QUALITY OF LIFE IN END STAGE RENAL DISEASE PATIENTS AFTER SUCCESSFUL RENAL TRANSPLANTATION, TANZANIA EXPERIENCE

By

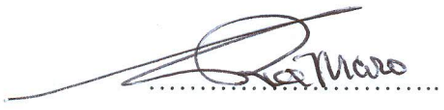
Onesmo A Kisanga

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree Master of Science (Nephrology) of the Muhimbili University of Health and Allied Sciences

April 2009

CERTIFICATION

The undersigned certify that he has read and hereby recommend for the examination a dissertation *entitled* ***"Quality of Life in End Stage Renal Disease Patients After Successful Renal Transplantation- Tanzania Experience"*** in fulfillment of the requirement for the degree of Master of Science (Nephrology) of the Muhimbili University of Health and Allied Sciences



Dr Eden E Maro

(Supervisor)

DECLARATION AND COPYRIGHT

I, Onesmo Adonikam Kisanga, declare that this dissertation is my own original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award

Signature.....

Date.....11.11.09

This dissertation is copyright material protected under the Berne Convention, the Copyright Act 1999 and other international and national enactments, in that behalf, on intellectual property. It may not be reproduced by any means, in full or part except for short extracts in fair dealings, for research or private study, critical scholarly review or disclosure with an acknowledgement, without permission of the Directorate of Postgraduate Studies, on behalf of both the author and the Muhimbili University of Health and Allied Sciences.

ACKNOWLEDGEMENT

I am sincerely grateful to my supervisor Dr Eden E. Maro for his untiring support, constructive criticisms, and encouragement during the preparation and write up of this dissertation.

Special appreciation goes to Prof Bjarne Iversen and the Renal Research Group of University of Bergen, Norway and Prof George T John and Nephro group of Christian Medical College Vellore, India for contribution and constructive criticisms.

My sincere thanks also go to Mr C Makwaya of the department of Epidemiology and Biostatistics of the Muhimbili University of Health and Allied sciences for his assistance during my data cleaning and statistical calculations.

My appreciation also goes to the management of Muhimbili National Hospital, Regency Medical Centre, IHI Aga Khan, TMJ, Lugalo Military Hospitals and MOH&SW headquarters for allowing me to use their patients for this purpose.

Lastly but not least I owe my gratitude to all the renal transplanted patients who participated in this study.

DEDICATION

This work is dedicated to my family. My wife Mrs Agnes O Kisanga for her kindness, tolerance and everlasting support throughout my studies and to my daughters Eva, Mkyeku and Mai for missing me most of this time.

ABSTRACT

CKD and eventually ESRD are becoming markedly increased across the world. The cost for RRT is becoming so prohibitive more so in developing countries like Tanzania. HRQoL is increasingly being used to assess chronic clinical conditions, CKD being one of them. HRQoL in nephrology involves determining efficiency and effectiveness of different forms of RRT; evaluating the efficiency and effectiveness of different types of other treatments applied to patients e.g. immunosuppressives, and follow-up of the evolution of individual patients.

Objectives; To determine the quality of life in ESRD patients after successful renal transplantation in Tanzania.

Study site and design; Cross- sectional study involving all renal transplanted patients in Tanzania.

Study procedure; a questionnaire was administered to all consenting renal transplanted patients. Information recorded includes demographic data, clinical characteristics and HRQoL using the SF-36 tool.

Results; The study sample included 44 renal transplanted patients of whom most were males 31(81.8%), married 37(84.1%), college educated 31(70.5%) and overweight 29(65.9%). Their age ranged from 22 to 66 years with a mean of 45.9 years ± 10.51.

Diseases leading to ESRD included Hypertension 25(58.8%), Glomerulonephritis 7(15.9%), both diabetes and hypertension 6(13.6%), Polycystic disease 3(6.8%), diabetes alone 2(4.5%).

Most transplants were sponsored by government 28(63.6%). Others included Employer or insurance 11(25.0%) and self or family 5(11.4%).

Most renal transplanted patients were on cyclosporine based immunosupression 20(45.5%). 11(25.0%) were on Tacrolimus, 7(15.9%) on Sirolimus and 4(9.1%) Azathioprine based immunosuppression.

Generally the HRQoL ESRD patients in Tanzania improved after transplantation. All 8 domains except 1 had total score above 50%. Physical Functioning =75%, Bodily Pain = 88.6%, General Health =73%, Vitality = 86.4%, Social Functioning =84.1%, Role Emotional = 52.3%, Mental Health = 95.5% and Role- Physical = 45%.

Some characteristics had statistical significant correlation to HRQoL like Age ($p< 0.043$), Marital status ($p< 0.036$), Education ($p< 0.002$), Employment ($p < 0.008$), serum Creatinine ($p< 0.032$), BUN ($p <0.021$), Immunosuppressives ($p <0.028$), DBP ($p< 0.000$), Haemoglobin ($p< 0.038$), Living donation ($p< 0.05$) and Smoking ($p< 0.038$).

Random Blood Sugar ($p<0.06$), BMI ($P<0.53$), HLA (0.53), Time since Transplantation were not statistically significantly associated to HRQoL. Likewise serum lipids ($p< 0.356$), serum protein (0.734) and serum albumin ($p<0.141$) were not statistically significant related. SBP ($p<0.060$), donor age ($p<0.66$, Urine routine ($p< 0.51$), donor relation ($p< 0.66$) and sex ($p<0.30$) were also not statistically related to HRQoL.

Conclusion; ESRD patients HRQol improves after renal transplantation. However transplantation is thus expensive and emphasis should be put on CKD prevention.

LIST OF ABBREVIATIONS

ACEI.....Angiotensin Converting Enzyme Inhibitor
AIDS.....Acquired Immunodeficiency Syndrome
ARB.....Angiotensin Receptor Blockers
BMI.....Body Mass Index
CAPD.....Continuous Ambulatory Peritoneal Dialysis
CKD.....Chronic Kidney Disease
CMV.....Cytomegalovirus
CRF.....Chronic Renal Failure
ECM.....Extra cellular Matrix
ESRD.....End Stage Renal Disease
ESRF.....End Stage Renal Failure
HBV.....Hepatitis B Virus infection
HCV.....Hepatitis C Virus infection
HLA.....Human Leukocyte Antigen
HRQoL.....Health Related Quality of Life
IPD.....Intermittent Peritoneal Dialysis
JNC.....Joint National Committee
MOH & SW...Ministry of Health and Social Welfare
MNH.....Muhimbili National Hospital
NODAT.....New Onset Diabetes After Transplantation
QoL.....Quality of Life
PTB.....Pulmonary Tuberculosis
RAAS.....Renin Angiotensin Aldosterone System
RBG.....Random Blood Sugar
RRT.....Renal Replacement Therapy
SADTR.....South African Dialysis and Transplant Registry
SF-36.....Short Form 36

UK.....United Kingdom

USA.....United State of America

USRDS.....United State Renal Data System

UTI.....Urinary Tract Infection

WBC.....White Blood Cells

LIST OF TABLES

Table 1.....22
Table 2.....23
Table 3.....24
Table 4a.....25
Table 4b.....25
Table 5.....27
Table 6 28
Table 7.....30
Table 8.....31
Table 9.....32

TABLE OF CONTENTS

Title.....i
Certification.....ii
Declaration.....iii
Acknowledgement.....iv
Dedication.....v
Abstract.....vi
List of Abbreviations.....viii
List of tables.....x
Table of contents.....xi
1. Background.....1
1.1 Epidemiology of chronic renal failure.....1
1.2 Mechanism of development of Chronic Renal Failure.....3
1.3 Renal diseases in Africa.....4
1.4 Renal Replacement therapy.....7
1.5 Quality of Life.....11
1.6 Combined Kidney and Pancreas Transplantation.....15
1.7 Quality of life following Transplantation of the Liver, Heart and Lung. 16
2. Problem Statement and Rationale 17
3. Research Questions.....18
4. Study Objectives.....18
4.1 Broad Objectives 18
4.2 Specific Objectives.....18
5. Methodology.....19
5.1 Study design.....19
5.2 Study setting.....19
5.3 Study population.....19
5.4 Data collection procedure.....19

5.4.1 Inclusion criteria 20
5.4.2 Exclusion criteria.....20
5.4.3 Ethical clearance.....20
6. Data entry and statistical analysis.....20
7. Results.....21
8. Discussion.....33
9. Conclusion.....42
10. Recommendations.....42
11. Study limitations.....43
12. References.....44
13. Appendix I (Consent form English Version).....53
14. Appendix II (Consent form Kiswahili Version).....56
15. Appendix III (Questionnaire on QoL- English Version).....58
16. Appendix IV (Questionnaire on QoL Kiswahili Version).....72

1. BACKGROUND

Chronic renal failure (CRF) is a permanent, usually progressive diminution in kidney function. It is caused by several renal diseases where immunological, metabolic and hypertensive disorders are the most common.

