical intervention, elimination of the source of infection, and peritoneal lavage. Since that time, surgeons have discussed the utility of irrigating and draining the peritoneal cavity. Postoperative lavage was already advocated in the beginning of 20th century, but generally regarded ineffective. Thus, the statement of Trendelenburg made one hundred years ago remains true, "...in medicine, the today is based on the yesterday, and to follow a gradual development is of immense interest". Many scoring systems have been created for assessing patients risks factor for death in peritonitis. These scoring systems will play an important role for objective and reliable classification of severity of peritonitis. The early prediction of outcome in terms of mortality is important to select patients for aggressive surgical interventions and pooling of limited resources for the best outcome. It is also useful to evaluate and compare results of different treatment regimens.

Peritonitis is inflammation of the serosal membrane lining the abdominal cavity and its

Over the past few decades, several scoring systems have been introduced. Acute Physiology and Chronic Health Evaluation (APACHE 2) score by Knaus and their coworkers (Knaus WA, 1985 Oct), integrated 12 physiological variables (both clinical and laboratory values), age and chronic health status. Its scores ranges from 0 to 71 and scores above 40 is uncommon. Because assessment of APACHE 2 score is both difficult, time consuming, and the need for evaluation after 24 hours of admission to intensive care unit, many other scoring systems were being developed. Two indices were developed specifically for peritonitis, which are Mannheim Peritonitis Index (MPI) and Peritonitis Index Altona 2. Other notable scoring systems available are Sepsis Severity Score (Elebute, 1983) and Multiple Organ Failure score (Goris RJ, 1985 Oct). Amongst all the scoring systems mentioned, analysis by Bosscha and collegues (Bosscha et al., 1997) reported hazard ratio for APACHE 2 score and MPI was 6.7 and 9.8 respectively. Only these two scoring systems contributed independently to the prediction of in hospital mortality outcome.

APACHE 2 has many parameters which should be scored 24 hours after intensive care unit admission. Meanwhile MPI scoring can be done during the first laparotomy or laparoscopic operation and has lesser criteria which can be manipulated for assessing the outcome. APACHE 2 score as well as MPI can correctly determine severity of intra-abdominal infections. They are both strongly and independently associated with prognosis but MPI has the advantage of simplicity and easy to apply (Pacelli *et al.*, 1996). MPI could also be confidently applied in retrospective studies because its data is easily available from the patient's medical records and its relevant.

Search in various local as well as international journals and internet search engines had few or no reports of such scoring index for peritonitis in our country. We hope that our study in HUSM would be useful in the management of peritonitis.

Mannheim is a name of a city in the southwest part of Germany and its amongst the 20 largest cities in Germany.

The Mannheim peritonitis index (Linder M and H., 1983) is based on data from 1253 patients with peritonitis treated between 1963 and 1979 and was developed by analysis of **17** possible risk factors (Linder M *et al.*, 1987; Wacha H, 1987). Eight of these parameters were of prognostic relevance and were entered into the current index, with weightage according to the predictive power. The information is collected during the first laparotomy, enabling immediate classification.

1.2 Anatomy of the peritoneal cavity

The endothelial lining of the primitive coelomic cavity of the embryo becomes the thoracic pleura and the abdominal peritoneum. It is invaginated by in growing viscera which thus come to be covered by a serous membrane and packed snugly into serous lined cavity, the visceral and parietal layer.

The peritoneum is a serous lining membrane which covers the abdominal cavity and the organs contained within it such as the liver, stomach, gall bladder, small and large intestine. It also covers the superior surfaces of the urinary bladder and the pelvic organs like the uterus, fallopian tubes and the ovaries in the females. It is divided into 2, parietal peritoneum and visceral peritoneum. In males, the peritoneal cavity is completely closed, but in females it is perforated by openings of the uterine tubes which constitute a possible pathway for infections.

Parietal peritoneum lines the outer surfaces of the abdominal cavity, and the lining membrane which covers the viscera of the peritoneal or abdominal cavity is called the visceral peritoneum. The potential space created by the parietal and visceral peritoneum is called the peritoneal cavity and this space contains peritoneal fluid. This fluid helps to lubricate and accommodates the expansion and movement of the gut. The doubling of the visceral peritoneum between the stomach and and its adjacent organs is called the omenta. The double peritoneal membrane between lesser curvature of stomach and porta hepatis of the liver is called the lesser omentum, while between greater curvature of stomach and the transverse colon it is called the greater omentum.

