

**PREVALENCE, MODES OF TREATMENT, AND
PATIENTS' SATISFACTION WITH KIDNEY
STONE DISEASE MANAGEMENT AT
HOSPITAL UNIVERSITI SAINS MALAYSIA**

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UNIVERSITI SAINS MALAYSIA

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by

AHMED IBRAHIM ABDEL RAHMAN NOURI

**Thesis submitted in fulfillment of the requirements
for the degree of
Master of Science**

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DECLARATION OF ORIGINALITY

I hereby declare that this thesis is my own work and none of the contents of this thesis contains substantial proportions of material that has been submitted and accepted for the reward of any other degree or diploma at any tertiary educational institution or organization. The information derived from the previously published work or written by any person has been acknowledged in the text, and a full list of references has been included in this thesis.

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LIST OF ABBREVIATIONS

| | |
|-------|---|
| ACP | American College of Physicians |
| ADH | Antidiuretic Hormone |
| AUA | American Urology Association |
| BPH | Benign prostatic hyperplasia |
| Ca | Calcium |
| CrCl | Creatinine Clearance |
| DM | Diabetes mellitus |
| EAU | European Association of Urology |
| ESRD | End stage renal disease |
| ESWL | Extracorporeal Shockwave Lithotripsy |
| GFR | Glomerular Filtration Rate |
| HTN | Hypertension |
| IHD | Ischemic heart disease |
| JEPeM | Jawatankuasa Etika Penyelidikan (Manusia) |
| K | Potassium |
| Kg | Kilogram |
| KSA | Kingdom of Saudi Arabia |
| KUB | Kidney-Ureter-Bladder |
| MDRD | Modification of Diet in Renal Disease |
| mm | Millimeter |
| Na | Sodium |
| NSAID | Nonsteroidal Anti-Inflammatory Drugs |
| PCNL | Percutaneous Nephrolithotomy |

| | |
|--------|---------------------------------|
| PUJ | Pelvic-uretric junction |
| QDA | Qualitative Data Analysis |
| RA | Research Assistant |
| RBC | Red Blood Cell |
| RPG | Retrograde Pyelography |
| sCr | Serum Creatinine |
| UN | United Nation |
| UPJ | Ureteropelvic Junction |
| URS | Ureteroscopy |
| USA | United States of America |
| VUJ | Vesicoureteric Junction |
| WBC | White Blood Cells |
| WiSQOL | Wisconsin Stone Quality of Life |

**PREVALENS, KAEDAH RAWATAN, DAN KEPUASAN PESAKIT
TERHADAP PENGURUSAN PENYAKIT BATU KARANG DI HOSPITAL
UNIVERSITI SAINS MALAYSIA**

ABSTRAK

Batu karang lazimnya terjadi disebabkan oleh pemendakan atau penghabluran mineral dan konstituen kencing. Ia adalah masalah biasa di seluruh dunia yang dimanifestasikan dengan episod kesakitan berulang, intervensi pembedahan serta penggunaan ubat yang menjejaskan kualiti hidup pesakit. Kajian ini bertujuan untuk menilai kebarangkalian penyakit batu karang di kalangan pesakit yang dimasukkan ke Hospital Universiti Sains Malaysia (HUSM), 2) - untuk menentukan ciri-ciri batu, cara rawatan, fungsi buah pinggang dan keadaan komorbid, 3) - untuk meneroka kepuasan pesakit dengan pengurusan penyakit batu karang, aspek sosial, persepsi, dan bagaimana penyakit yang mempengaruhi kualiti hidup mereka. Penyelidikan pelbagai kaedah, kuantitatif dan kualitatif digunakan. Bagi Fasa kuantitatif, reka bentuk kajian rentas keratan retrospektif telah di gunakan untuk mendapatkan data perlu bagi kajian ini. Senarai semua pesakit yang dimasukkan ke HUSM selama lima tahun (1 Januari 2012 hingga 31 Disember 2016) telah diambil menggunakan pengelasan ICD-10 untuk mengenal pasti kes-kes batu karang di HUSM. Analisis statistiks termasuk pengiraan statistik deskriptif, ujian Kolmogorov-Smirnov terhadap normaliti data kajian, dan ujian Mann-Whitney U untuk membandingkan median telah di guna pakai. Semua analisis dijalankan dengan program SPSS (Statistical Package of Social Sciences Version 22.0). Prevalens pesakit dengan penyakit batu karang adalah 1.8% di kalangan pesakit yang dimasukkan ke HUSM. Pesakit lelaki lebih daripada perempuan dengan nisbah 1.35: 1, majoriti pesakit