In its severe form it leads to End Stage Renal Disease (ESRD), a degree of renal failure that would cause death unless some form of Renal Replacement Therapy (RRT) is initiated. There are two forms of RRT-Dialysis (haemodialysis and peritoneal) and Renal transplant.

Epidemiology of chronic renal failure

Progression of chronic renal failure leads in the majority of instances to ESRD and when the residual renal function has largely been compromised, RRT is required. Since the mid 1980s there has being a marked increase in the incidence of ESRD across the world. The number of individuals treated in USA with dialysis and transplantation exceeded 320000 in 1998 and is expected to surpass 650000 in 2010(1). This is due to better medical treatment and demographic changes with increasing numbers of elderly people.

In the UK the incidence of ESRD varies between 45 and 85 new patients per million population, but it is much higher in the USA with 268 new patients per million population per year (1). The difference between Europe and USA is also shown by the difference in prevalence of patients on RRT. It was 462 patients per million in Europe and 1041patients per million population in the USA in 1996(1).

In general the incidence of ESRD increases with age reaching around 1000 patients per million per year above 65 years of age (1). As regards to age the incidence increased from 58 patients per million per year under the age of 50 years to 588 patients per million population per year from 80 years and over (2). In a French study,

the incidence of CRF was 1124 patients per million, with the highest incidence in elderly males (2).

Race and gender are of major importance as the incidence of renal disease and development of ESRD is different. While both hypertension and diabetes are more prevalent causes of ESRD in the developed world, chronic glomerulonephritis remains the most common cause in the underdeveloped countries (3).This is probably due to higher incidence of infections. Progression of the immunological nephropathy is dependant upon the type of glomerulonephritis and the level of proteinuria which seems to be an independent risk factor (3).

As regards to gender ESRD is more common in males than in the females. In the non diabetics, the rate of progression of renal failure has been found to be twice as high in males compared to females (2). Pathogenic mechanisms such as blood pressure are involved, as progression to ESRD was positively correlated with mean arterial blood pressure and a faster rate of progression to renal insufficiency was reported in males with Idiopathic membranous nephropathy, IgA nephropathy, Polycystic Kidney Disease, Hypertensive Nephrosclerosis and type 1 Diabetes(2).

The importance of race is demonstrated in studies from USA. Both the incidence and prevalence of hypertensive and diabetic renal disease have been found to higher in the African-Americans and Hispanic-Americans compared to Whites in the USA(1).The rate of progression of renal disease in both diabetic and non diabetic is more rapid in the African-Americans than in Whites(4).Furthermore, in a large single-centre study of 771 patients with ESRD in the USA, showed a higher incidence of diabetic nephropathy in patients from Indian sub-continent while Hypertensive renal disease was more prevalent in African and Caribbean descent(5).

Mechanisms of development of chronic renal failure

Several factors have a strong impact on the development of chronic renal failure. Proteinuria has been shown to be a single predictive factor in determining the progression to ESRD. Patients with heavy and sustained proteinuria invariably have a worse prognosis when compared to those with mild or remittent pattern of proteinuira (3).The role of proteinuria on the course of the renal disease, have been further clarified by changing the diet. The Modification of Diet in Renal Disease study as well as other studies has shown that baseline proteinuria was a strong predictor of subsequent decline in renal function (3, 6). The combined treatment with reduction of proteinuria by protein restriction (7) and Angiotensin Converting Enzyme Inhibitors (ACEI) (8) predict a better outcome in both diabetic and non diabetic renal diseases.
Hypertension is a very strong predictor of progression to CRF (2,3). The rate of progression to CRF is twice as fast in patients with diastolic pressure above 90mmHg as compared to lower levels. Progressive interstitial fibrosis or expansion of the extracellular matrix (ECM) by enhanced deposition of collagens is a morphological hallmark of chronic renal failure and is induced by hypertension. The interstitial fibrosis is characterized by an increased expression of collagen, the fibrous protein in connective tissue (9). This leads to expansion of the ECM which seems to destroy the tubular structures and cause functional deterioration of kidney function.

The role of lipid seems to play a role in development of chronic renal disease as there is a strong association, between lipoprotein and progression of renal failure (9). Progressive interstitial fibrosis or expansion of the ECM by enhanced deposition of collagens is a morphological hallmark of chronic renal failure. The interstitial fibrosis is characterized by an increased expression of collagen, the fibrous protein in connective tissue (9). This leads to expansion of the ECM which seems to destroy the tubular structures and cause functional deterioration of kidney function.

Furthermore, the role of lipids seems to play a role in development of chronic renal disease. In non diabetic nephropathies with elevated cholesterol and triglycerides appear to proceed faster to ESRD than those without hyperlipidaemia (9). Similar results are also found in patients with diabetic nephropathy (9).

The role of smoking in development of chronic renal failure has been debated, but some data seem to demonstrate deterioration both in diabetic and non diabetic nephropathies (10). The mechanisms may be related to increased blood pressure followed by elevated proteinuria and consequently progression in renal failure.

Renal diseases in Africa

Africa is a vast continent, extending over 30 million square km and comprising 53 countries with approximately 760 million people. Many millions live in overcrowded with poor hygienic conditions, where lack of clean water and inadequate sanitation foster breeding grounds for infectious diseases. Infectious diseases are the world's leading cause of death, 43% in the developing world compared to 1.2% in the developed world (11). Diseases such as tuberculosis and malaria that some places were recognized to be controlled have become a major health problem, mainly due to problems with resistance to therapy and shortage of money to buy the drugs. New diseases, such as AIDS, have reached epidemic proportions especially in sub-Saharan Africa.

The expenditure per capita per year on healthcare, show large differences between African countries. It ranges from11 US dollars (Tanzania), 9 US dollars (Nigeria), 29 US dollars (Senegal), 100 US dollars (North Africa) and 158 US dollars (South Africa). In contrast the healthcare expenditure per scapita in Europe is approximately 2000 US dollars. The health situation is increasingly influenced by social and economic circumstances and any improvements in total health thus demand an integrated, comprehensive action against all the determinants of all types of diseases in Africa.

As stated above, several studies have demonstrated the high incidence of chronic renal disease among African-Americans (1). Unfortunately, there are no reliable statistics in African countries. However, there is a general impression that renal diseases are at least three to four times more frequent than in more developed countries. These data are mainly based on analysis of the causes of death, reporting that uremia accounts for 1 to 1.5% of total annual deaths among Egyptians, (12). These figures are comparable with those of other countries in the region with similar socioeconomic standards.

Renal disease, especially glomerular disease, is more prevalent in Africa and seems to be of a more severe form than that found in Western countries. The most common mode of presentation is the nephrotic syndrome, with the age of onset at five to eight years (15). It is estimated that 2 to 3% of medical admissions to hospitals in tropical countries are due to renal-related complaints, the majority being glomerulonephritis. There are no reliable statistics for ESRD in all African countries. Statistics of the South African Dialysis and Transplant Registry (SADTR) reflect the patients selected for renal replacement therapy (RRT) and do not accurately reflect the etiology of chronic renal failure (CRF), where public sector state facilities will offer RRT only to patients who are eligible for a renal transplant. In 1994, glomerulonephritis was recorded as the cause of ESRD in 1771 (52.1%) and hypertension in 1549 (45.6%) of patients by the SADTR. In a six-year study of 3632 patients with ESRD, based on SADTR records., hypertension was reported to be the cause of ESRD in 4.3% of whites, 34.6% of blacks, 20.9% mixed race group and 13.8% of Indians. Malignant hypertension which is an important cause of morbidity and mortality among urban black South Africans accounted for 16% of all hospital admissions (13). In a ten-year study of 368 patients with chronic renal failure in Nigeria, the etiology of renal failure was undetermined in 62%. Of the remaining patients whose etiology was ascertained, hypertension accounted for 61%, diabetes mellitus for 11% and chronic glomerulonephritis for 5.9%. Patients with CRF constituted 10% of all medical admissions at this center (14). A 15-year review of children, who presented with CRF

to the University of Port Harcourt Teaching Hospital, Rivers State of Nigeria, was carried out. Forty-five children (28 boys, 17 girls) with CRF, defined as a glomerular filtration rate below 30 ml/min per 1.73 m^2 body surface area or a rise in serum creatinine above 120 µmol/l for at least 6 months, often accompanied by other biochemical abnormalities, were identified. The median annual incidence of CRF was 3.0 per million children. The prevalence of CRF increased from 12.5 in the 1985–1990 periods to 15 per million children after 1995. Acquired disorder was the major cause of CRF. Glomerulopathies were the cause in 53.3% of patients, mainly chronic glomerulonephritis (56.5%) and nephrotic syndrome (30.4%). Hepatitis B surface antigen was positive only in 2 patients. Congenital disorders accounted for 28.9% of all cases of CRF, which is lower than data from other countries. Posterior urethral valve was the only congenital disorder causing CRF in this study. No child with hereditary renal disorder as a cause of CRF was identified. Children with congenital disorders were diagnosed at an earlier age. The mortality rate was high (46.7%), as most patients were managed conservatively, since there were no permanent facilities for chronic dialysis or renal transplantation in Nigeria. The study shows that CRF is common in Nigerian children, and there is an urgent need for the establishment of facilities for renal replacement therapy (15).

