PSYCHOLOGICAL WELL-BEING FOCUSING ON ANXIETY AND DEPRESSION AMONG PATIENTS WITH LOWER URINARY TRACT SYMPTOMS IN BENIGN PROSTATIC HYPERPLASIA ON PHARMACOLOGICAL TREATMENT IN HUSM.

DR. SEJJEETRA RAYNEE TANAPALLA

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LIST OF SYMBOLS, ABBREVIATIONS OR NOMENCLATURES

BPH	Benign Prostatic Hyperplasia
HADS	Hospital Anxiety Depression Scale
HUSM	Hospital Universiti Sains Malaysia
IPSS	International Prostate Symptoms Score
LUTS	Lower Urinary Tract Symptoms
SPSS	Statistical Package for Social Study

ABSTRAK (BAHASA MELAYU)

Pengenalan : Simptom saluran kencing bawah *(Lower urinary tract symptoms (LUTS))* di kalangan pesakit pembengkakan prostat bukan kanser *(Benign Prostatic Hyperplasia (BPH))* boleh menyebabkan kesan yang negatif dalam kualiti hidup, termasuk gejala kegelisahan dan kemurungan. Tujuan kajian ini adalah untuk mengenalpasti kelaziman gejala kegelisahan dan kemurungan di kalangan pesakit ini serta menentukan korelasi di antara mereka.

Kaedah : Sebuah kajian keratan rentas telah dijalankan dari Jun 2019 hingga Oktober 2019 di kalangan 153 pesakit yang didiagnos dengan LUTS/BPH yang menghadiri temujanji Klinik Pembedahan di Hospital Universiti Sains Malaysia, Kelantan. Pesakit telah diberikan set soalan yang mengandungi soalan sosiodemografi, Skala Keresahan dan Kemurungan Hospital dan Skor Antarabangsa Simptom Prostat. Data yang telah dikumpul dianalisa menggunakan ujian *measure of frequency* untuk menentukan kelaziman kegelisahan dan kemurungan di kalangan pesakit LUTS/BPH dan *correlation analysis* untuk menentukan korelasi di antara mereka.

Keputusan : Kajian ini melaporkan kelaziman sebanyak 27.5% kemurungan dan 15.0% kegelisahan di kalangan pesakit LUTS/BPH. Keputusan kajian ini juga membuktikan bahawa terdapat korelasi yang positif di antara tahap keterukan kemurungan (r=0.426, *p-value* <0.001) dan kegelisahan (r=0.367, *p-value* <0.001) dengan tahap keterukan LUTS/BPH.

Kesimpulan : Kemurungan dan kegelisahan mempunyai tahap kelaziman yang ketara di kalangan pesakit LUTS/BPH. Selain itu, terdapat juga korelasi yang positif di antara tahap keterukan kemurungan dan kegelisahan dengan LUTS/BPH. Ko-morbiditi di antara situasi ini memerlukan perhatian oleh kedua-dua pihak psikiatri dan urologi serta meningkatkan lagi

pendekatan rawatan antara disiplin. Kajian prospektif dan *cohort* adalah penting untuk mendapatkan lebih banyak maklumat mengenai korelasi di antara LUTS dan gejala kegelisahan/kemurungan.

ABSTRACT

Introduction : Lower urinary tract symptoms (LUTS) in Benign Prostatic Hyperplasia (BPH) have a negative impact on the quality of life, and may relate to anxiety and depression. The aim of the present study was to investigate the prevalence of anxiety and depression among patients with LUTS/BPH as well as to determine their correlation.

Methodology : A cross-sectional study was conducted from July 2019 to October 2019 among 153 patients who had been diagnosed with LUTS/BPH under the Surgical Clinic Hospital Universiti Sains Malaysia follow up, by using a set of self-administered questionnaires which includes sociodemographic profile, the Malay version of the International Prostate Symptoms Score (IPSS) and the Malay version of Hospital Anxiety and Depression Scale (HADS). Data was analyzed using measure of frequency for prevalence of anxiety and depression in LUTS/BPH and correlation analysis to study the relationship between them.

Results : The study reported 27.5% prevalence of depression and 15.0% anxiety among patients with LUTS/BPH. The study results also indicated that there was positive correlation between severity of depression (r=0.426, p-value <0.001) and anxiety (r=0.367, p-value <0.001) with severity of LUTS/BPH.