The area where the double visceral peritoneum lining attaches the viscera such as the small bowels, the transverse colon and the sigmoid colon to the posterior abdominal wall is called the mesentery.

Intraperitoneal organs are those which are wrapped by the visceral peritoneum such as the liver, gall bladder though these organs are not entirely covered by this membrane. The spleen, stomach, small intestine, transverse colon, sigmoid colon and the upper rectum are completely covered by peritoneum. The retroperitoneal organs are those which only one of their surface is covered by the parietal peritoneum such as the duodenum except for the first 2.5cm of the first part, pancreas, kidneys, abdominal aorta, ascending and the descending colons. The lesser sac is the area in the peritoneal cavity which lies behind the stomach and liver. The greater sac is the part of the cavity which starts at the inferior surface of diaphragm above the liver surface extending all the way to the pelvic cavity (Figure 1.1). The communication between the greater and the lesser sac is the foramen of Winslow or the epiploic foramen (Figure 1.2).

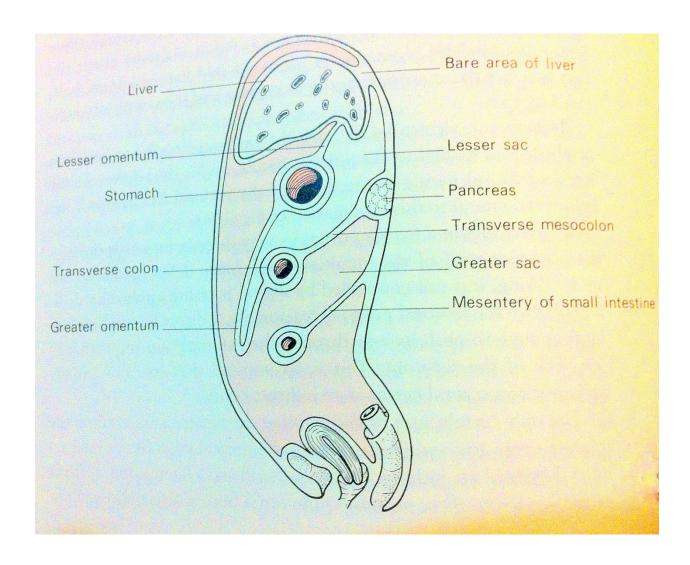


Figure 1.1 The peritoneal cavity in longitudinal section (female).

(Image adopted from Textbook of Clinical Anatomy by Harold Ellis published by Blackwell Science)

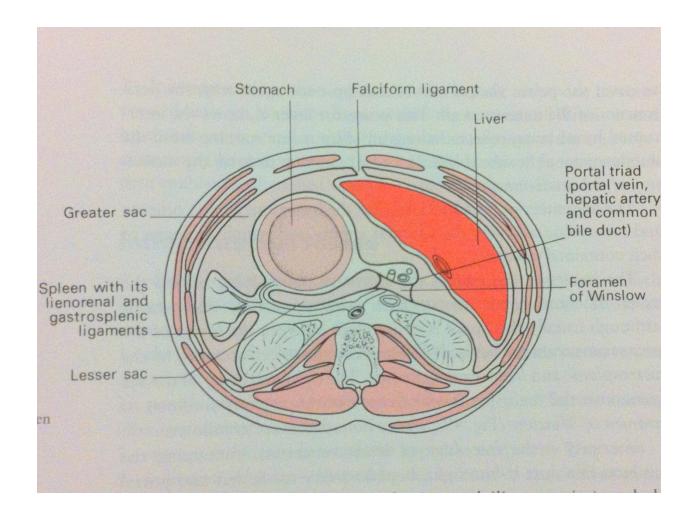


Figure 1.2 The peritoneal cavity in transverse section (through foramen of Winslow) (Image adopted from Textbook of Clinical Anatomy by Harold Ellis published by Blackwell Science)

