DEPRESSION AMONG END STAGE RENAL DISEASE PATIENTS ON REGULAR HAEMODIALYSIS; COMPARING THE HAEMOGLOBIN, NUTRITIONAL STATUS, BLOOD PRESSURE CONTROL, FLUID INTAKE AND ADEQUACY OF DIALYSIS THERAPY BETWEEN THE DEPRESSED VERSUS THE NONDEPRESSED PATIENTS.

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TABLE OF CONTENTS **PAGE**

CHAPTER 1: INTRODUCTION

ABBREVIATIONS

ANA	Antinuclear Antibody
Anti GBM	Anti Glomerular Basement Membrane
BDI	Beck Depression Inventory
BUN	Blood Urea Nitrogen.
C-ANCA	Antineutrophil Cytoplasmic Antibody (cytoplasmic)
CAPD	Continuous Ambulatory Peritoneal Dialysis
CKD	Chronic Kidney Disease
CrCl	Creatinine Clearance
DM	Diabetes Mellitus
DsDNA	Double stranded DNA
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
HADS	Hospital Anxiety Depression Scale
HD	Hemodialysis
HIV	Human Immunodeficiency Virus
HUSM	Hospital University Sains Malaysia
IDWG	Inter Dialytic Weight Gain.
K/DOQI	National Kidney Foundation Dialysis Outcome Quality Initiative

Kt/V	Kinetic Transfer/ Volume urea
MDTR	Malaysia Dialysis and Transplant Registry
MOH	Ministry of Health
NKF	National Kidney Foundation
NGO	Non Government Organization
P-ANCA	Antineutrophil Cytoplasmic Antibody (perinuclear)
SSRI	Selective serotonin reuptake inhibitors (SSRIs)
USRDS	United State Renal Data System
VDRL	Venereal Disease Research Laboratory

ABSTRACT

ABSTRAK BAHASA MELAYU

Pengenalan:

Penyakit kemurungan atau ketegangan jiwa adalah salah satu gangguan emosi yang kerap menyerang pesakit-pesakit kegagalan ginjal yang tenat. Ia juga mempengaruhi tahap kesihatan dan kematian mereka. Menurut Kimmel et al (1998), kadar prevalen penyakit kemurungan dalam pesakit kegagalan ginjal yang menjalani rawatan hemodialisis adalah 50%.

Walaubagaimanpun, tiada data tentang prevalen penyakit kemurungan di dalam populasi pesakit pesakit ginjal yang tenat yang menjalani rawatan dialisis di Kelantan. Oleh itu, kajian ini dijalankan untuk mengatasi masalah tersebut. Ia juga dijalankan untuk membandingkan perbezaan paras hemoglobin, status nutrisi, kawalan tekanan darah dan jumlah rawatan dialisis antara pesakit pesakit ginjal yang mempunyai kemurungan berbanding dengan mereka yang tiada masalah ini.

Metodologi:

Kajian ini merupakan satu kajian hirisan lintang yang dijalankan ke atas semua pesakit – pesakit kegagalan ginjal yang tenat di Hospital Universiti Sains Malaysia (HUSM) dan Pusat Rawatan Dialysis Renal Care. Semua

pesakit telah di soal siasat menggunakan satu set soalan iaitu "Hospital Anxiety and Depression Scale (HADS)" yang telah di validasikan ke bahasa melayu. Selain daripada itu, tekanan darah, jumlah kenaikan berat badan antara sesi dialisis dan darah pesakit telah diambil untuk penganalisaan jumlah preskripsi dialisis (Kt/V), hemoglobin, kandungan zat besi dan paras albumin.

Keputusan:

Kajian yang dijalankan ini mendapati, prevalen sebenar penyakit kemurungan dikalangan pesakit – pesakit kegagalan ginjal yang tenat di Kelantan adalah 56.8%.