Conclusion : Depression and anxiety are significantly prevalent among patients with LUTS/BPH. There is also positive correlation between severity of depression and anxiety with LUTS/BPH. Comorbidity of these conditions should draw the attention of both psychiatrists and urologists as well as enhance the interdisciplinary treatment approach.

Further prospective and cohort studies are essential to reveal more details of the correlation between LUTS and anxiety/depression.

Keywords: LUTS, BPH, Anxiety, Depression

CHAPTER 1: INTRODUCTION

1.1 Anxiety and depression among patients with LUTS/BPH

Benign prostatic hyperplasia (BPH), refers to the non-malignant growth of the prostate observed very commonly in aging men (1). Globally, BPH affects about 210 million males (6% of the population) as of 2010 (2).

BPH is the most common cause of lower urinary tract symptoms (LUTS) which can be conveniently divided into obstructive (voiding) and irritative (storage) symptoms (3). The prevalence of LUTS increases steadily with increasing age, starting at approximately age of 40. Observations to this effect have been obtained from many cross-sectional studies in various countries and racial groups (4). Moreover, it is estimated that nearly half of all patients with BPH will develop moderate to severe LUTS (1). A Malaysian study which was conducted in the Urology Clinic of Hospital Kuala Lumpur in 2001 reported that there were 39.3% who fulfilled the criteria of symptomatic BPH (5).

In a study, it was found that individuals with LUTS had a significantly higher prevalence of anxiety or depression than the matched controls (11.45% vs. 5.72%) (6). Although the mechanisms underlying the association of LUTS/BPH with anxiety/depression remain unclear, there are several possible reasons.

First, LUTS interfere with daily activities and sleep, and decrease the quality of life (7). Patients with LUTS may suffer from embarrassment, low self-esteem, stigma, and social isolation (8), which could cause significant emotional distress placing them at a higher risk for developing anxiety and depression (9).

Second, it has been suggested that stress accompanied by anxiety/depression may be a potent factor in the perception, development, and prolongation of LUTS (10)(11). In addition, antidepressants and anxiolytics have been reported to be risk factors for LUTS (12).

Third, some studies have shown that the serotonin system is involved in the genetic susceptibility and pathophysiology of LUTS (13) and in the process of anxiety/depression (14).

1.2 Association of severity between LUTS/BPH with anxiety/depression

A prospective study in Asia demonstrated that a temporal association between the presence of moderate-to-severe LUTS at baseline and increased risk of clinically relevant depressive symptoms (15). On the other hand, men with higher severity of depression were associated with significantly higher prevalence of voiding and storage symptoms (all $P<0.001$) which supports that subjects with more severe depression have greater probability of LUTS (16).

A previous study reported higher prevalence rates of anxiety in patients with LUTS compared with normal controls (17). It was identified that urinary incontinence with condition-specific functional loss predicted onset of newly-incident anxiety disorders among community-dwelling adults. Moreover, there were several findings which demonstrated that when anxiety and depression occurred together, there appeared to be an additive effect on the association with LUTS, which is consistent with the findings of Avery et al in 2013. This

association with anxiety/depression implies a psychological role in the pathogenesis or sequelae of LUTS.

1.3 Justification of study

Understanding that LUTS/BPH and anxiety/depression are frequently comorbid has important implications for the treating clinician. This area of research is important because clinical anxiety/depression is associated with a significant increase in mortality, hence improved understanding of the relationship, early detection, intervention, and treatment of clinically relevant symptoms are key factors in patient care (18).

In addition, patients with LUTS/BPH who screen positive for mental health disorders including depression and anxiety may benefit from referral to an appropriate provider, such as a psychiatrist, psychologist, or social worker. Clinician insight into the patient's emotional state may promote improved communication and prevent patient dissatisfaction with treatment. The response to medical management for LUTS/BPH may be improved by also treating the underlying mood disorder.

However, fewer studies in local settings have focused on the relationship between anxiety/depressive symptoms and LUTS/BPH, as well as the nature and direction of this relationship. A study had been done in the local community, however it was focused on the general quality of life among BPH patients. Therefore, a systematic review of the relationship between anxiety/depression and LUTS/BPH is needed. Hence, it is justified to conduct a

study to gather evidence on the prevalence and relationship between anxiety/depression among patients with LUTS/BPH.

1.4 Objectives

1.4.1 General objective

The aim of this study is to assess the psychological well-being focusing on anxiety and depression in patients with LUTS/ BPH on pharmacological treatment in HUSM.