adalah dari etnik Melayu (91.1%, n = 133). “Litotripsy shockwave ekstrakorporeal (ESWL)” adalah rawatan paling lazim digunakan di kalangan pesakit (45%, n = 67 dari 146). Bagi fasa kualitatif, pendekatan fenomenologi telah diguna pakai. Pensampelan purposif digunakan untuk merekrut dan mendekati pesakit di atas 18 tahun yang telah didiagnosis dengan penyakit batu karang. Wawancara separuh berstruktur telah dijalankan dengan pesakit dengan bertanya soalan siri terbuka. Wawancara yang dirakam suara adalah kata kerja yang ditranskripsikan dan diterjemahkan, maka analisis kandungan dijalankan. Wawancara dilakukan untuk 15 pesakit dengan 8 lelaki dan 7 wanita berumur 24 hingga 79 tahun. Kepuasan terhadap pengurusan batu karang dipengaruhi oleh pilihan rawatan yang dipilih untuk setiap pesakit, jangkaan dan persepsi terhadap rawatan dan penyakit, dan isu berkaitan sistem penjagaan kesihatan. Memahami perspektif, pengalaman, dan pengetahuan pesakit batu buah pinggang boleh membantu dalam menyediakan penjagaan kesihatan yang lebih baik. Oleh kerana etiologi penyakit batu karang adalah bersifat pelbagai faktor, keperluan untuk maklumat lanjut mengenai pengaruh diet, iklim, perkauman perlu dilaksanakan. Adalah disyorkan untuk menjalankan kajian kebangsaan terperinci ke dalam epidemiologi, sosioekonomi, diet dan faktor-faktor lain yang bertanggungjawab untuk wujudnya penyakit batu karang dalam kalangan rakyat di Malaysia. Apabila kajian sedemikian dijalankan, faktor-faktor ini dapat difahami secara mendalam bagi tujuan pencegahan bukan sahaja insiden tetapi juga morbiditi dan mortaliti yang sering dikaitkan dengan penyakit ini. Oleh itu, memahami pengaruh aspek sosial, persepsi dan kepuasan pesakit terhadap pengurusan batu karang membantu dalam menyediakan penjagaan yang sesuai dan pendidikan pesakit yang memastikan hasil kesihatan yang diharapkan.

**PREVALENCE, MODES OF TREATMENT, AND PATIENTS’
SATISFACTION WITH KIDNEY STONE DISEASE MANAGEMENT AT
HOSPITAL UNIVERSITI SAINS MALAYSIA**

ABSTRACT

Kidney stones form by the precipitation or crystallization of minerals and urinary constituents. It is a common problem worldwide manifested with recurrent intermittent pain episodes, surgical interventions and medication consumption which affect the quality of life of the patients. This study aimed 1) - to assess the prevalence of kidney stone disease among patients admitted to Hospital Universiti Sains Malaysia (HUSM), 2) - to determine the characteristics of stones, modes of treatment, renal function and comorbid conditions, 3) - to explore the patients’ satisfaction with the management of kidney stones disease, the social aspects, perceptions, and how the disease affecting their quality of life. A multi-method research adopting both quantitative and qualitative methodologies were applied. Quantitative phase was a retrospective cross-sectional study design. A list of all patients admitted to HUSM for five years (January 1st, 2012 to December 31st, 2016) was retrieved using ICD-10 to identify cases of kidney stones in HUSM. The statistical analysis included the calculation of descriptive statistics, Kolmogorov-Smirnov test of normality, and Mann–Whitney U test to compare medians. All analysis were carried out with SPSS (Statistical Package of Social Sciences Version 22.0) program. The prevalence of patients with kidney stones disease was 1.8% among patients admitted to HUSM. Male patients were more than females with a ratio of 1.35:1, the majority of patients were of Malay ethnicity (91.1%, n= 133). Extracorporeal shockwave lithotripsy was the most prevalent mode of treatment

among patients (45%, n= 67 of 146). On the other hand, a phenomenological approach was applied in the qualitative phase. Purposive sampling was adopted to recruit and approach patients above 18 years old and diagnosed with kidney stones disease. Face-to-face semi-structured interviews were conducted with patients by asking series of open-ended questions. The voice-recorded interviews were verbatim transcribed and translated, then content analysis was carried out. Interviewing was done for 15 patients with 8 male and 7 female of age 24 to 79 years old. The satisfaction towards the management of kidney stones was influenced by the treatment option chosen for each patient, expectations and perceptions of the treatment and disease, and healthcare system related issues. Understanding kidney stones patients' perspectives, experiences, and knowledge can help in providing better proper health care. As the etiology of stones disease is multifactorial, the need for further information on dietetic, climatic, racial influences needs to be implemented. It is recommended to carry out a detailed national study into the epidemiology, socio-economic, dietary and other factors responsible for urolithiasis. When such a study is carried out and these factors understood that it may be possible to undertake preventive measures which will reduce not only the incidence but also the morbidity and mortality from urinary stones disease in the Malaysian population. Listening and investigate the stories about experiences and limitations of therapy is equally essential in the patient care. Hence, understanding the influence of social aspects, perceptions and patients' satisfaction toward management of kidney stones help in providing appropriate care and patient-education that ensures the best expected health outcomes.

CHAPTER 1:

INTRODUCTION

1.1 Background

Kidneys, two bean-shaped organs, function in essential roles to maintain the harmony of body systems. Kidneys maintain body fluid homeostasis, producing urine by clearing and removing excessive amounts of substances such as water, minerals, and waste products. Also, they reabsorb nutrients and synthesize certain hormones, such as erythropoietin, calcitriol, and renin.(Mukoyama and Nakao, 2005) Along with acid-base balance, blood pressure, electrolyte balance, and activation of vitamin D.(Atherton, 2015)

The precipitation and accumulation of waste materials and minerals that are supposed to be washed out from the body lead to the formation of solid materials (crystals) inside kidneys or so-called stones. (Sakhaee, 2009) A kidney stone, or calculi, can be formed by the precipitation or crystallization of minerals and urinary constituents such as calcium oxalate, calcium phosphate, cystine or uric acid.

The stones formed in the kidneys vary in size, big as a ball or small as a fine sand, it can migrate to any part of the urinary tract causing obstructions, symptoms of patients making them lie on the floor because of the pain or it can be asymptomatic where the patient can be surprised when the urine turned bloody, reddish, or sandy.

Kidney stones disease, or urolithiasis, is a common problem worldwide with remarkable health and economic burden. It is regarded as a common cause of morbidity.(Alexander et al., 2012) After urinary tract infections and prostate

diseases, kidney stone disease is considered as the third most common disease in urology.(Yanagawa et al., 1997, Bartoletti et al., 2007). Urolithiasis is spreading all over the world with an increasing prevalence affecting males and females. However, it is more predominant in males compared to females with an average ratio of 2:1. (Xu et al., 2013).