Chronic glomerulonephritis and hypertension are the main causes of CRF in tropical Africa and East Africa, together with diabetes mellitus and obstructive uropathy. The availability of dialysis and transplantation is quite variable in Africa: treatment rates in North Africa are 30 to 186.5 per million of the population (pmp) in countries with more established programs: Algeria 78.5; Egypt 129.3; Libya 30; Morocco 55.6 and Tunisia 186.5. In South Africa, treatment rates of 99 pmp have been reported (16). Dialysis and transplant programs in the rest of Africa are dependent on the availability of funding and donors. Services are still predominantly urban and therefore generally inaccessible to the poorer and less educated rural patient. There is not enough money for healthcare in Africa particularly for expensive and chronic treatment such as RRT

(16). The goal should be to have a circumscribed chronic dialysis program, with as short a time on dialysis as possible, and to increase the availability of transplantation (both living donor and donor from dead persons). Efforts should be made to prevent and optimize therapy of renal disease and renal failure globally and particularly in developing countries with lack of resources. Strategies should be developed to screen for and manage conditions such as hypertension and diabetes mellitus at the primary healthcare level in an effort to decrease the incidence of chronic renal failure. Any improvements in health thus demand integrated, comprehensive action against all the determinants of ill health. In Tanzania the prevalence of ESRD is estimated to be 75 patients per million population. Studies of follow-up of 26 transplant patients the main primary cause of ESRD was Hypertension (30.8%), Chronic glomerulonephritis (23.8%), Nephrotic syndrome (15.4%), Obstructive uropathy (7.7%), Ischaemic nephrosclerosis (3.9%), Polycystic kidney (3.9%) and undetermined (15.4%) (17, 18).

Renal replacement therapy

Renal Replacement Therapy comprises Dialysis (haemodilysis and peritoneal) and Renal Transplant. If every patient with ESRD was started on dialysis, the incidence rate of new dialysis patient would reflect the epidemiology of renal disease. This incidence varies across the world due to different criteria in offering any mode of dialysis if ever available.

Among the factors that influence the criterion for dialysis is their availability (19). Availability of nephrologists is also an important factor as patients have been denied dialysis by general practitioners due to lack of nephrologists (20).

Cultural differences and diverse attitudes influence the decision to initiate dialysis. Nephrologists in the UK would hesitate to initiate dialysis in a severely mentally incapacitated patient as compared to nephrologists in the USA.

Due to limited resources available, it has been argued that patients who are not expected to survive for more than a few months should not be offered dialysis. This is

supported by the view that it is preferable to avoid suffering by not starting dialysis than to withdraw treatment when the patient condition becomes disastrous (21). Withdrawing dialysis seem more like actively causing death than withholding dialysis, where death is allowed to occur naturally. This utilitarian approach to the allocation of resources is contrary to the instincts of most doctors to act in the patient's best interest and may be unacceptable to many physicians. Furthermore it does not take into account of even a short extension of life which allows the patient and his or her family to prepare for death. Nevertheless, most physicians would agree that patients who are certain to have an unacceptable quality of life should not be accessed to this treatment. Although advanced age was used as a simple exclusion criterion in the early days when resources were limited, the elderly are now the most rapidly growing group of the dialysis population. Their quality of life can be good; indeed their expressed satisfaction with life may be greater than that of younger dialysis patients (22).

One Canadian study has attempted to identify other predictive factors (23).822 patients starting dialysis were studied prospectively. A Cormobidity scoring system was used to quantify factors likely to predict early death, including increasing age, heart failure, symptomatic ischaemic heart disease, cardiac arrhythmias, severe peripheral vascular diseases, malignancy and severe liver diseases. The predictive value of this scoring system was compared with the value of an estimate made by the patient's nephrologist of the probability the patient would die within 6 months. Although 14% patients died within 6 months, it was not possible to predict early death accurately using the Cormobidity scoring system or the clinician's opinion. It was even impossible to identify the small proportion of patients with poor prognosis. Clinicians were more accurate than the scoring system in identifying patients with less than a 50% risk of death by 6 months, but they tended to overestimate the risk of death in the worst prognostic groups. For example, 30% of patients whose probability of death was considered to be >80%, in fact survived for more than 6 months. This important study should strengthen the resolve of clinicians to resist the imposition of rationing criteria on dialysis provision. Furthermore, it warns clinicians against

making self fulfilling prophecies of early death in patients with ESRD who are denied dialysis.

Nephrologists may be encountered by a dilemma of a competently patient who does not wish to be dialyzed or a close relative of an incompetent patient, on behalf speaking not to start dialysis (21). From ethical viewpoint, decision not to start dialysis or withdrawing dialysis is justified by individual's autonomy. Where a patient is able to express a clear wish, it is the duty of a physician to respect the patient's decision; denying a patients treatment may constitute an assault. The physician must nonetheless ensure that all reversible factors have been addressed such as unfounded fears about what dialysis will entail or a depressive illness which will affect patient's judgment.

There is a wide discrepancy as to the choice of either peritoneal or haemodialysis. In the UK 45% of the patients compared to only 10% in France are offering peritoneal dialysis indicating non medical influences on dialysis (24).

It behooves all nephrologists to ensure that the resources dedicated to renal failure treatment are used to best effect. As dialysis has advanced the goal of treatment has moved from merely sustaining life to achieving as near normal a quality of life for patient as possible.

Renal transplantation is a modality of RRT that has proven to be highly effective in increasing both life expectancy and quality of life. New maintenance immunosuppressive therapies, potent agents to combat acute rejection episodes, a better understanding of the role of transplantation immunobiology, and a closer medical monitoring and treatment of patients of cormorbid conditions have resulted in a steady improvement in both short and long term graft survival (25).A successful kidney transplant frees the patient from dialysis and provides the kidneys other metabolic functions.

Kidney was the first organ which was successfully transplanted. The event to place in Boston, USA, and was performed between two identical twins. Transplantation

between twins evokes the least immune reaction as the HLA types are identical and no immunosupppresion therapy is necessary (26).
In 2001 there were 14000 kidney transplants of which 63% were from dead persons. Patients survival using kidneys from dead persons is .90% 1year after the transplant and 60-90% after 5 years while for living donor it is >98% after 1 year and 71-98% after 5years (27).

Dialysis and transplant programs in Africa are dependent on the availability of funding and donors.

Tanzania has intermittent hemodialysis facilities for patients with acute renal failure and patients with chronic renal failure have been prepared for kidney transplants abroad. Dialysis services were offered in the 1980s at the Muhimbili Medical Centre; todate haemodialysis is only offered by private hospitals and there is no peritoneal dialysis in Tanzania. We do not have transplant services in Tanzania; a few are referred abroad initially to UK and currently to India (17,18).

Nigeria offers hemodialysis, CAPD and IPD (Intermittent Peritoneal Dialysis) depending on availability of funds. Patients were previously referred to Europe for renal transplantation, which is currently being established in Nigeria (16).

Cameroon offers all modalities of dialytic support to limited numbers of patients, depending on funding (16).

Cote d'Ivoire has a few hemodialysis and renal transplant patients, with the patients being transplanted in other countries (16).

Ethiopia has hemodialysis and peritoneal dialysis facilities for acute renal failure (16).

Quality of life

The evaluation of Health Related Quality of Life (HRQoL) in chronic diseases is becoming more and more important. The reasons for the importance of HRQoL assessment can be summarized as follows: 1. to determine the efficacy of medical intervention; 2.to improve the process of making clinical decisions; 3. to evaluate the quality of care; 4. to estimate the health care needs of the general population; and 5. to gain a better understanding of the causes and consequences of the differences in health (28). For some authors the assessment of perceived health status is especially important in the evaluation of the consequences of chronic diseases, because clinicians require information about the effects of a specific disease on patients, and also of the effect of a specific treatment, in order to improve its management and the assessment of the evolution of the patient (28).

In the Nephrology field, the evaluation of HRQoL involves: 1st determining the efficiency and effectiveness of the different forms of renal replacement therapy (RRT) (hemodialysis, peritoneal dialysis and kidney transplantation); 2nd evaluating the efficiency and effectiveness of the different types of other treatments applied to patients of immunosuppressive treatments); 3rd follow-up of the evolution of individual renal patients (28).

The World Health Organization defined Quality of Life (QoL) as 'the individual's perception of their life status concerning the context of culture and value system in which they live and there goals, standards expectations, and concerns' (29).

Kidney transplantation is the treatment of choice for end stage renal disease patients. Recent advances, including newer immunosuppressants, revision of organ allocation policies, and better medical care of renal transplant recipients, have resulted in an increased number of transplants with improved outcomes. The major obstacles include the lack of improvement in long term outcomes, shortage of organs and long-

term morbidity of candidates with chronic kidney disease (25). Kidney transplantation should be strongly considered for all patients who are medically suitable with chronic and end-stage renal disease (ESRD). A successful kidney transplant offers enhanced quality and duration of life and is more effective (medically and economically) than chronic dialysis therapy. Transplantation is the renal replacement modality of choice for patients with diabetic nephropathy and pediatric patients.