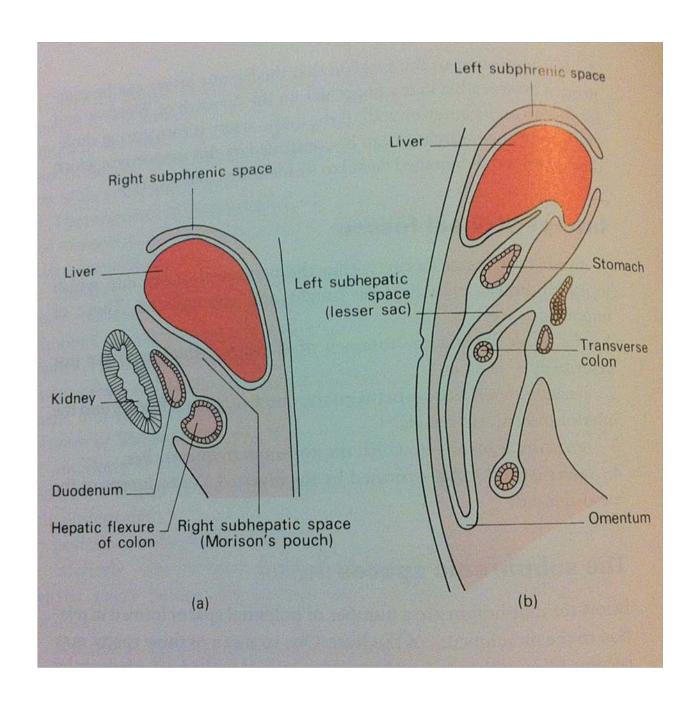


Figure 1.3 Anatomy of (a) the right and (b) the left subphrenic spaces in sagittal section. (Image adopted from Textbook of Clinical Anatomy by Harold Ellis published by Blackwell Science)

CHAPTER 2

LITERATURE REVIEW

2.1 Epidemiology

The commonest causes of peritonitis in developing countries are perforated appendicitis, perforated peptic ulcer disease and thyphoid perforations (Levinson, 2005). In a study of Nigerian children, 50% had thyphoid perforations (Adesunkanmi AR *et al.*, 2003). In the western countries, appendicitis remains the most common cause of peritonitis followed by colonic perforations due to diverticulitis (Malangoni M and T, 2006).

Mortality in secondary peritonitis had significantly decreased over the last century from 90% to about 20% (Weigelt, 2007) but it varies according to the specific cause: 0.25% for appendicitis and 45% for feculent peritonitis. The degree of contamination and ability to control the source of the contaminant plays the most important role in predicting the outcome (Malangoni, 2005).

2.2 Types of peritonitis

In surgical practice, peritonitis is usually divided to primary, secondary and tertiary peritonitis. Primary peritonitis usually occurs in chronically ill patients such as chronic kidney disease and liver cirrhosis patients due to immunocompromised state. This type of peritonitis is also called spontaneous bacterial peritonitis. Primary peritonitis is an inflammation of the peritoneum from a suspected extraperitoneal source, often via hematogenous spread. It occurs in children and in adults and can be a life-threatening illness, particularly in patients with cirrhosis. The spectrum of bacteria causing this and the population primarily affected have changed over recent decades. Primary or spontaneous bacterial peritonitis is now more common in adults than in children. Children with nephrosis (eg: nephrotic syndrome), formerly the group most commonly affected, have been replaced by adults with cirrhosis systemic lupus or erythematosus (SLE). Spontaneous peritonitis in adults is seen most commonly in patients with ascites and is a monomicrobial infection (i.e., only a single species of bacteria is present). The infective organism is usually gram positive, most commonly Streptococcus pneumonia and group A streptococci.

Secondary peritonitis or suppurative peritonitis is due to gastrointestinal perforation, injury, anastomotic dehiscence, haemoperitonitis, or a gangrenous or infected hollow viscus organ. In contrast to primary peritonitis, secondary peritonitis has polymicrobial infection due to gram negative organisms such as, *E.coli, Klebsiella pneumonia* and anaerobs such as *Bacteriodes fragilis* and *Peptostreptococcus*.

Tertiary peritonitis is persistence or recurrence intra abdominal infection following apparently adequate treatment of primary or secondary peritonitis. Those with tertiary peritonitis have a longer ICU stay and more advanced organ dysfunction reflected in higher ICU mortality (64% vs 33%) than patients with uncomplicated secondary peritonitis (Schwartz, 1999).