Humans have been suffering from kidney stones disease thousands and thousands of years back. (López and Hoppe, 2010, Shah and Whitfield, 2002) A fact that was confirmed by many archeologists and ancient writings that have passed through ages. In the 8th century B.C, an Indian surgeon described a surgery to treat kidney stones. Also, Hippocrates mentioned in his oath bladder stones, and he recommended not to cut patients and take out the stones.(Tefekli and Cezayirli, 2013) Historically, kidney stones used to be considered as a killer disease, many of the patients who suffered from painful stone colic ended up dead either because of the disease itself or the treatment method used back then. Treatment of kidney stones changed drastically through ages, from using open surgery, endoscopic interventions to recently most patients are being treated in outpatient settings with minimally invasive procedures, and patients getting treated using conservative approaches. (López and Hoppe, 2010, Shah and Whitfield, 2002).

Therapy for urolithiasis has undergone many changes. The advent of non-invasive and minimal-invasive procedures has revolutionized the surgical approach to kidney stones treatment.(Türk et al., 2016c) However, the mode of treatment is individualized from patient to patient, as it depends on a variety of factors such as stone location, stone size, stone physicochemical properties, and patient's preferences.

Patients with urolithiasis seek medical help usually complaining of renal colic. Renal colic is the acute cramping and intermittent abdominal and flank pain caused by kidney stones. The increased wall tension caused by urinary flow obstruction together with the contraction of the ureteral smooth muscle in an attempt to move the stone stimulates the synthesis of prostaglandins. This will cause inflammation, edema formation, and the painful spasms. Sometimes, it is accompanied by hematuria, nausea, and vomiting. (Golzari et al., 2014, Beltrami et al., 2016, Masarani and Dinneen, 2007, Ahmad et al., 1991)

Aims of treatment are unified for all patients, preventing recurrence of stones and maintenance of renal function. (Eisner et al., 2013, Campschroer et al., 2014, Saita et al., 2004, Hollingsworth et al., 2006)

Several approaches and guidelines are available for treatment of kidney stones, most of them choose the treatment based on the physicochemical properties of patient's stones. However, assessment of physicochemical is not always feasible. Generally, guidelines agree on that pain management and hydration is part of the acute treatment of all types of stones. Initially, evaluation to exclude infection shall be obtained, then identification of location and size through imaging studies. Consequently, decisions to consider medical expulsive therapy or surgical interventions according to guidelines.

All in all, treatment could depend on the experience and the culture of the treating physician for kidney stones. For the same location and size, physicians might put a patient under watchful waiting as a conservative measure, letting the stone to pass within a certain period with providing symptomatic relief. Other physicians may go for more advanced treatment options from the beginning such as interventional

options. Medical expulsive therapy is a strategy used for facilitating stones passage through the urinary tract by using drugs such as alpha blockers or calcium channel blockers.

Kidney stone disease is not considered a mortal disease anymore, however, it is a devastating disease. Recurrent intermittent pain episodes, surgical interventions, medication consumption and facing the risk of side effects, all of which affect the quality of life of the patients. (Rule et al., 2009, Donnally et al., 2011)

As a complex disease, by means of symptoms diversity and individualized treatment with high risks of disease recurrence after treatment. Surgical management aims to treat the patient and eliminate the stones, medical management aims to treat and prevent recurrence of disease, also, minimizing the frequency of painful episodes and their acuity. (Penniston and Nakada, 2013) However, it is more relevant to patients to care about daily life and how the disease or its treatment is affecting their life. Hence, understanding and exploring the perceptions of the patients, expectations, and satisfaction towards the various treatment options will provide opportunities for healthcare improvement, cost reduction, design effective management, enhancing decision making by involving patients in the process.

1.2 Kidney stone disease epidemiology

As a disease that occurs in all parts of the world, the understanding of kidney stones disease epidemiology is crucial to specify the significance of the disease in each country worldwide. (Knoll, 2010) Urolithiasis is regarded as the third most frequent urological disease.(Kovshilovskaya et al., 2012) Many studies showed that prevalence and incidence of kidney stones disease are increasing in all parts of the world.(Curhan, 2007, Lee et al., 2002, Soucie et al., 1994, Stamatelou et al., 2003,

Morgan and Pearle, 2016) Hence, reducing the risk of disease formation is possible by the understanding of its epidemiology, risk factors, and variations between countries and ethnicities.

1.2.1 Prevalence and incidence of renal stones: A global picture

Prevalence, the proportion of a population of having a disease or a characteristic, of kidney stones disease was reported to be increasing worldwide. While, the incidence, the number of *new* cases that develop in a given period of time, was reported to be increasing as well.(Noordzij et al., 2010)

The risk factors that are population dependent made the variation in epidemiological disease profile of kidney stones between countries. (Romero et al., 2010b, Yasui et al., 2008, Alatab et al., 2016, Fisang et al., 2015).

The variation in prevalence is demonstrated in the Afro-Asian stone forming belt as shown in Figure 1-1, which is an area of the world extends from the North African countries to the Arabian Gulf, Iran, India, and Malaysia down to the Philippines. In this area, the disease affects all age groups with a male-to-female ratio of 2:1 and prevalence of 10 - 15%, some studies reported up to 20%, and some studies reported lower values. (Fisang et al., 2015)

A review by (Romero et al., 2010a) was made to capture the *global* picture of prevalence, incidence, and risk factors for kidney stones disease. By reviewing studies from more than 20 countries, it came to conclude that prevalence and incidence are increasing globally, where the changes in dietary habits had a key role in these effects.