1.4.2 Specific objectives

i. To determine the prevalence of anxiety and depression among patients with LUTS/BPH on pharmacological treatment in HUSM.

ii. To determine the correlation between the severity of LUTS/BPH with severity of anxiety and depressive symptoms.

1.5 Methodology

A cross-sectional study was conducted from June 2019 to October 2019 among 153 patients who had been diagnosed with LUTS/BPH under the Surgical Clinic Hospital Universiti Sains Malaysia follow up by using a set of self-administered questionnaires which includes sociodemographic profile, the Malay version of the International Prostate Symptoms Score (IPSS) and the Malay version of Hospital Anxiety and Depression Scale (HADS). The data entry and analysis were performed by using Statistical Package for Social Study (SPSS) Version 24.

1.6 Dissertation organization

This dissertation is arranged according to the Format B: Manuscript ready format based on the guideline by Postgraduate Office, School of Medical Sciences (2016). The following chapters would be the study protocol that has been submitted for ethical approval. Chapter 3 is the manuscript of 'Psychological Well-being Focusing on Anxiety and Depression among Patients with LUTS/BPH on Pharmacological Treatment in HUSM' which is ready for submission to the Malaysian Journal of Medical Sciences with the author instruction. The raw data is included in the attached CD.

CHAPTER 2: STUDY PROTOCOL

2.1. Introduction & Literature Review

Benign prostatic hyperplasia (**BPH**), refers to the non-malignant growth of the prostate observed very commonly in aging men. It develops as a strictly age-related phenomenon in nearly all men, starting at approximately 40 years of age. In fact, the histologic prevalence of BPH, which has been examined in several autopsy studies around the world, is approximately 10% for men in their 30s, 20% for men in their 40s, reaches 50% to 60% for men in their 60s, and is 80% to 90% for men in their 70s and 80s. No doubt, when living long enough, most men will develop some histologic features consistent with BPH (1).

BPH is the most common cause of lower urinary tract symptoms (LUTS). The LUTS symptom complex can be conveniently divided into obstructive (voiding) and irritative (storage) symptoms. These symptoms may be accompanied by bladder pain or pain while urinating, called dysuria.

Among the obstructive symptoms are hesitancy (a delay between trying to urinate and the flow actually beginning), intermittency, straining to void, weak urinary stream, prolonged voiding, partial or complete urinary retention, a sensation of incomplete emptying, terminal or post-micturition dribbling (uncontrollable leaking after the end of urination) and, ultimately, overflow incontinence. The often more bothersome irritative symptoms consist of increased frequency, urgency (compelling need to void that cannot be deferred), with urge incontinence (urine leak following a strong sudden need to urinate), nocturia, and painful urination, as well as small voided volumes (3), (19), (20).

The prevalence of LUTS increases steadily with increasing age. Observations to this effect have been obtained from many cross-sectional studies in various countries and racial groups (4).

It must be recognized, however, that not all men with histologic BPH will develop significant LUTS, although other men who do not have histologic BPH will develop LUTS. Such men might have other conditions of the prostate (prostatitis or prostate cancer), other causes for subvesical outlet obstruction (urethral stricture, bladder neck sclerosis), conditions of the bladder (carcinoma in situ, inflammation, stones), or other conditions (21).

LUTS associated with BPH are often accompanied by sexual dysfunction, including erectile dysfunction (ED) and ejaculatory problems. Interest in sexual intercourse declines with severity of LUTS. Men with more severe LUTS have significantly lower libido, greater difficulty maintaining an erection, and lower levels of sexual satisfaction than men with less severe LUTS. The severity of urinary symptoms in men with LUTS appears to exert the greatest influence on the degree of sexual dysfunction (22).

According to the U.S. National Health and Social Life Survey, both premature ejaculation difficulties and ED are associated with LUTS. Frankel and colleagues reported that men with storage-related complications from LUTS, particularly incontinence, had approximately twice the probability of experiencing sexual dysfunction, especially impotence, as men without such complications (23).

Epidemiology

BPH has a high prevalence that increases with age; about half of all men at age 60 years have histological BPH, and by 85 years the prevalence is approximately 90% (47). Moreover, it is estimated that nearly half of all patients with BPH will develop moderate to severe LUTS (1).

Globally, benign prostatic hyperplasia affects about 210 million males as of 2010 (6% of the population) (2).