Analisis univariasi mendapati bahawa, pesakit - pesakit kegagalan ginjal kronik yang mengalami kemurungan mempunyai purata tahap hemoglobin yang lebih rendah (10.4 vs 11.5; $p < 0.009$) dan purata tekanan darah sistolik yang lebih tinggi (149.0 vs 138.6; $p< 0.031$) berbanding dengan pesakit pesakit kegagalan ginjal kronik yang tidak mengalami masalah kemurungan. Analisis univariasi juga menunjukkan bahawa lebih ramai pesakit wanita yang cenderung untuk mengalami masalah kemurungan. (32.1% vs. 24.7%; $p<0.027$).

Keputusan purata paras hemoglobin dan tekanan darah sistolik masih tetap signifikan selepas dikaji dengan analisis multivariasi (masing masing dengan $p<0.023$ dan $p<0.008$). Analisis multivariasi juga mendapati bahawa lebih ramai pesakit kencing manis yang mempunyai masalah kemurungan berbanding dengan pesakit pesakit kegagalan ginjal kronik tanpa penyakit kencing manis ($p<0.033$).

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Kesimpulan:

Konklusinya, prevalen sebenar penyakit kemurungan dikalangan pesakit – pesakit kegagalan ginjal yang tenat di Kelantan adalah 56.8% dan prevalen ini agak sama berbanding dengan kajian lain yang pernah dijalankan sebelum ini.

Penyakit kemurungan di kalangan pesakit – pesakit ginjal kronik sangat berkait rapat dengan tahap hemoglobin yang lebih rendah dan tekanan darah sistolik yang lebih tinggi. Ia juga menunjukkan bahawa penyakit diabetes juga boleh mempengaruhi kewujudan masalah kemurungan di kalangan pesakit – pesakit ini.

ENGLISH ABSTRACT

Background:

Depression is the most commonly encountered psychiatric problem in patients with end stage renal disease (ESRD) and has been shown to have a significant impact on the morbidity and mortality of these patients.

The prevalence rate of depression in ESRD patients on haemodialysis as quoted by Kimmel et al (1998) was 50%. Unfortunately there was no local data on the prevalence of depression in ESRD patients undergoing haemodialysis; hence this study was conducted to address this issue. The objective of the study was also to compare the differences in parameters such as haemoglobin, nutritional status, blood pressure control and adequacy of dialysis between the depressed versus the non depressed ESRD patients.

Methodology:

This was a cross sectional study conducted on all ESRD patients undergoing haemodialysis in Hospital University Sains Malaysia (HUSM) and Renal Care dialysis centre. The subjects were interviewed using a validated Malay version of Hospital Anxiety and Depression Scale (HADS) questionnaire as

a screening tool for depressive illness. The blood and dialysis parameters such as haemoglobin, serum iron, renal function, serum albumin, interdialytic weight gain and blood pressure were obtained and analyzed. Amount of dialysis delivered was measured by urea kinetic modeling (Kt/V).

Result:

The local prevalence of depressive illness among ESRD on regular haemodialysis (using 11 as the cutoff point) obtained from this study was 56.8%.

On univariate analysis, this study had shown a significantly lower haemoglobin level (10.4 vs 11.5; $p < 0.009$) and higher systolic blood pressure (149.0 vs 138.6; $p< 0.031$) among the depressed group as compared to the non depressed group of patients. Univariate analysis had also significantly showed more proportion of female in the depressed group as compared to the non depressed group (32.1% vs 24.7%; $p<0.027$)

On further analysis with multivariate analysis, the haemoglobin and systolic blood pressure control remain statistically significant with $p<0.023$ and

$p<0.008$ respectively. Multivariate analysis had also significantly showed more proportion of diabetics had depression as compared to non diabetics with $p<0.033$.

Conclusion:

In conclusion, local prevalence of depressive illness amongst end stage renal disease patients on haemodialysis was comparable to previous studies. We also found that depressive state was significantly associated with lower haemoglobin level and higher systolic blood pressure. Diabetes was also shown to become an independent risk factor of developing depression.