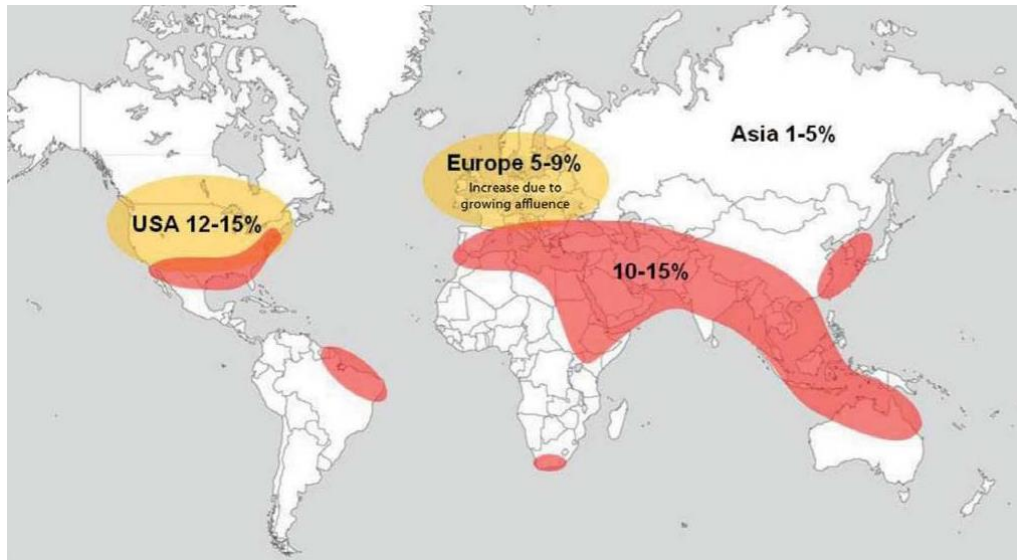


Figure 1.1 Afro-Asian Stone Forming Belt (red area) “adopted and used with permission from (Fisang et al., 2015)”

It was reported that the disease formation in Western countries is high compared to the Eastern countries. (López and Hoppe, 2010) However, there were differences in disease formation from century to century and from decade to decade. This attributed to the development of treatment strategies and diagnostic measures. The occurrence of kidney stones in Asia in the 20th century was similar to the occurrence of kidney stones in Europe in the 19th century as reported by the study by Asper. (Asper, 1984)

1.3 Etiology and factors influencing on kidney stones development

Urolithiasis has no single or definite cause; it is considered as a multifactorial disease; several factors increase the risk of forming stones. (Pak, Resnick, & Preminger, 1997; Prince, Scardino, & Wolan, 1956) Different factors play a role in disease formation in different populations, such as:

- Socio-economic status
- Dietary habits and obesity
- Dehydration
- Digestive diseases

- Geographical and environmental area
- Racial differences
- Family history

This variation in risk factors around the world made the variation in epidemiological disease profile between countries.(Claros et al., 2012; Hughes & Caring for Australians with Renal, 2007; Romero et al., 2010a; Shoag, Tasian, Goldfarb, & Eisner, 2015)

Gender plays a role in the development of kidney stones where the risk of having stones in male dominates over females without specified reasons in literature. Nevertheless, many studies reported that this ration is decreasing due to the increasing occurrence in females.(Strope, Wolf, & Hollenbeck, 2010) Furthermore, all age groups are at risk of kidney stones formation with a peak incidence of 35 – 45 years that differs from country to country. In terms of racial differences, researchers found that it is higher in whites, followed by Hispanics, Blacks, and Asians.

Though the relationship between overweight and kidney stones has limited studies, obesity and high body mass index found to be a risk factor for kidney stones in Japanese men. Moreover, members of a family with kidney stones history has two to three folds higher relative risk of having kidney stones compared to those who do not have history, genetic factors can play a role in this. (Yoshimura et al., 2016)

Geographical or environmental aspects such as hot climate, daily lifestyle, low-consumption of an adequate amount of water are causes of dehydration, which causes the concentration of urinary constituents.

Also, dietary habits like over or under-consumption of calcium-containing nutrients, over-consumption of vitamin C products, digestive diseases and many other medical

conditions like insulin resistance and metabolic syndrome, all of which found to contribute in causing kidney stone disease.(de Oliveira, Hauschild, Leite, Baptista, & Carvalho, 2014)

1.4 Classifications of kidney stones

Treatment of kidney stones differs in one patient compared to another, based on the size, composition, or location of stones.(Asplin, 2008) Therefore, kidney stones diagnosis and management influenced by properties of the kidney stones that the patient has. Classifications of kidney stones are summarized in table 1-2. (Türk et al., 2016a)

Size

- Less than 5mm to ≥ 25 mm
- Staghorn (Stones large enough to fill the renal calyces)

Radiology

- Radiopaque (Ca oxalate, Ca phosphate)
- Radiolucent (Uric acid, Ammonium Urate, Xanthine)
- Poor radiopacity

Location

- Bladder
- Kidney
- Urethra
- Ureter
- Pelvic-Ureteric Junction (PUJ)
- Vesicouretric Junction (VUJ)

Composition

- Calcium Stones (Ca Oxalate, Ca Phosphate)
- Uric Acid
- Cystine
- Struvite (Magnesium ammonium phosphate)