The prostate gets larger in most men as they get older. For a symptom-free man of 46 years, the risk of developing BPH over the next 30 years is 45%. Incidence rates increase from 3 cases per 1000 man-years at age 45–49 years, to 38 cases per 1000 man-years by the age of 75–79 years. While the prevalence rate is 2.7% for men aged 45–49, it increases to 24% by the age of 80 years (24).

A Malaysian study was conducted in the Urology Clinic of Hospital Kuala Lumpur in 2001. There were 226 (39.3%) who fulfilled the criteria of symptomatic BPH. The prevalence of symptomatic BPH for Malay, Chinese and Indian were 52.7%, 39.3% and 30.4% respectively. Although there is a higher prevalence of symptomatic BPH among Malay as compared to Chinese and Indian, this has not reach statistical significance ($p \sim 0.052$). The mean age of subject with and without symptomatic BPH were 60.1 and 58.8 respectively. The difference was statistically significant ($t=2.488$, $p<0.01$). The proportion of subjects with symptomatic BPH for age group 50 - 59, 60 - 69 and 70 or more were 35.0% 43.0% and 52.6% respectively. The prevalence of symptomatic BPH increased 8% per decade, however this was not statistically significant (Chi square test $X2 = 6.58$ $DF = 2$, $p =$

0.06). There were 91 subjects (15.8%) with obstructive symptoms with a mean age of 61.2 years. 72 of them had moderate to severe LUTS (79.1%) (5).

The Association between LUTS with psychological disorders

The association between LUTS and psychological disorders, especially anxiety and depression, has gathered increasing attention recently. In a study was found that individuals with LUTS had a significantly higher prevalence of anxiety or depression than the matched controls (11.45% vs. 5.72%) (6).

Although the mechanisms underlying the association of LUTS and anxiety/depression remain unclear, there are several possible pathways:

(i) anxiety and/or depression are the consequence of LUTS;

(ii) anxiety and/or depression per se induce LUTS;

(iii) LUTS, anxiety and/or depression share common etiological factors.

First, LUTS interfere with daily activities and sleep, and decrease the quality of life (7). Patients with LUTS may suffer from embarrassment, low self-esteem, stigma, and social isolation (8), which could cause significant emotional distress placing them at a higher risk for developing anxiety and depression (9).

Second, it has been suggested that stress accompanied by anxiety/depression may be a potent factor in the perception, development, and prolongation of LUTS (10), (11). In addition, antidepressants and anxiolytics have been reported to be risk factors for LUTS (12).

Third, some studies have shown that the serotonin system is involved in the genetic susceptibility and pathophysiology of LUTS (13) and in the process of anxiety/depression (14). Furthermore, serotonin and noradrenaline reuptake inhibitors, a class of antidepressant, have been shown to be effective in the treatment of LUTS (25).

Pathophysiology of LUTS and Depression/Anxiety

Storage symptoms are more common than voiding symptoms (13–42% vs. 6–22% of adult males, respectively). LUTS has been demonstrated to have an equivalent or greater impact on health-related quality of life (HR-QoL) as other major chronic diseases, such as heart disease, diabetes, and cancer. Storage symptoms (especially nocturia) in particular seem to adversely impact HR-QoL, while voiding symptoms are associated with elevated distress (26).

Several physiologic mechanisms have been proposed that may account for a relationship between depression/anxiety and LUTS secondary to BPH. One possibility is that central physiologic abnormalities such as increased adrenergic tone, which cause depressive symptoms, may also contribute to urologic symptoms (27). Johnson and colleagues inferred that chronic inflammation may be a possible common cause of these two diseases (28).

It is well known that inflammation contributes to the pathophysiology of major depression (29); depressed patients often exhibit significant increases in inflammatory biomarkers such as C-reactive protein, interleukin-6, and tumor necrosis factor-α. These inflammatory pathways might also contribute to the relationship between depression and other inflammatory disease states.

There is speculation that depression and LUTS secondary to BPH are linked with certain neurotransmitters that also play a role in depression, possibly contributing to the development of clinical symptoms and even treatment outcomes in patients with LUTS secondary to BPH (30).

Association of LUTS and Depression

Previous research has established that LUTS increase the odds of having depressive symptoms. Wong and colleagues found that, in elderly men, moderate to severe LUTS are associated with an increased risk of having clinically relevant symptoms of depression (31).