2.3 Pathophysiology of peritonitis

Peritonitis is an inflammatory reaction to peritoneal injury. Irritation or injury results in an influx of protein rich fluid, activation of the complement cascade, up-regulation of peritoneal mesothelial cell activity and invasion of the peritoneum with polymorphonuclear neutrophils and macrophages (Hall JC, 1998). Cytokine and chemokine production are triggered. Major cytokines are tumour necrosis factor, interleukin-1, interleukin-6, and interferon gamma. Bacteria are opsonized and destroyed by leucocytes and cleared through the lymphatics. The pathogenesis of intra-abdominal infections is determined by bacterial factors which influence the transition from contamination to infection along with its inflammatory cascade. The local consequences of this activation are the transmigration of granulocytes from peritoneal capillaries to the mesothelial surface and a dilatation of peritoneal blood vessels resulting in enhanced permeability, peritoneal edema and lastly the release of protein rich peritoneal exudates (Farthmann EH, 1998, October). The first line defense is clearance of noxious agents via the lymphatics of the parietal peritoneum, diaphragm and omentum. The formation of fibrin acts to wall off the infection and is associated with abscess formation. The response to intraabdominal infection depends on 5 factors: (a) inoculum size (b) virulence of the contaminating organisms (c) the presence of contaminants within the peritoneal cavity (d) adequacy of local, regional, and systemic host defenses and (e) the adequacy of initial treatment (Malangoni, 2005). The specific microbial characteristics of different regions of the gut determines the types of infecting organisms found.

Inflammation within the peritoneal cavity evokes a series of secondary changes that produce systemic responses. These features are part of the Systemic Inflammatory Response Syndrome (SIRS), whose characteristics include two or more of the following: temperature >38° C or <36° C, heart rate >90 beats/minute, respiratory rate >20 breaths/minute or partial pressure carbon dioxide <32 mm Hg, total white cell counts >12,000 cells/mm³ or <4000 cells/mm³, or >10 % immature (band) forms. SIRS is caused by a wide variety of conditions. Sepsis is when SIRS is present with a known infection, for example in peritonitis where the term intra-abdominal sepsis is used. Severe sepsis is when there's presence of organ dysfunction distant from the site of infection (renal, cardiac, respiratory or brain) or hypotension (systolic blood pressure < 90mm Hg or mean arterial blood pressure < 70mm Hg). Septic shock is sepsis with hypotension unresponsive to fluid resuscitation and requiring vasopressor agents (Bone, 1991).

The acute inflammatory process within the abdomen results in sympathetic activation, and suppression of intestinal peristalsis, or ileus. Fluid absorption through the wall of the bowel is impaired, and significant amounts of fluid may be sequestered within the lumen of the gut, resulting in hypovolemia. Moreover reduced intestinal peristalsis promotes microbial overgrowth, leading to translocation of bacteria and their products from the gut lumen into the peritoneal cavity and the portal circulation (JC., 2004).

2.4 History of Mannheim Peritonitis Index (MPI)

The Mannheim peritonitis index is based on data from 1253 patients with peritonitis treated between 1963 and 1979 and was developed by analysis of **17** possible risk factors (Linder M *et al.*, 1987; Wacha H, 1987).

Eight of these parameters were of prognostic relevance and were entered into the current index, with weighting according to the predictive power. The information is collected during the first laparotomy, enabling immediate classification. The original reports by Linder and Wacha in 1987 excluded patients with post operative peritonitis and appendicitis, but further investigation by Fuegger in 1988 revealed that extension to these groups did not reduce the predictive value (Linder M *et al.*, 1987; Wacha H, 1987; Fuegger R, 1988). Further single centre studies have increased experience with the index (Krenzien J, 1990; Seifert J, 1990; Van Laarhoven CJ, 1998).

2.5 The Mannheim Peritonitis Index

The MPI scoring is done by assessing the patient who has been diagnosed for peritonitis after history taking, examination and imaging modalities. During the first laparotomy or laparoscopy, the scoring can be completed by giving scores for the type of exudative fluid noted intraoperatively and the extent of contamination. If the exudative fluid had involved more than 2 quadrants of the peritoneal cavity, diffuse generalized peritonitis is scored for the patient. There are 8 criteria which is involved during MPI scoring as shown in table 1.

Table 1 MPI scoring with its weighting for each of the 8 criteria.

Number	Risk factor	Weighting if present
1	Age >50 years old	5
2	Female sex 5	
3	Organ failure**	
4	Malignancy	4
5	Preoperative duration of peritonitis >24 hours	4
6	Origin of sepsis not colonic	4
7	Diffuse generalized peritonitis	6
8	Exudate (intra operative):	
	Clear	0
	Cloudy/ purulent	6
	Feculent	12

^{**}Definitions of organ failure:

Kidney	Creatinine level >177 umol/L
	Urea level >16.7 mmol/L
	Oliguria <20 ml/h
Lung	$PO_2 < 50 \text{ mmHg}$
	PCO ₂ >50 mmHg
Shock	(systolic blood pressure <90mmHg without ionotropes)
Intestinal obstruction	Paralysis >24h or complete mechanical obstruction

Total MPI score =.....