Cause

- Non-infectious Stone
- Infectious stone
- Genetic

Figure 1.2 Kidney stones classifications

1.5 Clinical presentation

Patients with urolithiasis seek medical help usually complaining of loin pain or renal colic which is an acute onset of severe cramping and intermittent abdominal and flank pain. (Ahmad et al., 1991, Cole et al., 1988) This pain may often be accompanied by fever, dysuria, urgency, or nausea and vomiting. (Pedersen et al., 2011) Nonetheless, even with no or minimal pain sensation, many patients hurry for physicians because of hematuria or sandy urine. Renal stones can also be asymptomatic, where diagnosis occur during a routine medical checkup or visiting for a non-urological disease (Wimpissinger et al., 2007) Common clinical presentations are summarized in Table 1-1. (Frassetto and Kohlstadt, 2011)

Table 1.1 Common clinical presentations of patients with kidney stones

| Common Renal Stones Symptoms |
|--|
| Dysuria (urinating small amount) |
| Urgency (persistent need to urinate) |
| Fever and chills |
| Hematuria, sandy urine |
| Nausea, vomiting |
| Pain and cramps (abdominal, flank, loin, side) |
| Pain in urination |
| Asymptomatic |

Renal colic is episodic in nature; pain induction occurs when the stone blocking urine passage is trying to move due to peristaltic movement of the ureter or when the patient is trying to force urination. Moreover, the blockage of urine flow and urine retention cause hydroureter or hydronephrosis based on the obstruction location.

Renal colic involves prostaglandin-mediated pain due to the elevated intra-pelvic pressure caused by obstruction of urinary flow and subsequent contraction of smooth muscle of ureter as an attempt to move and expel the stone. (Cole et al., 1988, Ahmad et al., 1991, Holdgate and Pollock, 2004) All of which, pain comes to the patient as

waves or episodes that lasts from minutes to up to one hour.(Pearle et al., 2014)
Hence, renal colic is considered as an emergency that needs prompt action and causes the patient to seek medical attention.

1.6 The role of the pharmacist in urology related issues

Kidney stone management requires a thorough patient history, definitive diagnosis, supportive care, and possible surgical intervention. Long-term management focuses on addressing the underlying etiologies and preventing complications of treatment. (Mohammad et al., 2013) Pharmacists continue to identify drug-induced causes, promote public health information, and counsel patients on methods to avoid recurrent stone formation. Along with other health care professionals, pharmacists are of drug-induced causes and counsel patients to adhere to definitive therapies and recommended diets.

Pharmacists develop interventions in urology including participating in ward rounds and making drug treatment plans for clean operations in urology, and extracting the medical records of inpatients who receive antibiotics in urology and assessing their responsible use. Also, participating in consultations on complicated infection cases in urology.(Zhou et al., 2015)

Pharmacist team works with physicians to ensure provision of clinical support and affordable medication to meet needs and expectations of the patients. Among patients with kidney stones rates of adherence to thiazide diuretics, alkali citrate therapy and allopurinol, collectively referred to as preventive pharmacological therapy, are low. This lack of adherence may reduce the effectiveness of secondary prevention efforts, leading to poorer clinical health outcomes in patients with kidney stones. The consequences of nonadherence to preventive pharmacological therapy

among patients with kidney stones. To improve adherence further research is needed to understand patient and provider level factors that contribute to lower rates of adherence.(Dauw et al., 2016)

The relationship between nephrolithiasis and urinary tract infections (UTIs) is complex and difficult to analyse both on a physiopathological and clinical point of view.(Zhou et al., 2015)

Most kidney stones are composed of calcium oxalate or calcium phosphate, and they may lead to urinary obstruction, flank pain, hematuria, and an increased infection predisposition. Urinary tract infections (UTI) and urosepsis are complications which can precede or follow a kidney stone treatment.

The relationship between urinary stones and UTIs is well known and has different clinical pictures, namely, stones that develop following UTIs (infection stones) and stones complicated by UTIs (stones with infection). (Miano et al., 2007) Thus, there is agreement on the need for prophylaxis and antibiotic therapy, the most recent literature has shown excellent results with fluoroquinolones both in prophylaxis and therapy, concerning post-operative infection control after percutaneous as well as ureteroscopic removal of stones. No agreement has yet been reached on antibiotic prophylaxis modalities prior to percutaneous or ureteroscopic removal and its usefulness for ESWL.(Zanetti et al., 2008) Hence, antibiotic stewardship programme with pharmacist participation including real-time interventions can promote improved antibiotic-prescribing and significantly decrease costs.(Zhou et al., 2015) the prevalence of infection might also be different, depending on the pathogenic mechanism of nephrolithiasis and on the geographical, social and economic environment.

1.7 Study Objectives

The current study divided into two parts

1.7.1 The quantitative phase

1. To determine the prevalence of kidney stones disease among patients admitted to Hospital Universiti Sains Malaysia (HUSM) in the period of 1st January 2012 to 31st December 2016.
2. To present the common modes of treatment options used by physicians to treat patients with kidney stones disease.
3. To evaluate clinical characteristics of kidney stones patients in HUSM.

1.7.2 The qualitative phase

1. To explore patients' satisfaction and experiences with the management of kidney stones disease.
2. To explore patients' perceptions of kidney stone disease and its treatment.

Along with the study objectives, the research took three phases (two quantitative and one qualitative) to achieve its objectives. The research flow chart is shown in Figure 1.1.