In a cross-sectional, population-based study, men with LUTS had an increased risk of reporting not only depression, but suicidal ideation as well. In addition, men with more severe depression measured by the Patient Health Questionnaire-9 (PHQ-9) were at greater risk of having LUTS (32).

Impact of BPH on Depression

Several studies provided evidence on the impact of LUTS secondary to BPH on depression. Huang and colleagues prospectively collected Taiwanese population-based data to help determine the relationship between BPH and depressive disorder (18). These findings suggest a unidirectional effect of BPH on the incidence of depressive symptoms and subsequent diagnosis of depressive disorder compared to the control group.

Another prospective study found that the presence of moderate to severe LUTS at baseline was associated with an increased risk of clinically relevant depressive symptoms at 2-year follow-up (OR 3.25; 95% CI, 1.91–5.52) (15).

Impact of Depression on BPH

Some studies have provided evidence on the impact of psychiatric parameters, specifically depression, on the clinical manifestation of LUTS secondary to BPH. A Korean population-based study found that elderly men with depression are likely to have more severe LUTS than those without depression, particularly if urinary urgency is present (33).

It is possible that this relationship may extend to treatment response as well. Yang and associates conducted the first study to investigate the influence of depression, anxiety, and somatization on clinical symptoms and treatment response in patients with LUTS secondary to BPH (30).

Depression was also associated with an increased risk of LUTS progression independent of other lifestyle and medical factors. Depression at baseline, which was defined by self-report, Beck Depression Inventory score, and/or use of antidepressants, preceded progression of storage and voiding symptoms over 5 years (34).

Another factor to consider in the relationship between depression and BPH is the possibility that depressed patients may report elevated subjective symptom scores due to the tendency of these patients to catastrophize. A cross-sectional study revealed that depressed patients using the Geriatric Depression Scale (GDS); reported significantly higher American Urological Association Symptom Index (AUA-SI) scores (16.61 ± 9.89; $F = 40.19$; $P < .001$), compared with the non-depressed patients (28).

Reciprocal Relationship Between BPH and Depression

The direction of causation remains unclear. Aside from the theories of potential pathophysiologic relationship between depression and LUTS in men with BPH, one hypothesis is that the negative impact of LUTS on quality of life in men with BPH results in the development of depression.

It is well known that chronic illnesses can lead to depression, and it has been established that LUTS secondary to BPH can seriously impact quality of life. LUTS may also lead to depression indirectly through sleep deprivation caused by nocturia, a major LUTS subset. It is also possible that depression plays a role in the subjective severity of BPH symptoms, particularly in the context of depressed patients' tendency to catastrophize. Depressed patients might report subjective suffering or greater AUA-SI scores than represents their true pathologic state.

Considering the evidence that exists to support an impact of LUTS on depression, as well as the impact of depression on LUTS, a final hypothesis involves a reciprocal or bidirectional relationship. Perhaps LUTS triggers depression in men with BPH, which in turn exacerbates LUTS severity and results in worsening depression.

LUTS/BPH and psychiatric symptoms

Previous studies have mainly focused on the negative effect of LUTS on quality of life, overall perception of bladder problems, general health status and mental health. Pre-existing studies suggest that putative role of psychiatric parameters in the development of LUTS/BPH and proposes that the current treatment for LUTS/BPH may not fully ameliorate

urinary issues if the underlying psychiatric disturbances are not properly resolved (35). Hence, proper evaluation and management of depression and anxiety has important implications for the appropriate management of patients with multiple facets of LUTS/BPH and also warrants further in-depth studies regarding the specific mechanisms underlying such relationship (36).

BPH Treatment and Depression

Treatments used for patients with LUTS secondary to BPH may be associated with depression as well. Frequently used medications to treat LUTS secondary to BPH include 5-α-reductase inhibitors (5-ARIs; eg, finasteride and dutasteride) and α-adrenergic antagonists (α-blockers; eg, prazosin, terazosin, doxazosin, and alfuzosin) (37). Side effects of these treatments, which may include incontinence and erectile dysfunction (ED), may contribute to depression. ED, a potential side effect of treatment with either medical therapy or transurethral resection of prostate (TURP), has been found to be associated with increased rates of LUTS and depression (27).

5-ARIs have been approved for the treatment of BPH and the subsequent LUTS that develop. Adverse effects on sexual function, depression, and quality of life are associated with the use of these medications. Studies have reported that 5-ARIs contribute to reduction or loss of libido and ED. Psychological impact may be explained by an association between depression and androgen deficiency, which may occur as a result of the medication. Low androgen levels are associated with symptoms of irritability, dysphoria, increased risk of depressive symptoms, and depression (38).