2.6 Studies done on Mannheim Peritonitis Index(MPI)

The largest study done on MPI was by A.Billings et al. (A. Billing et al., 1994). In their study, MPI scoring was done at seven different surgical centres in three different countries in Europe for a total number of 2003 patients.

In Mexico, MPI validation study was done at the Hospital General De Durango (Rodolfo L. Bracho-Riquelme MC, 2002). This study was done for a period of 4 years from 1995 till 1999 with 174 data samples.

In Rwanda Africa, prediction of outcome using the Mannheim peritonitis index in patients with peritonitis at Kigali University Teaching Hospital from period of 1st May 2009 till 30th April 2010 was done. Study population consisted of 100 consecutive patients who were operated due to peritonitis.

CHAPTER 3

MATERIAL AND METHODS

3.1 General objective

To evaluate MPI in patients with secondary peritonitis in HUSM

3.2 Specific objectives

- I. To survey the demographics of patients who present with secondary peritonitis in HUSM.
- II. To determine the associated factors of mortality in patients with secondary peritonitis in regards to the 8 parameters in MPI.
- III. To predict mortality based on MPI score in patients with secondary peritonitis in HUSM.

3.3 Study design

Retrospective case control review of all patients diagnosed with peritonitis and had been operated between 1st January, 2013 to 31st October, 2014 in HUSM.

3.4 Sample population

All patients who got operated for secondary peritonitis, in Hospital Universiti Sains Malaysia, during the study period that fulfill the study criteria.

3.5 Sample size

Power and Sample size calculation (PS) Software version 3.0.43 was used to calculate the sample size.

Simple logistic regression via dichotomous/binary- two proportions formula was used to calculate the sample size.

Type of study: Dichotomous/binary- two proportions formula

Design: Independent

alpha=0.05

power=0.8

 $\underline{p_0}$ =0.11 *(proportion of absence of malignancy with higher chance of death)

 $p_1 = 0.35$ (proportion of presence of malignancy with higher chance of death)

m = 1

Sample size=47 for subjects for each arm (survive and non survive)

Acceptable sample fall out 10% from each arm

Sample size should be at least 103

*F. Ntirenganya et al- Prediction of Outcome Using the Mannheim peritonitis Index in Patients with Peritonitis at Kigali University Teaching Hospital – The mean MPI was 26.78 and the odd ratio was ⁺. 6.32

Sample size calculation using dichotomous/binary- two proportions formula;

n=
$$p_1(1-p_1)+p_2(1-p_2)$$

 p_1-p_2 $(z_{\alpha}+z_{\beta})^2$

n = required sample size

 α = level of significance

 $1-\beta$ = power of study

 z_{α} = value of the standard normal distribution cutting off probability α in one tail for a one - sided alternative or $\alpha/2$ in each tail for a two - sided alternative.

 z_{β} = value of the standard normal distribution cutting off probability β

Commonly used values are -

$$z_{\alpha} = 1.96$$
 for $\alpha = 0.05$ (two tailed) or 2.58 for $\alpha = 0.01$ (two tailed) $z_{\beta} = 0.84$ for 80% power or $z_{\beta} = 1.28$ for 90% power.

When we substitute numbers into the equation;

$$n = 2.26$$

Number of samples required is 226 divided by 2 = 113

Taking into consideration that sample fall out rate is 10%.

Number of samples required is 102.

3.6 Inclusion criteria

- 1. All patients with secondary peritonitis
- 2. Patients who underwent laparoscopic or laparotomy operation.
- 3. Age more than 12 years old.

3.7 Exclusion criteria

- 1. Primary and tertiary peritonitis.
- 2. Patients who did not undergo operation or operated outside HUSM for the similar pathology within last 6 months.
- 3. Age less than 12 years.
- 4. Records which are not complete.

3.8 Ethical approval

Ethical approval was obtained from HUSM Ethics and Research Committee in September

2014 to conduct the study. Permission to use hospital patients' records was sought and

given by the Director of HUSM, Malaysia.

3.9 Data collection

List of patients who had undergone operation for secondary peritonitis was obtained from

the General Surgical operative record book in the operation theater. Patient folders were

then traced from the Medical Record Department. Relevant information of patients in the

folders was collected in data performa. Patient's data were reviewed and statistically

analyzed.

See appendix: data proforma (Page 94, 95)

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