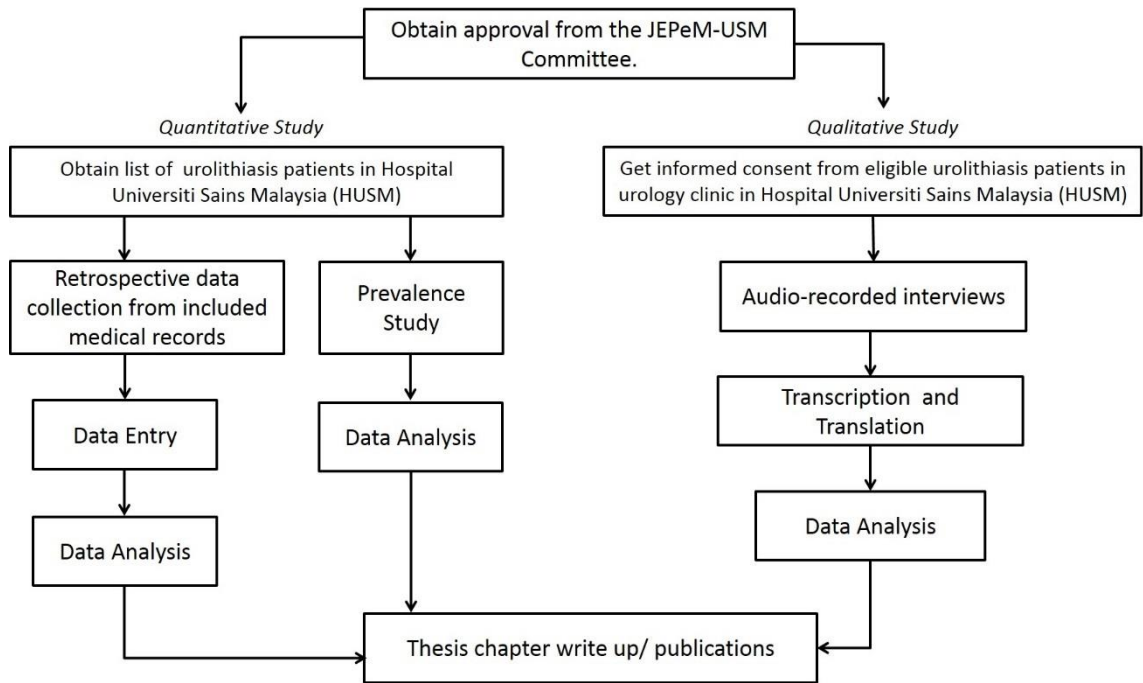


Figure 1.3 Research flow chart

1.8 Significance of the study

- In a multi-ethnic country like Malaysia, there are very limited data about kidney stones, and the disease has no priority compared to other urological diseases. This study will provide an insight and fresh information about the disease in Malaysia.
- Studying the prevalence of kidney stones, modes of treatment, disease progression, comorbidities and clinical characteristics of kidney stones patients, can help the health care authorities in designing better strategies to provide effective treatment and preventive maneuvers.
- Besides RCT or evidence-based health care as a guide for therapy selection, listening and investigate the stories about experiences and limitations of therapy is equally essential in the patient care.
- Understanding the influence of social aspects, perceptions and patients' satisfaction toward management of kidney stones will help in providing appropriate care and patient-education that ensures the best expected health outcomes.
- Giving insights into the influence of social aspects, perceptions and patients' satisfaction toward their stones management; the understanding of what is influential from the patients' perspective and how far patients are satisfied with their disease management, what do they do to improve pain relief, how the disease is affecting their quality of life. All of this will give the ability to deliver optimum care, patient education, and therapeutic plans; which will ensure achieving their expectations with minimum let-downs and contribute to better outcomes and satisfaction.

1.9 Outline of the thesis

This thesis is organized into the following sequence to address the study objectives:

In Chapter 2, literature review presents a comprehensive background of kidney stone disease, clinical presentation, classification, investigations, and renal function with kidney stones. Nonetheless, the review had a focus on the epidemiology of the disease and the treatment options by international guidelines. Moreover, the chapter reviews evidence on the perceptions of stone formers, satisfaction toward disease management, and patient-reported outcomes importance in health-related quality of life.

Chapter 3 addresses the methodology undertaken to attain the quantitative objectives of the research that lead to the results and outcomes. After discussion and interpretation of the results, eventually, limitations and conclusions were stated.

Chapter 4 provides the qualitative research methodological approaches and sampling techniques implemented in the present study. Recruitment and the qualitative interviewing process of patients with kidney stones. Moreover, it presents how the qualitative data was managed and handled for interpretation and analysis. Eventually, discuss the emerged themes from analyzed interviews to come up with the conclusions.

CHAPTER 2:

LITERATURE REVIEW

2.1 Overview

The current chapter aims to provide a comprehensive background information to guide the research objectives in chapter 1, in which the outcomes of the study will be discussed in Chapter 4, 5, and 6.

This chapter begins with reviewing kidney stones disease, from the aspect of pathophysiology, etiology, symptomatic evaluation, and diagnostic investigations. Information regarding the epidemiology of kidney stones disease will be further discussed from a global perspective and Malaysian perspective.

As management of renal stone disease varies based on several factors, herein, a review to summarize the evidence-based guidelines and current modes of treatments. Furthermore, there is a brief review to discuss the effect of kidney stones disease on the deterioration of kidney function.

Finally, the chapter reviews relevant articles to the satisfaction of patients toward the treatment of kidney stones diseases such as patient-reported outcomes and health-related quality of life of patients with kidney stones disease.

Research articles and review articles that reported epidemiology of kidney stones disease, causes, treatment options or medication used among kidney stones disease patients, and literature reporting satisfaction or studying quality of life of kidney stones patients were included whereas the data published focusing on herbal products and dietary therapy were excluded as it is out of scope of this research.