A cohort analysis (39) which assessed the risk of depression in patients with BPH and those exposed to α-inhibitor medication found that the risk of depression was significantly higher in men with BPH compared with those without BPH (incidence rate ratio 2.17, 2.12–2.22). However, the study concluded that the relationship between depression and exposure to α-blockers is confounded by concurrent disease states.

LUTS and Anxiety Disorders

A previous study in 2011 reported higher prevalence rates of anxiety in patients with LUTS compared with normal controls. It was identified that urinary incontinence with condition-specific functional loss predicted onset of newly-incident anxiety disorders among community-dwelling adults. Urinary incontinence with functional loss predicts onset of anxiety disorders. Panic disorder predicts onset of urinary incontinence with functional loss. Agoraphobia predicts onset of urinary incontinence with functional loss (17).

Moreover, there were several findings which demonstrated that when anxiety and depression occurred together, there appeared to be an additive effect on the association with LUTS, which is consistent with the findings of Avery and colleagues in 2013 (6), (7). This association between LUTS and anxiety/depression implies a psychological role in the pathogenesis or sequelae of LUTS.

Association of severity of LUTS to depression/anxiety

A prospective study in Asia demonstrated that a temporal association between the presence of moderate-to-severe LUTS at baseline and increased risk of clinically relevant depressive symptoms after a period of 2 years, adjusting for other confounders including

demographic, lifestyle, medical factors, weight status, stressful life events as well as baseline depressive symptoms (15).

On the other hand, compared to men without depression, mild, moderate, and severe depression were associated with significantly higher voiding symptoms prevalence (aOR, 3.04, 3.28, and 5.58; all $P<0.001$). The same significant associations were also observed in storage symptoms (aOR, 2.43, 3.43, and 2.89; $P<0.001$, $P<0.001$ and $P=0.011$, respectively). Furthermore, increasing severity of depression was also associated with increasing trends of voiding and storage symptoms (all $P<0.001$). Therefore this supports that subjects with more severe depression have greater probability of LUTS (16).

2.2. Problem Statement

- There is lack of study of psychological assessment among patients with LUTS/BPH in the local study.
- There is lack of study associating LUTS/BPH with prevalence of anxiety/depression in Malaysia.
- There is lack of study correlating the severity of LUTS/BPH to severity of anxiety/depression in the local study.

2.3. Justification to Conduct the Study

Understanding that BPH and depression are frequently comorbid has important implications for the treating clinician. Rom and colleagues recommended that clinicians screen for depression in all patients presenting with LUTS suggestive of BPH, as well as for LUTS in patients presenting with depressive symptoms (40).

Research has suggested that psychiatric parameters such as depression may have a putative role in the development of LUTS secondary to BPH. Furthermore, depression may pose an impediment to effective treatment for these patients. Improved understanding of the relationship between BPH and depression could lead to improved management.

This area of research is important because clinical depression is associated with a significant increase in mortality, and early detection, intervention, and treatment of clinically relevant depressive symptoms are key factors in patient care (18).

Fewer studies have focused on the relationship between depressive symptoms or depressive disorders and BPH, or the nature and direction of this relationship in the local setting. Thus, a systematic review of the relationship between depression and BPH is needed.

In addition, patients who screen positive for mental health disorders including depression and anxiety may benefit from referral to an appropriate provider, such as a psychiatrist, psychologist, or social worker. Patients who screen positive for depressive disorder may require more extensive counselling before diagnostic testing or surgery. Clinician insight into the patient's emotional state may promote improved communication

and prevent patient dissatisfaction with treatment. The response to medical management for BPH may be improved by also treating the underlying mood disorder.

In a study by Beiramijam and associates, patients with BPH were included in a study of the impact of a self-care educational program on anxiety, stress, and depression in this population (41). The authors found that, in the group of patients who received the self-care educational program, there was a decrease in depression in comparison with the control group. These results may suggest that interventions may be helpful for patients with depression in BPH.

A high level of depressive and anxiety symptoms have important implications for management of patients with LUTS secondary to BPH and warrant further study of the potential relationship between psychiatric symptoms and treatment response in these patients. Patients with BPH could be best managed using a multidisciplinary approach, including routine psychological assessment.