Currently in the US, more than 80,000 persons are living with a functioning kidney transplant. This number represents 27% of the nearly 300,000 persons enrolled in the US ESRD program

Renal Transplant is very expensive procedure. With the scarce health budget there is a need to assess the QoL gained and factors related to that.
We do not have renal transplant services in the country and a few patients whom the government can sponsor are referred abroad at an exorbitant price.
There is an increasing attention that is being paid as to the QoL that is offered to the patient, family and society in general.

The definition of QoL is difficult in the context of Renal Replacement Therapy.
Such parameters e.g., 1.employment 2.education 3.physical performance (objective indicators) 4.ability to lead satisfactorily social life with hobbies and interests and 5.to be able to have sex and affectionate relationship (subjective indicators).
Whilst it is desirable that all patients achieve complete rehabilitation in practice this is not achieved in the majority of cases.
In a multi-center study in the USA out of 859 patients 79% of Transplanted patients were able to function at near normal levels cf 47.5% on CAPD and 59% on haemodialysis. (30)
On three subjective measures (life satisfaction, well being and psychological affect) the transplanted had a greater QoL.

Studies in the UK were not dissimilar, they classified patients above and below 60years of age with and without risk factors (diabetes, cerebral vascular accidents (CVA), severe disability, mental illness, social isolation, unemployment, IQ, health care compliance)(31). The patients that did well were males below 60 years and with risk factors. On a few psychological scales Continuous Ambulatory Peritoneal Dialysis (CAPD) patients perceived life better than haemodialysis and an important finding was that patients over 60 years even in presence of risk factors perceived life to be good (32).

Employment status, surfers significantly in ESRD. In an American study only 25% of those employed were working after starting CAPD cf 60% for home dialysis and 75% for Transplants (33).

Although high risk patients can adapt to adverse life circumstances and perceive good QoL evidence of successive rehabilitation does not exists except in Transplant and some dialysis patients (34).

QoL following Transplant is difficult to assess (35). The popular concept is that vast improvement in QoL takes place after Transplant (36). But this is not always the case as has being confirmed by subjective measurements and particularly with failed Transplants do particularly badly (37). Although renal transplantation offers survival and quality of life advantages as a renal replacement therapy, a substantial proportion of transplant recipients develop worsening of preexisting medical diseases or new complications, including sequelae of rejection, new onset diabetes after transplantation (NODAT),hyperlipidemia, opportunistic infections, cancer, and other systemic diseases secondary to immunosuppression. Management of these problems can be a complex endeavor due to medication interactions that often affect immunosuppression levels. However, successful management of the chronic medical problems associated with renal transplantation can prolong the life span of the graft and the patient (38).

Uncontrolled clinical observations suggest that QoL after transplant is equal to that of normal population (39).Unfortunately most studies have failed to have satisfactory

control population or to follow up patients subsequently through dialysis and Transplant.

Previously many assessment of QoL depended on rehabilitation in terms of employment or education but these have become less valid as the criteria for transplant particularly regarding age has become less rigid (40).

In a survey of children in Europe starting haemodialysis before 15 years majority attended or completed secondary education but over 10% were unable to attend. However at least 11% started University, although the average proportion of patients aged between 20 and 30 years employed whether part or full time was only 60%(41). As in most studies the level of attainment at work was not included and much more detailed studies of rehabilitation and QoL are required.

Studies of sexual function have all suggested an improvement after Transplant.

The most objective assessment of sexual function is the ability to become parents.

In one study 433 Transplants, 55 on haemodialysis and 20 on CAPD were reported to become pregnant (42, 43).

The proper measures for assessing (QoL) in patients with chronic kidney disease (CKD) remain unclear. QoL measures are subjective or objective, functional or satisfaction-based, and generic or disease-specific. Treatment of end-stage renal disease with transplantation and treatment of anemia with erythropoietin in patients with CKD have been associated with dramatic improvements of QoL. Other factors such as age, ethnic or national background, stage of CKD, modality of dialytic therapy, exercise interventions, sleep disturbances, pain, erectile dysfunction, patient satisfaction with care, depressive affect, symptom burden, and perception of intrusiveness of illness may be associated with differential perception of QoL. Recent studies showed an association between assessment of QoL and morbidity and mortality in ESRD patients, suggesting the measures do matter. Further studies are necessary in patients with early stages of CKD and in children. QoL measures should include validated psychosocial measures of depressive affect, perception of burden

of illness, and social support. The challenge for the next decade will be to continue to devise interventions that meaningfully increase the QoL of patients with CKD at all stages (44).

Until now no single tool or method has been shown to be ideal in transplantation, to measure HRQoL in all circumstances. It has been shown that very different HRQoL results can be obtained in the same population if different tools are used (44). With more than 2000 publications SF-36 is one of the most widely used HRQoL used worldwide (44). It is a self administered survey containing 36 items. It includes one multi item scale that assesses 8 health domains. These include 1.Phsical Functioning-limitation of physical activities because of health problems. 2. Role-Physical-limitation in usual role activities because of physical health problems. 3. Social Functioning-limitation of social activities because of physical or emotion problems. 4. Bodily Pain-limitation of activities due to pain. 5. General Mental Health. 6. Role Emotion-limitation in usual role activities because of emotional problems. 7. Vitality. 8. General Health perception.

These domains are measured on a likert or sumative scale with scores transformed between 0 (worst) and 100 (best) (44).

Combined pancreas and kidney transplantation

In patients with type 1 diabetes mellitus and ESRD, combined pancreas and kidney transplantation improves metabolic control and obviates the need for insulin therapy. This as well may prevent diabetic nephropathy in the transplanted kidney (41) and has been shown to improve certain aspects of QoL compared to renal transplant alone (41).

Quality of life following transplantation of the heart, liver and the lungs

In the study that described the quality of life of patients who have received a transplant of the heart, liver, and lungs documented how the different patient groups faired in relation to each other with respect to physical, psychological, and social functioning, as well as in relation to published normative data and also wished to identify factors that contribute to better functioning. A questionnaire was sent by mail and responses were received from 55 heart, 149 liver, and 59 lung transplant recipients (82% response rate). Measures included the SF-36, Mental Health Inventory, the State Anxiety Inventory, the Loneliness Scale-Revised, a QoL measure that rated degree of improvement since transplantation, a measure of degree of difficulty in following medical and lifestyle regimens, sleep disturbance, and the Illness Intrusiveness Rating Scale. Results indicated that lung transplant patients reported better functioning than heart or liver transplant patients in all three domains of physical, psychological, and social functioning. Lung patients' level of functioning was equivalent to or better than published norms for the SF-36. Heart and liver recipients reported equivalent functioning to published norms in some domains, but reported impairment in the areas of physical and social functioning. Heart patients especially reported greater intrusiveness of their illness on their daily lives and indicated more difficulty complying with their lifestyle regimen. In all three groups, a large majority of patients reported feeling that life had improved since transplant with respect to health, energy level, activity level, and overall quality of life. Fewer patients reported improvements in the areas of sex life, marriage, family relationships, and social relationships. Where there were differences among the three patient groups, again it was the lung patients who reported more improvement in life since transplantation. Patients with better physical functioning tended to have more energy and pep, to be younger, to see themselves as being in better health, to feel less intrusion on their lives of their illness, and to be employed. Those with better psychological functioning tended to report less sleep disturbance, less loneliness, better social functioning, more vitality, and to be older. Better social functioning was

associated with better mental health, less illness intrusiveness, and less role impairment as a result of physical or emotional factors. Relatively few patients roughly a quarter of the total sample reported that they were working either full or part time. They concluded that transplantation results in improved quality of life overall, but that problems persist for some patients in their physical and social functioning. Interventions aimed at improving rehabilitation in specific targeted areas may enable patients to resume a more fulfilling lifestyle post transplant. (46)

2. PROBLEM STATEMENT AND RATIONALE

The prevalence of chronic renal disease is increasing worldwide and most of these patients end up in ESRD (11, 16). Globally attention is being paid to chronic renal disease because of five factors, (a) The rapid increase in its prevalence. (b) The enormous cost of treatment. (c) Recent data indicating that overt disease is the tip of an iceberg of covert disease. (d) An appreciation of its major role in increasing the risk of cardiovascular disease and (e) The discovery of effective measures to prevent its progression. (11)

End stage renal disease inevitably reduces the life span of its victims. In African countries the problem remains in assessment of QoL among renal transplanted patients and there is inadequacy in determining the efficacy of this medical intervention.

The treatment of choice for many patients is transplantation, but this does not affect a cure. Its aim is to improve renal function and thus to enhance the patients ability to enjoy as full a life as possible. In our country, no research has been done concerning the QoL of our renal transplant patients.

3. RESEARCH QUESTIONS

(1.) What is quality of life of patients with end stage renal disease who had renal transplantation in Tanzania?

(2) What problems do they encounter before and after renal transplantation?