2.2 Kidney stone disease epidemiology

A population-based study in the United States of America (USA) to determine the disease prevalence over a 20-year period, involving USA residents in 1976 to 1980 and USA residents in 1988 and 1994. It was found that disease formation was increasing between 1980 and 1994, where 1988 to 1994 had a prevalence of 5.2% and 1976 to 1980 of 3.8%, ($p < 0.05$). It was greater in males over females and strongly associated with ethnicity and residence area. (Stamatelou et al., 2003)

The Kingdom of Saudi Arabia (KSA) had the highest disease prevalence all-over the world with a percentage of 20%. (Asper, 1984) The prevalence rate in KSA among males was of 8.1%. (Abdel-Halim et al., 1989). The study by (Abomelha et al., 1990) came to find that there is a seasonal variation kidney stones disease formation with a strong correlation between kidney stones and monthly temperature, also, the geographical area has a high atmospheric pressure was found to be correlated with disease formation. On the contrary, humidity did not show any correlation. As an Islamic country, data were analyzed peri-fasting month and peri-pilgrim period, no significant correlation was found. All in all, these findings were similar to studies in the same geographical area such as Iraq (Al-Dabbagh and Fahadi, 1977), Kuwait (Salem and ABU, 1969), and the United Arab Emirates (UAE) .(Husain et al., 1979)

In a more recent study of the same geographical area of KSA, analysis of the records of urolithiasis cases in UAE for the period of 2007 to 2009 found that male to female ratio was 5.2:1. The study focused on the age of disease formation and clinical presentation. The mean age at onset was 33.1 ± 8.6 years. However, it did not find statistically significant differences in age. (Venkatramana et al., 2010)

In a study by Robertson et al; 2012, the study reviewed the kidney stone formation in the Middle East, the Arabian Gulf countries in particular. (Robertson, 2012) Having a high incidence of renal stones in the Gulf Countries, the review revealed that these findings attributed to high consumption of animal protein and high consumption of oxalate-containing food. Also, a hot and dry climate that causes dehydration and low volumes of urine was a factor of the higher incidence. Despite including studies from a limited period (1980 to 1990), (Robertson, 2012) many more recent studies reported the high consumption of animal protein in Arabian Gulf countries as well. (Musaiger et al., 2012, Ng et al., 2011)

In Japan, kidney stones are one of the most common urological diseases as well. (Yoshimura et al., 2016) Using a nationwide survey, epidemiology of upper urinary tract stones in Japan was evaluated. Japanese reports have shown that a steady elevation in the incidence of urinary calculi and the age-adjusted annual incidence of upper urinary tract stones in 2005 was more than double the incidence in 1965. The study included almost all urologists in Japan, inclusion was to patients visited urologists in the year 2005 and diagnosed with kidney stones for the first time. Compared to a nationwide survey done between 1965 and 1995, the estimated annual incidence was 114.3 per 100,000 in 2005 compared to 53.8 per 100,000 in 1965 and 92.5 in 1985 with a male to female ratio of 2.5:1.(Yoshida and Okada, 1990) In regard to age, the annual incidence had increased in all age groups. (Yasui et al., 2008)

Similarly, in Taiwan, the annual incidence was increasing with male patients being more dominant compared to female patients. The number of kidney stones cases in each 5-year period from 1956 to 1999 at a university hospital in Taiwan increased from ~65 cases/year between 1956 and 1960 to ~410 cases/year between 1996 and

1999. The lifestyle and dietary habits changes were attributed to the similarity between Taiwan and Western countries kidney stones patterns. (Hsu et al., 2002)

Based on the National Health Insurance Research Database of Taiwan, an epidemiological analysis was done to patients diagnosed with upper urinary tract stones between 1997 and 2010. The prevalence was 7.38% with a male to female ratio of 1.55:1. The recurrence rate was 6.12% at one year and of 34.71% at 5 years, with males being of higher recurrence rate also. In regards to age, the peak prevalence was in the 60 to 69-year age. (Huang et al., 2013)

In Hong Kong, a study was conducted to report the prevalence of renal stones, patients' characteristics, and awareness towards prevention by surveying the general public using phone calls. A total of 1010 individual were surveyed in 2007, 25 of them reported to have a history of kidney stones disease, (2.5% point prevalence). Despite the relative quality of evidence, it showed results that are consistent with other studies, where the male had a higher percentage of having kidney stones with a ratio of 3:2 and older age groups were more common to have kidney stones especially 50 – 59 years old. The study also reported poor knowledge of proper strategies to prevent renal stones. Considerably, Hong Kong had lower prevalence (2.5%)(Chan et al., 2008) compared to countries in same geographical area, such as Seoul (3.5%)(hoe Kim et al., 2002), Japan (5.4%)(Yoshida and Okada, 1990), and Taiwan (7.38%)(Huang et al., 2013)

Alatab et. al. published a review comparing between developing and developed world showing that the incidence of urolithiasis had a steady increase around the world. (Alatab et al., 2016) It was reported that urolithiasis incidence has been increasing in both developing and developed countries, however, younger age

population in the developing countries had higher risks of renal stones formation compared to developed countries. Also, developing countries had higher uric acid stones than developed countries.

2.2.1 Kidney stones in Malaysia

Malaysia is located in Southeast Asia, it consists of 13 states and 3 federal territories. With a population over 30 million, Malaysia has various ethnicities, namely, Malay, Chinese, Indian among minorities of other ethnicities. The healthcare in Malaysia has been considered as one of the best in the world. Also, Malaysia healthcare system was complemented by the United Nation development program and other developing countries should look up to it. A thorough literature review was done to learn about the epidemiology of the disease, however, the review failed to find recent studies. Apparently, the disease has no priorities to do studies about it, and there is no available statistics about it. A review published in 1990 by Sreenevasan was the latest pieces of information about kidney stones in Malaysia.