In conclusion, preliminarily studies demonstrate that clinicians may need careful evaluation of depression, anxiety and somatization issues for the proper management of patients with LUTS/BPH, despite study limitations. Subsequent studies with adequately-powered and better design may be crucial to validate and support the present exploratory study findings (30).

2.4. Research Gap

i. Fewer studies have focused on the relationship between depressive/anxiety symptoms and BPH, or the nature and direction of this relationship (42).
ii. Limited local studies that associate anxiety and depression with LUTS/BPH.
iii. The relationship between anxiety and depression with higher severity of LUTS/BPH.

2.5. Objectives

2.5.1. General Objectives

The aim of this study is to assess and evaluate the psychological well-being focusing on anxiety and depression in patients with lower urinary tract symptoms (LUTS) in BPH on pharmacological treatment in HUSM and the associated factors.

2.5.2. Specific Objectives

i. To determine the prevalence of anxiety and depression among patients with LUTS/BPH on pharmacological treatment in HUSM.
ii. To determine the correlation between the severity of LUTS and severity of anxiety and depressive symptoms.
iii. To determine the associated factors involved in patients with anxiety and depression among patients with LUTS in BPH on pharmacological treatment in HUSM.

2.6. Research Question

i. Is LUTS/BPH a contributing factor in causing anxiety and depression?

ii. Is anxiety and depression more prevalent among patients with more severe degree of LUTS/BPH?

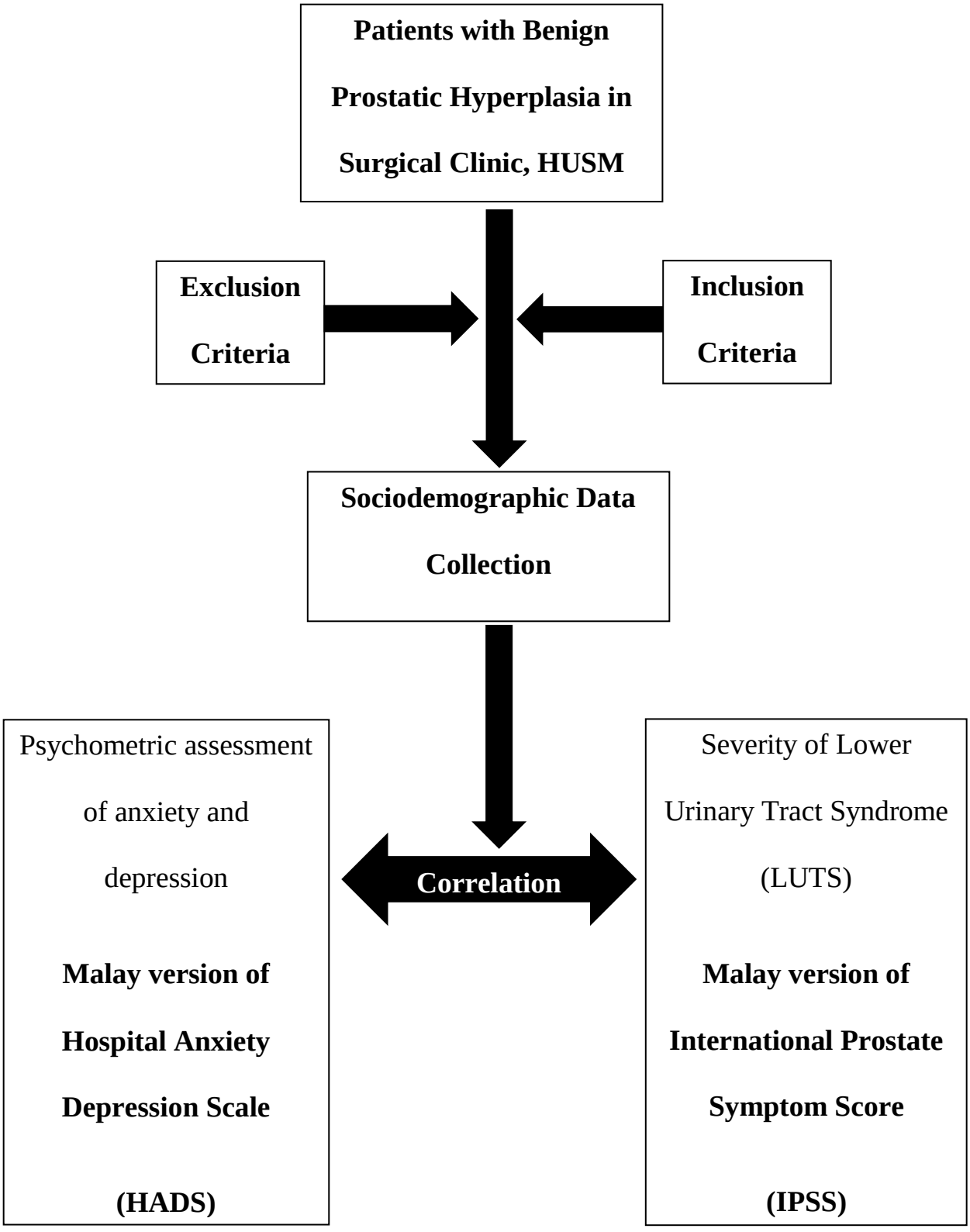
iii. What are the other sociodemographic factors contributing to anxiety and depression in patients with LUTS/BPH?