4. STUDY OBJECTIVES

4.1 Broad Objective

To determine the quality of life in end stage renal disease patients after successful renal transplantation in Tanzania.

4.2 Specific Objectives

1. To determine the demographic characteristics of patients who had renal transplant in Tanzania.
2. To determine the causes of End Stage Renal Disease in renal transplant patients in Tanzania.
3. To determine the socioeconomic challenges associated with renal transplantation in Tanzania.
4. To determine the treatment pattern and follow up arrangements of renal transplant patients in Tanzania.
5. To determine the impact of transplantation on overall health related quality of life of renal transplant in Tanzania.

5. METHODOLOGY

5.1 Study design- Cross- sectional descriptive study.

5.2 Study setting –The study was done at

1. Muhimbili National Hospital (MNH).
2. Ministry of Health and Social Welfare (MOH&SW) Headquarters.
3. Regency Medical Centre, Hindu Mandal Hospital, Agakhan Hospital and TMJ hospital (Centres with haemodialysis services in Dar-es- Salaam).

5.3.Study population-All patients who have had renal transplant in Tanzania.

5.4 Data collection procedure

1. Written and informed consent.
2. Self administered questionnaire-SF 36 with translation in both English and Kiswahili.
3. Pilot testing of the questionnaire.
4. The following demographic data including age, sex, marital status, education status, employment status and relevant clinical variables were collected. Patient's native kidney disease was obtained from transplant discharge summaries. Other important information like time since transplant, time on dialysis, donor relationship and HLA typing were also collected.

Other information collected include history and amount of smoking, current medication i.e immunosuppressive drugs and other drugs like anti hypertensives and anti-diabetics.

The source of these drugs and the sponsors of transplantation were collected.

Other clinical parameters like height, weight, BMI, haemoglobin, WBC, RBG, serum creatinine, urine were also collected.

Disease that occurred after transplantation e.g. UTI, PTB, CMV, Herpes, Malignancy, Surgeries and side effects of the immunosuppressive drugs like cushingoid, hirsutism, gum hypertrophy were also obtained.

Episodes of acute or chronic allograft rejection and referral abroad for check-ups were also noted.

Inclusion criteria

All Tanzanian patients who had renal transplant and who consented.

Exclusion criterion

Renal transplant associated with other solid organ transplant e.g. the pancreas.

Non Tanzanian renal transplanted patients.

5. 5 Ethical clearance

Informed written consent was requested from all interviewed patients and the medical record sections. Institutional ethical clearance was obtained from MUHAS ethical committee.

6. Data entry and statistical analysis

Questionnaire data entry and analysis was done using SPSS package software version 15.Continous variables were presented as frequencies, Mean and Standard Deviation. Student T-test was used for numerical variables. And Chi-Square test was used for categorical variables. Significance was assumed at a two - tailed value $P < 0.05$.

MUHIMBILI MEDICAL UNIVERSITY COLLEGE LIBRARY DSM

7. RESULTS

Demographic characteristics

Demographic characteristics are shown in Table 1. The study sample included 44 transplant patients. Their age ranges from 21 to 66 years with a mean of 45.89 ±10.513 years. In the age group 0- 19 years had no patient. There were 5(11.4%)in age group 20-29 years, 3(6.8%)in age group 30-39years,21(47.7%)in age group 40-49 years,11(25%) in age group 50-59 years and 4(9.1%)in age group 60years and above.

There were 36(81.8%) males and 8(18.2%) females. 37 (84.1%) were married, 6(13.6%) single and 1(2.3%) was widowed.

31(70.5%) had college education, 9(20.5%) secondary and 4(9.1%) primary education.

28(63.6%) had full time employment, 3(6.8%) part time employment, 9(20.5%) were on sick leave and 4(9.1%) were retired.

Weight ranged from 43 kg to 98 kg with a mean of 74.07 ± 11.06 kg.

Height ranged from 142 cm to 182 cm with a mean of 167.± 8.363cm.

Systolic blood pressure ranged from 110 to 160 mmHg with a mean of 128.98 ± 13.320 mmHg.

Diastolic blood pressure ranged from 70 mmHg to 100 mmHg with a mean of 81.36 ± 7.951mmHg.

Body Mass Index ranged from 20 to 38 kg/m2 with a mean of 26.39 ± 3.731 kg/m2.

MUHIMBILI UNIVERSITY COLLEGE LIBRARY DSM

Table 1 ; **Demographic characteristics**

Age group (years)		Number	Percentage
0-19		0	0
20 –29		5	11.4
30-39		3	6.8
40-49		21	47.7
50-59		11	25.0
60+		4	9.1
Sex:	Males	36	81.8
	Females	8	18.2
Education:	Primary	4	9.1
	Secondary	9	20.5
	College	31	70.5
Marital status:	Single	6	13.6
	Married	37	84.1
	Divorced/widow	1	2.3
Employment:	Full time	28	63.6
	Part time	3	6.8
	Sick leave	9	20.5
	Retired	4	9.1
BMI: (Kg/m2):	Underweight (< 18.5)	0	0
	Normal (18.5 -24.9)	15	34.1
	Overweight (25 -29.9)	21	47.7
	Obese (> 30)	8	18.2

Causes of ESRD in renal transplants

Hypertension alone contributed to 25(58.8%), Glomerulonephritis 7(15.9), 6(13.6%) were due to both Diabetic and Hypertensive, 2(4.5%) Diabetic alone, 3(6.8%) had Polycystic kidney disease.1 (2.3%) native kidney disease was not known. (Table 2)

Table 2; **Disease leading to ESRD**

		Number	Percentage
1.	Hypertension	25	56.8
2.	Glomerulonephritis	7	15.9
3.	Diabetes/Hypertension	6	13.7
4.	Polycystic Kidney disease	3	6.8
5.	Diabetes alone	2	4.5
6.	Unknown	1	2.3
	Total	44	100

Socio-economic issues

28(63.6%) transplant patients were sponsored by the government, 15(34.1%) were sponsored by their employers or insurance services and 5(11.4%) were self sponsored or supported by their families. (Table 3)

15(34.1%) had their cost of medication incurred by the government, 15(34.1%) by employer or insurances and 14(31.8%) had their cost of medication met privately or supported by their families. (Table 3)

Table 3; **Sponsors for kidney transplantation and anti rejection medication expenses**

Sponsor	Transplant	%	Medication expenses	%
Government	28	63.6	15	34.1
Insurance/Employer	11	25.0	15	34.1
Self/Family	5	11.4	14	31.8
Total	44	100	44	100

Treatment pattern and follow-up arrangements

Despite a varied transplant sponsorship and cost of medicines, majority 35(79.5%) started attending the newly established renal clinic at the Muhimbili National Hospital and the rest 9(20.5%) continued to attend private services for follow-ups. As regards to immunosuppressives, 20(45.5%) were on Cyclosporine Mycophenolate and Prednisolone; 11 (25.0%) were on Tacrolimus Mycophenolate and Prednisolone; 7 (15.9%) were on Sirolimus, Mycophenolate and Prednisolone; 4 (9.1%) were on Azathioprine and prednisolone; 2(4.5%) were on other combination that included Evorolimus.(Table 4a)

On other drugs 20(45.5%) were on antihypertensives, 14(31.8%) on antihypertensive and antidiabetics, 9(20.45%) on antilipemics, 7(15.9%) on anti tuberculous therapy, only 1(2.3%) was on ant diabetic alone and 1 on other medications. (Table 4b)

As regards to follow-up abroad either for complications or trough drug levels, 30(68.2%) were referred and 14(31.8%) were not referred.

Time since transplant ranged from 58 to 4380 days with a mean of 750.59 ± 909.91 days.

Time on dialysis before transplant ranged from 0 to 13 months with a mean of 6.03 months.

Table 4a; **Immunosuppressive regime**

	Number	**Percentage**
Cyclosporine, Prednisolone, Mycophenolate	20	45.5
Tacrolimus, Prednisolone, Mycophenolate	11	25.0
Sirolimus, Prednisolone, Mycophenolate	7	15.9
Azathiprine, Prednisolone	4	9.1
Evorolimus, Mycophenolate, Prednisolone	2	4.5
Total	44	100

Table 4b; **Other drugs treatment**

	Number	**Percentage**
Anti-hypertensive	20	45.5
Anti-hypertensive/anti-diabetes	14	31.8
Anti-TB	7	15.9
Anti-diabetes	1	2.5
Anti-Lipemics	9	20.5
Others	1	2.3

Impact of transplantation on health related quality of life

Laboratory parameters of kidney transplant patients are in Table 5. Serum creatinine ranged from 88 to 599 µmol/litre with a mean of 153.1 ± 97.528 µmol/litre. Blood Urea Nitrogen ranged from 5.1 to 36.0 mmol/litre with a mean of 8.514 ± 5.092 mmol/litre.

23(52.3%) transplant patients had serum creatinine below or equal to 120 µmol/litre and 21(47.7%) had serum creatinine above 120 µmol/litre.