CHAPTER 1

INTRODUCTION

1.1 OVERVIEW OF END STAGE RENAL DISEASE.

1.1.1 Introduction

The National Kidney Foundation of the United States – Disease Outcome Quality Initiative (K/DOQI) 2005 guideline defines chronic kidney disease (CKD) as structural or functional kidney abnormalities (abnormal urine analysis, abnormal imaging studies or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR). It is characterized by progressive renal mass destruction with irreversible sclerosis and loss of nephrons. The term CKD should be reserved for patients with GFR less than 60ml/min. CKD usually ends up as end stage renal disease (ESRD).

ESRD is defined as a clinical state or condition in which there has been an irreversible loss of endogenous renal function leading a patient to be permanently dependent upon renal replacement therapy to avoid life threatening uraemia. The term ESRD should be reserved for CKD patients with GFR less than 15ml/min.

1.1.2 Pathophysiology

Each kidney has approximately one million nephrons. Each functioning nephron contributes to the total glomerular filtration rate (GFR). In the event of an injury, reduction of renal masses causes structural and functional hypertrophy of the surviving nephrons to maintain the GFR. This adaptability allows for the continuity of normal clearance of plasma solutes i.e. urea and creatinine. As GFR declines to as low as thirty percent of normal, patients may remain asymptomatic, only then plasma creatinine and urea will start to rise. The residual nephrons hyperfiltration and hypertrophy has been hypothesized to represent a major cause of progressive renal damage.

1.1.3 Prevalence.

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States, there is a rising incidence and prevalence of kidney failure. The number of patients enrolled into end stage renal disease (ESRD) program has increased from 10 000 beneficiaries in 1973 to 86 354 in 1983 and 431 284 in 2002. The rising prevalence of treated ESRD can be attributed to the increase in the number of patients who start renal replacement therapy each year, and to smaller extent, increased survival of

patients with end stage renal disease (ESRD). The NKF – K/DOQI CKD Guidelines workgroup, using glomerular filtration rate (GFR) < 60ml/min/1.73m2 as a definition for chronic kidney disease (CKD), states that the prevalence of CKD in the United States in the year 2000 is 4.7 % or 8.3 million. The exact incidence of CKD in Malaysia is unknown due to under reporting. At the end of 2004, there were a total of 11554 dialysis patients, one third receiving dialysis treatment provided by Ministry of Health (MOH) hospitals, another third by non government organization centers (NGO) and about 28% by the private sector (the twelfth report of The Malaysian Dialysis and Transplant Registry, 2004).

1.1.4 Race.

There are striking racial and ethnic differences in the incidence and prevalence rates of CKD and ESRD in the United States. It is higher in African American and Asian American as compared to Caucasians. Unfortunately there are no local data to reveal local prevalence racial differences in Malaysia.

1.1.5 Gender.

In United States, males are more commonly affected than females to suffer from chronic kidney disease (CKD); United State Renal Data System, 1999. Similarly in Malaysia, males make up 55% of all new dialysis patients, 58% on haemodialysis and 52% on continuous ambulatory peritoneal dialysis (CAPD) patients. (The twelfth report of The Malaysian Dialysis and Transplant Registry, 2004).

1.1.6 Age.

End stage renal disease (ESRD) is found in all ages. In Malaysia, the dialysis treatment rates for patients 55 to 64 years old continue to rise. The younger age group 45 to 54 years old is seen in new CAPD patients.

1.1.7 Clinical symptoms.

Patients with mildly diminished renal reserve are asymptomatic, and renal dysfunction can be detected only by laboratory testing. A patient with mild to moderate renal insufficiency may have only vague constitutional symptoms despite elevated blood urea nitrogen (BUN) and creatinine. Lassitude, fatigue, and decreased mental acuity often are the first manifestations of uremia. Hakim and Lazarus (1989) found in their study

that patients are mostly asymptomatic until glomerular filtration rate (GFR) is less than 30ml/min.