2.7. Research Hypothesis

i. There is an association between anxiety/depression and patients with LUTS/BPH.

ii. There is an association between higher scoring of IPSS and HADS score.

2.8. Conceptual Framework



2.9. Methodology

2.9.1. Study Design: Cross-sectional (survey)

2.9.2. Study Duration: This study will be conducted from June 2019 to October 2019

2.9.3. Study Location: Surgical Clinic, Hospital Universiti Sains Malaysia

2.9.4. Sampling Frame

2.9.4.1. Reference Population: All the patients with LUTS/BPH in Malaysia on pharmacological treatment.

2.9.4.2. Source Population: All the patients with LUTS/BPH in Kelantan on pharmacological treatment.

2.9.4.3. Sampling Frame: All the patients with LUTS/BPH in HUSM on pharmacological treatment.

2.9.4.4. Study Sample: Patients with LUTS/BPH in HUSM on pharmacological treatment and agrees (consents) to participate in the study.

2.9.4.5. Study Subject : Patients with LUTS/BPH in HUSM on pharmacological treatment and agrees (consents) to participate in the study, in which during the period of study fulfill the inclusion and exclusion criteria.

2.9.5. Operational Definition

In this study, patients who experience Lower Urinary Tract Symptoms (LUTS) due to underlying Benign Prostatic Hyperplasia (BPH) and receiving pharmacological treatment in HUSM will be studied.

2.9.6. Selection Criteria

2.9.6.1. Inclusion Criteria

i. Patients who have been diagnosed with LUTS/BPH for at least 6 months duration before study by clinical and laboratory assessment including Digital Rectal Examination (DRE) and Prostate Specific Antigen (PSA).

- LUTS/BPH is a chronic illness among elderly which requires lifestyle modification of patient's daily routine. Therefore, there may be an adjustment period which may last from 3-6 months. According to Diagnostic and Statistical Manual of Mental Disorders, 5th Edition by the American Psychiatric Association (DSM-5), Adjustment disorder is the development of emotional or behavioural symptoms in response to an identifiable stressor occurring within 3 months of the onset of the stressor(s). Once the stressor or its consequences have terminated, the symptoms do not persist for more than an additional 6 months. The condition may be further specified; (i) with depressed mood, (ii) with anxiety, or (iii) with mixed anxiety and depressed mood. Therefore, duration of 6 months is taken as inclusion criteria as participants are

more suggestible of having depressive and anxiety disorders by this point of time rather than adjustment disorder.

ii. Patients who are on pharmacological treatment for LUTS/BPH

iii. Patients who have never undergone surgical intervention for prostate-related condition.

iv. Patients who can understand Malay language.

2.9.6.2. Exclusion Criteria

i. Patients with severe cognitive impairment.

- Based on this criteria, patients who are suspected with cognitive impairment would be assessed objectively using the Elderly Cognitive Assessment Questionnaire (ECAQ). It is a 10-question screening tool for assessment of cognitive function in the elderly. A score of 5 points and below is suggestive of having a high risk of cognitive impairment, thus would be excluded from this study.

ii. Patients with underlying severe mental illness.

- A severe mental illness is a condition that affects a person who currently or at any time in the past have been diagnosed to have mental, behaviour, or emotional disorder that has resulted in serious functional impairment. Mental illnesses which typically meet the criteria for severe mental illness include schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder), bipolar disorder, and major depressive disorder (43).