Random Blood Sugar ranged from 4.1mmol/litre to 13.4 mmol/litre, with a mean of 6.132 ± 2.0 mmol/litre. 41(93.2%) had Random Blood Sugar below 11.1mmol/litre and only 3(6.8%) had their Random Blood Sugar levels above 11.1 mmol/litre.

Haemoglobin ranged from 7.6 to 14.5 g/dl with a mean of 12.09 ± 1.482 g/dl 34(77.3%) had low Haemoglobin and 10(22.7%) had normal Haemoglobin levels.

Total serum protein ranged from 58 to 84 g/litre with a mean of 70.41 ± 5.970 g/ldl. 42(95.5%) had normal serum protein levels and only 2(4.5%) had low protein levels.

Serum albumin ranged from 30 to 53 g/litre with a mean of 39.34 ± 4.937g/litre. 41(93.2%) had normal albumin levels and 3(6.8%) had low albumin levels.

35(79.5%) had normal lipid levels and 9(20.5%) had abnormal lipid levels.

White Blood Cells ranged from 2300 to18600x10^3/litre with a mean of 6397x10^3 ± 2787x10^3/litre. 41(93.2%) had normal White blood cell count, 2(4.5%) had high white blood cell count and 1(2.3%) had a low count.

Platelet count ranged from 134 to 413x10/litre with mean of 205.43x10^3 ± 43 58.69x10^3/litre. 43(97.7%) had normal platelet count while only 1(2.3%) had low count.

Urine routine was normal in 36(81.8%), 2(4.5%) had White blood cells, 2(4.5%) Red blood cells, 2(4.5%) were positive for sugar and 1(2.3%) had both White and Red cells, none had casts in their urine.

21(47.7%) transplants patients had no complication after transplantation while 9(20.5%) developed diabetes after transplantation, 3(6.8%) developed tuberculosis, 3(6.8%) Urinary Tract Infection, 3(6.8%) malignancy and 2(4.5%) developed Cytomegalovirus disease.3 (6.8%) had surgical complication (lymphocele). (Table 6)

41(93.2%) transplant patient did not developed side effects due to immunosuppressive drugs while 3(6.8%) developed Cushing features.

39 (88.6%) transplant patients had no episode of rejection while 2(4.5%) had acute rejection and 3(6.8%) had chronic rejection.

Table 5; **Laboratory parameters of the Kidney transplant patients**

Variables		Number	Percentage
Serum creatinine (μmol/l)	≤ 120	23	52.3
	≥ 120	21	47.7
Random Blood Sugar (mmol/l)	≤ 11.1	41	93.2
	≥ 11.1	3	6.8
Haemoglobin	Normal	10	22.7
	Low	34	77.3
Serum protein	Normal	42	95.5
	Low	2	4.5
Serum albumin	Normal	41	93.2
	Low	3	6.8
Serum lipids	Normal	35	79.5
	Abnormal	9	20.5
White blood cells	Normal	41	93.2
	High	2	4.5
	Low	1	2.3
Platelets	Normal	43	97.7
	Low	1	2.3
Urine routine	Albumin	2	4.5
	WBC	2	4.5
	RBC	1	2.3
	RBC/WBC	2	2.3
	Sugar	2	4.5
	Normal	36	81.8
Rejection	Acute	2	4.5
	Chronic	3	6.8
	None	39	88.6
HLA	Single	17	38.6
	Haplo	15	34.1
	Total	12	27.3

Table 6; **Diseases after transplant**

	Number	Percentage
Diabetes	9	20.5
Pulmonary tuberculosis	3	6.8
Malignancy	3	6.8
Urinary Tract Infection	3	6.8
Cytomegalovirus disease	2	4.5
Surgery/Lymphocoele	3	6.8
No complications	21	47.7

As regards to Quality of Life total scores are given in Table 7. Total score in Physical Functioning ranged from 0 to 100% with a mean of 62.84 ± 24.001%. 33(75%) scored above 50 %.

Total score in Bodily Pain ranged from 0 to 90% with a mean of 67.41 ± 22.982%. 39(88.6%) scored above 50%.

Total score in General Health ranged from 25 to 97% with a mean of 62.02 ± 20.513%. 32(72.7%) scored above 50%.

On Vitality total score ranged from 5 to 95% with mean of 63.64 ± 19.301%. 38(86.4%) scored above 50%.

Total score on Social Functioning ranged from 0 to 100% with a mean of 68.30 ± 26.464%. 37(84.1%) scored above 50%.

Total score on Role Emotion ranged from 0 to 100% with a mean of 49.30 ± 44.04%. 23(53.2%) scored above 50%.

Total score on Mental Health ranged from 24 to 100% with a mean of 74.18 ± 16.157%. 42(95.5%) scored above 50%.

Total score on Role Physical ranged from 0 to 100% with a mean of 43.55 ± 45.462%. 20(45%) scored above 50%.

Table 8 shows the relationship between clinical parameters and HRQoL. Age was statistically significant associated with HRQoL (P< 0.043) with 2 degrees of freedom on Mental Health score.

Marital status was statistically significant related to HRQoL (P<0.036) with 2 degrees of freedom on Vitality score.

Education was statistically significant related to HRQoL on General Health score (P< 0.0.002) with 2 degrees of freedom.

Employment was statistically significant related to HRQoL on Role- Physical score (P<0.008) with 3 degree of freedom.

Serum creatinine level was statistically significant related to HRQoL on Role Physical score (P<0.032) with 1 degree of freedom.

Blood Urea Nitrogen was statistically significant associated to HRQoL on Mental Health score (P<0.021) with 1 degree of freedom.

Use of immunosuppressive therapy was statistically significant associated to HRQoL on General Health score (P<0.028) with 4 degrees of freedom.

Haemoglobin level was significantly associated to HRQoL on Physical Functioning score (P<0.038) with 1 degree of freedom.

Diastolic Blood pressure level was significantly associated to HRQoL on Mental Health score (P<0.000) with 5 degrees of freedom.

Living donor was statistically associated to HRQoL on Mental Health score (p<0.05) with 4 degrees of freedom.

Smoking was statistically associated with HRQoL on General health score (p<0.038) with 1 degree of freedom.

There was no statistically significant association on Random Blood Sugar level (P<0.06), BMI level (p<0.53), HLA level (P<0.53) and on Time since transplant (P<0.346) all on Role Emotion score.

Likewise there was no statistically significant association on serum lipid level (P<0.356), serum protein level (P<0.734), serum albumin level (P<0.141) and SBP (P<0.060) level all on Vitality score.

Donor age level (P<0.660) and Urine routine (P<0.501) were all not statistically not associated with HRQoL all on Social Functioning score.

Equally there was no statistically significant association to HRQoL on donor relation (P<0.660), sex (P<0.30) and diseases leading to ESRD (P< 0.330) all on General Health score.

Table 7; **Trend of Health Related Quality of Life.**

Domain	**Range**	**Mean**	**SD**	**% score above 50%**
Physical Functioning (%)	0 - 100	64.84	24.00	75.0
Vitality (%)	5 - 95	63.64	19.30	86.4
Mental Health (%)	24 - 100	74.18	16.16	95.5
Bodily Pain (%)	0 - 90	67.41	22.98	88.6
Social Functioning (%)	0 - 100	68.30	26.46	84.1
General Health (%)	25 - 97	62.02	20.51	72.0
Role Emotion (%)	0 -100	49.30	44.04	52.3
Role – Physical (%)	0 - 100	43.55	45.46	45.0

Table 8; **Relation of clinical parameters to Health Related Quality of Life**

Variable	**Domain**	**P-value <**
Age	Mental Health	0.040
Marital status	Vitality	0.036
Education status	General Health	0.002
Employment status	Role - Physical	0.008
Serum Creatinine	Role - Physical	0.032
Blood Urea Nitrogen	Mental Health	0.021
Immunosuppressive	General Health	0.028
DBP	Mental Health	0.000
Haemoglobin	Physical Functioning	0.038
Living donor	Mental Health	0.050
Smoking	General Health	0.038
Random Blood Sugar	Role - Emotion	0.060
BMI	Role - Emotion	0.530
HLA	Role - Emotion	0.530
Time since transplant	Role - Emotion	0.346
Serum Lipids	Vitality	0.356
Serum Total Proteins	Vitality	0.734
Serum albumin	Vitality	0.141
SBP	Vitality	0.060
Donor Age	Social Functioning	0.660
Urine Routine	Social Functioning	0.510
Donor Relation	General Health	0.660
Sex	General Health	0.300
Underlined disease	General Health	0.330

Donor perspectives

There were 43(97.7%) living donors and 1(2.3%) cadaveric donor. 29 (65.9%) were males and 14(31.8%) females. Their ages ranges from 19 to 54 years with a mean of 36.84 ± 8.147 years. 42(95.5%) had their age below 50 years and only 2 (4.5%) were above 50 years (Table 5).

20(45%) were siblings, 11(25%) were second degree relatives like cousins, 3(6.8%) were spouses, 3(6.8%) were sons or daughters and others were 6(13.6%). There was no twin nor parent donation (Table 9).