Neuromuscular features include coarse muscular twitches, peripheral neuropathies with sensory and motor phenomena, muscle cramps, and convulsions (usually the result of hypertensive or metabolic encephalopathy). Anorexia, nausea, vomiting, stomatitis, and an unpleasant taste in the mouth are almost uniformly present.

1.1.8 Clinical signs.

Malnutrition leading to generalized tissue wasting is a prominent feature of chronic uremia. In advanced chronic kidney disease (CKD), gastrointestinal ulceration and bleeding are common. Hypertension is present in > 80% of patients with advanced renal insufficiency and is usually related to hypervolemia and occasionally to activation of the renin-angiotensin-aldosterone system. Cardiomyopathy (hypertensive, ischemic) and renal retention of sodium and water may lead to congestive heart failure or dependent edema. Pericarditis, usually seen in chronic uremia, may occur in acute, potentially reversible, uremia. The skin may appear yellow-brown;

occasionally, urea from sweat may crystallize on the skin as uremic frost causing pruritus.

1.1.9 Relevant investigations.

(i) Assessment of severity and complications of CKD.

Definitive assessment of severity of renal insufficiency depends on laboratory findings of blood urea nitrogen (BUN), creatinine and creatinine clearance. Assessment of anaemia, metabolic acidosis, hypocalcaemia, hyperphosphataemia and hyperuricaemia are also important.

Creatinine clearance is the most important investigation in chronic kidney disease (CKD). It is measured by calculation (Cockcroft – Gault) formula or using twenty-four hours urine creatinine clearance.

(ii) Investigations for complications of CKD.

(a)Renal osteodystrophy (abnormal bone mineralization resulting from hyperparathyroid function, calcitriol deficiency, elevated serum phosphorus, or low or normal serum calcium) usually takes the form of hyperparathyroid bone disease (osteitis fibrosa). Serum parathyroid hormone should be done to assess parathyroid function as well as serum phosphate and serum calcium level.

(b)Abnormalities with lipid metabolism may occur with chronic kidney disease (CKD), patients on dialysis and post renal transplantation. The primary finding in CKD and dialysis is hypertriglyceridemia; the total cholesterol level is usually normal.

(iii) Assessment for chronicity of CKD.

Imaging studies, usually ultrasound, need to be done to assess the chronicity of the disease.

(iv) Investigations to determine the primary cause of CKD.

Investigations to look for primary illness are also indicated i.e. antinuclear antibodies (ANA) and double stranded DNA antibody levels for lupus nephritis, serum complements, c-ANCA, p- ANCA, anti-GBM antibodies for underlying glomerulonephritis as well as viral hepatitis particularly B and C.

1.1.10 Causes of ESRD.

Diabetes and hypertension are the two commonest causes and account for approximately two thirds of the cases of CKD and end stage renal disease (ESRD). Other major causes include glomerulonephritis of any type (one of the most common causes), polycystic kidney disease, Alport syndrome, reflux nephropathy, obstructive uropathy, kidney stones and infection, and analgesic nephropathy.

According to the twelfth report of The Malaysian Dialysis and Transplant Registry 2004, the prevalence of diabetes in Malaysia is rising and the glycaemic control is suboptimal. Thirty three percent (33%) of adult Malaysian is hypertensive and the blood pressure control is poor. Fifty one percent (51%) of new dialysis patients were diabetics in 2004. (The twelfth report of The Malaysian Dialysis and Transplant Registry, 2004).

1.1.11 Treatment of ESRD

Over the past 35 years, renal replacement therapy using dialysis and transplantation has prolonged the lives of thousands of patient with end stage renal disease (ESRD). Renal replacement therapy should not be initiated when the patient is asymptomatic; however, dialysis and/or transplantation