In 1990, Sreenevasan presented the incidence of kidney stones in Malaysia by comparing between a study conducted in 1980 covered the years of 1962-1976 and a study conducted in 1989 covered the period of 1977-1981. It studied ethnicity, sex, and age distribution of kidney stones among the three major races of Malaysia (Chinese, Malay, and Indians). (Sreenevasan, 1981, Sreenevasan, 1990) It concluded that in Malaysia, the incidence of renal stones formation was increasing in the periods 1962-1966, 1967-1971, and 1977-1981. The study also concluded that there was no significant variation consistent with Malaysia population.(Sreenevasan, 1981, Sreenevasan, 1990) The study showed the increasing incidence between 1962 and 1981; incidence of ~200 per 100,000 in 1961 was doubled to up to more than 400 per

100,000. Ethnicity, sex, and age distribution of more than four thousand diverse subjects with kidney stones showed ~48% Chinese, while ~37% were Malay and around 13% Indian. The highest incidence found to be between the ages of 30 to 50 years old in all groups and female dominated by males with a male-to-female ratio of 3:1 which is consistent with international findings. As shown in Figure 2-1. (Sreenevasan, 1990)

Since there are no prevalence studies and no population-based studies on the incidence of kidney stones in Malaysia in the last two decades. Thus, several reviews and meta-analysis have been done by several researchers found in the health literature studying Malaysian results in their reviews (Romero et al., 2010b, Yasui et al., 2008, Sreenevasan, 1990, Alatab et al., 2016). Bearing in mind the evolving epidemiology of urinary tract stones and evolving nature of Malaysian population, including obsolete Malaysian information about renal stones will not capture or present evidence of high quality about the country.

For example, Alatab et al in 2016 published a review using the same references showing that the incidence of urolithiasis had a steady increase, although it presented only the incidence of kidney and ureter stones without showing the incidence of stones in other parts of renal tracts, the included incidence was of the study made many decades ago.

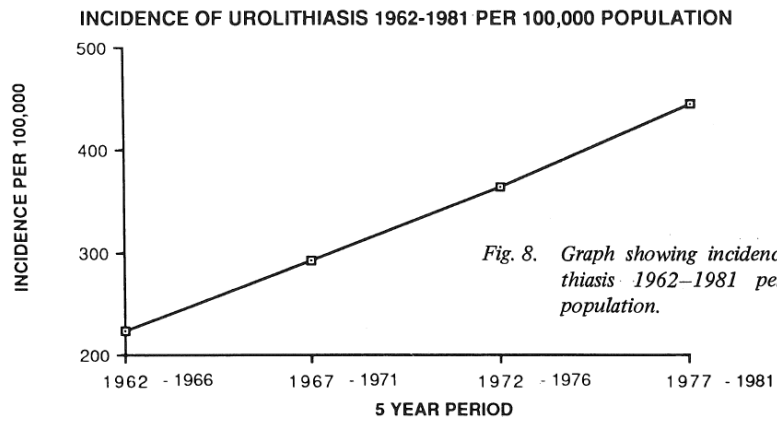


Fig. 8. Graph showing incidence of urolithiasis 1962-1981 per 100,000 population.

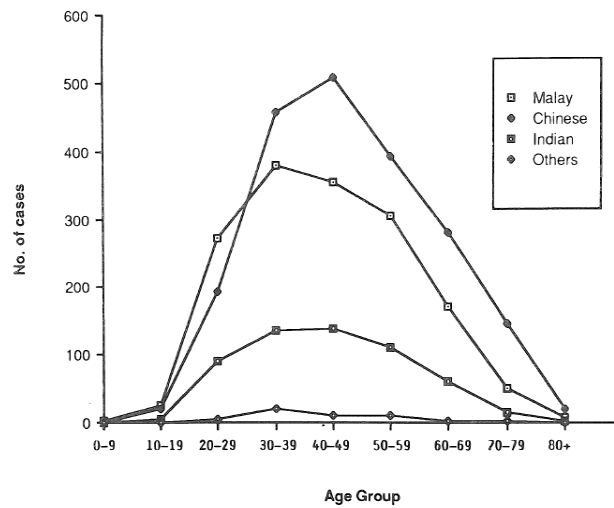


Fig. 11. Graph showing age distribution of urinary calculi.

Figure 2.1 Figures showing kidney stones disease distribution

2.3 Treatment of kidney stones disease

This section provides a comprehensive summary of the treatment modalities for kidney stones disease. Many international guidelines, such as American Urology Association (AUA) and European Association of Urology (EAU), offer evidence-based plans for evaluation, investigations, symptomatic management, surgical approaches, pharmacological therapy, and preventive measures. Table 2-1 summarizes the medical and surgical treatment options for each renal stone type.

Table 2.1 Summary of renal stones management strategies

| Stone type | Procedures | Medications |
|---|--|--|
| Calcium Phosphate, Calcium Oxalate | ESWL* Open surgery PCNL [€] URS [¥] | Allopurinol Amiloride Cellulose Phosphate Chlorothiazide Chlorthalidone Cholestyramine Hydrochlorothiazide Magnesium citrate Potassium citrate Potassium magnesium citrate Potassium Phosphate Sodium Phosphate Trichlormethiazide |
| Uric Acid | ESWL* Open surgery PCNL [€] URS [¥] | Allopurinol Potassium citrate Sodium bicarbonate |
| Struvite | Open surgery | Acetohydroxamic acid (AHA) Aluminum hydroxide gel Antibiotics |
| Cystine | Open surgery | Amercaptopropionylglycine (tiopronin) Captopril d-penicillamine Sodium bicarbonate |

*ESWL: Extracorporeal shockwave lithotripsy,

[€]PCNL: Percutaneous nephrolithotomy, [¥]URS: Ureteroscopy