As regards to HLA antigen matching 12(27.3%) had total matching, 15(34.1%) were haplomatching 17(38.6%) had single antigen matching. None had total mismatch.

All were x –matching negative (Table5).

Table 9; **Donor Relation**

	Frequency	**Percentage**
Sibling	20	45.0
Son/daughter	3	6.8
2nd degree relative	11	25.0
Spouse	3	6.8
Unrelated	6	13.6
Total	44	100

8. DISCUSSION

This study demonstrates that generally ESRD patients in Tanzania have their HRQoL improved after renal transplantation. Although this study did not assess these patients before transplantation, they themselves acted as a control. All domains scores except for Role-Physical had their total scores above 50%. This confers with studies done elsewhere. Ogutmen and colleagues in a teaching hospital analysed 302 transplant patients and compared them with dialysis patients and general population and they found that renal transplant patients had a better HRQoL ($p<0.001$) than patients on dialysis (47).In a Greece study Balaske and colleagues found better scores on HRQoL in transplanted patients than those on Haemodialysis (48).A similar study by Jofre and coworkers found in 88 out of 93 transplant patients that served as their own control to have exhibited improved scores after transplant(49).

Age was statistically significantly related to HRQoL because most of the transplants were of lower age level ($P< 0.040$). Only 4(9%) were of the age above 60 years. Despite the fact that there is no formal upper age limit at which patients may no longer be accepted for transplant, elderly fair less well mainly because of cormobidity . In the USA the age at which transplant is initiated is shifting upwards with an estimated 9% of patients aged more than 65years on waiting list for cadaveric transplants (50).However data from USRDS suggest that transplant recipients aged 60-74 years have better transplant survival than age-matched controls on waiting list (51).

Marital status was significantly related to HRQoL ($P< 0.036$) probably due to social support as has been noted in a Chinese study by Taylor L and colleagues (52).

Education was equally significantly related to HRQoL probably these are highly motivated and may well cope with complex medication and compliance issues as has been noted by Robolo and colleagues in a Spanish study (53).

Likewise employment was statistically significantly associated to HRQoL as that, those who are likely to maintain their job are certainly those with better HRQoL as has been noted by Chen Wan-Chi in a Southern Taiwan correlation study (54).

Serum creatinine and Blood Urea Nitrogen were also significantly associated to HRQoL and this denotes graft function and certainly will influence HRQoL as has been found by Rebeca J and Brian B on new transition in life after transplantation (113).

Use of immunosuppressives was also significantly associated to HRQoL not supprisingly that only 3(6.8%) were cushingoid, the only side effect noted and as well there were fewer rejection episodes 2 acute(4.5%) and 3 chronic(6.8%).

Haemoglobin was significantly associated to HRQoL. Despite the fact that 34(77.3%) transplant patients were found to be anemic its only 5(11.4%) had Haemoglobin level below 11.0g/dl a factor that may be contributed by our patients in the tropics ability to accommodate for lower Haemoglobin levels (55).

Diastolic Blood pressure was also associated with HRQoL. Hypertension occurs in 60 to 80 % of transplant recipients (56) and it is associated with poorer long term graft survival. A large registry study by Olpez G and colleagues showed that recipients with well controlled blood pressure have improved long term survival (57). In this study 31(70.5%) renal transplant patients had their Diastolic blood pressure below 85mmHg and 33(75%) had their Systolic Blood pressures below 130mmHg.JNC VII recommends Blood pressure below 130/85 in CKD patients (58).

Living donation was significantly related to HRQoL ($P< 0.050$). Almost all 43(97.7%) were living related donors and only 1(2.3%) had a cadaveric donation. The half-life living kidney donor is 21.6 years compared to 13.8 years of cadaveric donors (59).

Smoking was significantly associated to HRQoL ($P< 0.038$). In this study no transplant patient was actively smoking but 15(34.1%) smoked before transplantation. Some studies reported similar smoking prevalence among renal transplant recipients and the general population a reason that may explain the outcome in this study (60). It is well known that despite cessation in smoking the cardiovascular risk persist though at a reduced magnitude while stopping smoking markedly reduce the risk in malignancies like lung cancer(61).

Despite the fact that only 3(6.8%) renal transplants had random blood sugar in the diabetic range, 8(18.2%) were diabetic before transplantation, 15(34.1%) were on anti diabetics and 9(20.5%) developed diabetes after transplantation. This may be a reason why random blood sugar alone may not be used to asses the HRQoL .However there was no simultaneous Pancreas and Kidney transplantation where there is greater improvement in HRQoL than in kidney transplant alone particularly in the area of diabetes specificity and physical health (62).

Kasiske and colleagues worked for risk factors for post transplant diabetes mellitus and they found that African Americans, Hispanic Americans, BMI>30,Tacrolimus and viral Hepatitis C infection to be independent risk factors for post transplant diabetes mellitus(63).

This study did not look for viral Hepatitis C infection and BMI was not significantly related to HRQoL (P< 0.530). Eleven (25.0%) renal transplant recipients were using Tacrolimus based immunosuppressant. However both Cyclosporine and Prednisone are as well known to be associated with post transplant Diabetes Mellitus though Tacrolimus being 5 fold more diabetogenic than Cyclosporine (56).

Gender was not statistically associated to HRQoL in this study (p<0.3).This is contrary to a study by Johnson and colleagues that they evaluated HRQoL after the first year of renal transplantation and found that despite improved HRQoL women consistently scored lower than men(64). This could be due to a low number of females 8 (18.2%) in this study.

Role- Physical total score was low of which a possible explanation could be that in a period immediate after renal transplant, patients are usually liberated from dialysis dependence and some restrictions eg with diet but as time goes, they have to cope with several somatic (drug complications) and psychosocial (return to work, social life etc) problems(65).Likewise Neipp M and colleagues on following transplant recipients for more than 15 years after kidney transplantation comparing their HRQoL with general population they found satisfactory HRQoL 4 of the 8 domains ie Role- Physical, Social Functioning, Role Emotional and Mental Health(66).

As regards to underlying causes of CKD leading to ESRD in this study, data may not be a true representation as no histology were performed for there are no established renal units in the country. A study in a University Hospital in Nigeria had before histology services found 62% of ESRD being unknown but after histology services 53% were due to Chronic Glomerulonephritis(14,15).

Likewise there are a lot of discrepancies to drugs supply especially in the government services where oftentimes the immunosuppressive drugs were out of stock. This is likely to influence HRQoL as Hariharan S et al in the USA found that regular intake of immunosuppressives and other medications is the key to prevent graft rejection and a number of late acute rejection occur as of non compliancy or stopping medication (59).

Living donation as noted above might have contributed to the outcome in these patients and likewise the donor age was rather appreciable as only 2(4.5%) donors were of age above 50 years. Donor age is an important determinant of long term graft function and this confers with findings by Davis that 5- year graft survival of donors in their mid twenties cf to donors in their mid sixties fall by approximately 5% each decade (27).

Challenges

Patients with ESRD are likely to represent the tip of the iceberg of the entire burden of CKD. It has been estimated that the number of earlier CKD i.e. stages 1 to stage 4 are likely to exceed as much as 50 fold of those reaching ESRD i.e. stage 5(67).

Early detection of CKD and intervention aimed at preventing its progression into more advanced stages are likely to be key factors in alleviating the future burden of ESRD as has been noted in Okinawa study (68).

It is increasingly recognized that the burden of CKD is not limited to its impact on RRT but has a major impact on overall population health. It is now well established that the prognosis and in particular the cardiovascular morbidity and mortality of diabetes and hypertension depend on renal involvement (69,102).

Consequently early detection and prevention of progression of CKD will not only alleviate the future burden of ESRD but also reduce cardiovascular morbidity and mortality with highly prevalent hypertension and diabetes (70).

CKD is emerging in the 21st century as a global public health issue. Worldwide 1million patients are on RRT and predicted to double by 2010(71).

The cost RRT is prohibitive for many economies and countries, because there is a clear and a direct relationship between GDP and availability of RRT (72).

Within the next 10 years, it is estimated that the annual cost of ESRD management in the United States will rise to approximately US 30 billion dollars, consuming a considerable part of health budget (73.)

Worldwide about 50 million people suffer CKD with 1 million on RRT of whom 85% are from industrialized countries. The incidence of ESRD requiring ESRD has doubled over the past 15 years with further doubling predicted in the next 10 years, largely to an increased incidence in type 2 diabetes and obesity (74,75,76,77).

Also developing countries continue to suffer from massive burden of infectious diseases and infestations with associated renal involvement. The global burden of HIV infection is 40million people and most of them in sub Saharan Africa(78), HCV infection is 170 million(79),malaria 300 million (80), Schistosomiasis 200 million(81) and Tuberculosis 200 million(82).

Development of strategies for early detection and prevention is the only realistic strategy to avert an imminent global health care worldwide. This has to involve gathering of biostatistical and demographic data for CKD and as well an establishment of precise programs for early detection of CKD as well as primary and secondary prevention.

Such programs should be multidisplinary and require strong and require government, public and health care commitments.

The scientific basis for these programs would assist the capacity building in medical sciences in renal, cardiovascular and diabetic care which are crucial in providing the necessary infrastructure, thus contributing to enhancement of health status and economic status of poor nations.

Before any preventive program for chronic illness like CKD on a community basis is planed few other issues need to be addressed .1.Is the disease easy to detect? 2. Can the disease be easily be prevented? 3. Is the cost of prevention less than treatment? 4. Can the preventable programs be sustainable? (83)

Because CKD is a clinical syndrome, one has to understand its aetiology as has been noted on hospital based studies in India that Diabetes is a major contributor to ESRD(41%) followed by hypertension(22%) and Chronic glomerulonephritis(16%) ;a picture different to this study where majority are hypertensive (70.5%) followed by Diabetes (18.2%) and Chronic glomerulonephritis (15.9%)(84,85).Thus if we concentrate on these 3 diseases on a community basis for a prevention programme on CKD, we may be able to prevent a large number of CKD cases.

It is thus obvious that clinical examination for blood pressure, urine protein and sugar, spot urine albumin and creatinine, random blood sugar are simple to perform; a prerequisite for diagnosis and management of CKD and its 3 major aetiologies ie hypertension, diabetes and chronic glomerulonephritis. This will lead to retarding CKD progression, reduced cost and an improved Quality of Life.

Public awareness programs e.g. on obesity have proved success in Arab world where 18% of school children are obese and at least one third of Arab population is categorized obese (86, 87).

In addressing challenges posed by worldwide CKD pandemic, diet and lifestyle modification, tight diabetic and blood pressure control are imperative (88,89,90,91).

Smoking has been implicated in the onset of albuminuria in both diabetics and non diabetics and cessation of smoking will undoubtedly be beneficial in individuals at

risk of renal disease as well as cardiovascular diseases. In this study none of the transplant patient was currently smoking but 15(34.1%) smoked before transplantation.

Control of hypertension is a single most important intervention to reduce both albuminuria and proteinria and subsequent development of CKD in both diabetics and non diabetics (92).It is imperative to detect pre hypertensive states, aiming at lowering blood pressure levels in the general population and be even more aggressive with reduction in blood pressure in hypertensive and underlying CKD (93).

It has been suggested that every elevation of SBP above 115mmHg in the general population is associated with doubling the risk of CKD. In patient with CKD, transplants inclusive should be less than 130/85 mmHg in the absence of diabetes and protenuria above 1gm/24 hours. In this study 33(75%) SBP below130 mmHg and 31(70.5%) had DBP below 85 mmHg.

The control of glycemia has being shown to be a major factor in the prevention and progression of Diabetic Nephropathy. Target HbA1 levels around 7% have been recommended (94, 95, 96).The setback has been fatal hypoglycemic events as noted in ADVANCE (97) and ACCORD (98) studies.

Control of albuminuria and proteinuria is also an important factor in slowing the progression of CKD in both diabetics and non diabetics (99,100).

For that reason antihypertensive using ACEI and ARB have been widely advocated (101).Their impact on renal function is often proportional to their proteinuria lowering effect. Inhibition of the RAAS may also have an additional Reno protective effect through inhibition of renal inflammation and fibrosis. Further more, these agents are also known to be cardio protective and therefore minimal cardiovascular complications of CKD.

Dyslipidemia has been implicated in the progression of CKD. Subsequently , lipid lowering largely by statins has been shown to be protective in experimental CKD and may have additive effect when combined with inhibitors of RAAS (69).A systematic

review of lipid lowering trials in CKD suggested a potential benefit in slowing the progression of renal failure(103).

A growing body of evidence suggests that conventional risk factors for cardiovascular disease are also associated with increased risk of CKD. The Framingham Offspring study investigated new onset CKD in 2585 health participants who attended baseline examination from1978-1982 and follow-up examination from 1998-2001(104). 244(9.4%) developed CKD. Identifiable risk factors included increased age (OR2.36), Diabetes (OR 2.38), Smoking (OR 1.42) and hypertension (OR 1.57). Similar observation was noted with both the Okinawa and MRIFT studies (105,106).

Emphasis on infectious diseases eg scaling up of antiviral drugs all along with other preventive measures, Vaccination against HBV eg vaccination has dropped infection from 10 -12% in early 1980 to 6% at the end of last century in Arab world (107).Despite having no vaccine to HCV in countries with strikingly high prevalence like Egypt 18%, the incidence of associated glomerulonephritis may be largely reduced by public education, needle stick injury, blades, barbers and barrier technique in high risk groups(107). Tuberculosis can cause renal failure by fibrosis and stricture of urinary system, Immune complex glomerulonephritis and renal amyloidosis and therefore emphasis in Tuberculosis prevention and treatment is paramount. Genitourinary Tuberculosis is one of the more common forms of extra pulmonary constituting 30% of them (108). Tuberculosis is an important cause of morbidity and mortality in renal transplant recipients and its incidence varies according to the general population eg it is 0 to 1.3% in the USA,0.8 to 1.6% in Spain, 3.5% in Saudi Arabia, 11% in South Africa ,11.8% in India and 14.5% in Pakistan (110). In this study 3(6.8%) developed Tuberculosis after renal transplantation.

In the absence of state funded medical treatment and medical insurance facilities for CKD/ESRD there are various sources from which patients gets money for treatment One study in India concluded that 63% had a help from employer or charity, 26% took loan, 34% sold assets or pooled their family resources but despite of all this only3 to5% of all ESRD in India gets some form of RRT (111), a picture not very different

to our setup. In all major studies in India, most of them hospital based(84,85), men in their 30s were the most commonly affected by CKD/ESRD and thus an employed patient with ESRRD must reach for finances for his treatment not only for direct cost but also for indirect cost of loss of job or working days which is enormous. The government sector in India can not afford to provide Maintenance Haemodialysis-majority offering 2 shifts of Haemodialysis and only 2% of ESRD are afforded Haemodialysis. Although the first Continuous Ambulatory Peritoneal Dialysis in India was initiated in1990 only about 3000 patients have been initiated on this modality of RRT (112). India has nearly 700 nephrologists and approximately 400 dialysis units, majority in the private sector but only 3-5% of all ESRD get some form of ESRD and thus prevention for CKD the only practical solution for India and other emerging countries like Tanzania.

Funding of detection and prevention of CKD programs will have to engage Governments, Non-Governmental Organisations, Charitables as well as Pharmaceutical Industries. Commitment of local government agencies at regional and national level is a prerequisite to the implementation of such activities.

Non-Governmental organizations and Charitables have an important role to play in lobbying and encouraging Governments to take up and support such programs.

Finally the Pharmaceutical industry will have to face up to its responsibility in supporting such detection of CKD programs, knowing that many patients identified will undoubtedly require their products to prevent progression of underlying kidney diseases.

9. CONCLUSION

1. Most successfully renal transplanted patients in Tanzania were males and aged below 60 years of age. Majority had college education, fully employed and married. Most were normotensive but overweight.
2. The causes of ESRD in Tanzania are similar to those in other developing countries. Most were Hypertensive followed by Glomerulonephritis and then Diabetes.
3. The government in Tanzania is the main sponsor of transplant costs and cost of medication including immunosuppressives as well as referring patients abroad for review.
4. Most renal transplant patients in Tanzania have started attending the newly established renal clinic for follow-up.
5. Generally HRQoL of ESRD in Tanzania improves after being successfully renal transplanted. However patients with ESRD are likely to represent the tip of the iceberg of CKD and prevention is the best approach.

10. RECOMENDATIONS

HRQoL is increasingly been used in chronic diseases. In renal transplant it is necessary to determine the effectiveness of medical intervention, to improve clinical decision, to manage physical, functional, psychological and social aspects of patient course and to plan for psychosocial and rehabilitation intervention.

Whenever possible suitable patients with ESRD should be transplanted as has been shown that transplanted patients in Tanzania have improved QoL

Young donor age preferably below 50 years lead to a better outcome as has been shown in this study.

However since ESRD is only the tip of iceberg prevention is the most feasible approach.

A multifaceted approach is urgently needed to stem the global tide of ESRD. This calls for concerted efforts from government agencies international bodies and organizations including pharmaceutical industry. It calls for a rethinking of medical and nephrology training and that of associated health workers to meet community based demands. Ultimately, population-increased education and awareness will contribute to its wellbeing.

11. STUDY LIMITATION

The registry at MOH&SW has been updated from 2000.There is no data of patients who were transplanted before 2000 and this may have influenced my results. The study was done in Dar es Salaam and there is a possibility of missing those transplanted patients before 2000 or those who did not seek government sponsorship.

REFERENCES

1. United States Renal Data System (USRDS). 2000 Annual Data Report. National Institute of Diabetes and Digestive and Kidney Disease Bethaseda MD. The National Institute of Health.2000.
2. Locatelli F, Del Velchio L, Natural history and factors affecting progression of Chronic Renal Failure .In EL Nahas AM, Anderson S, Harris KPG, eds Mechanisim and management of progressive renal failure. London; Oxford University Press,1999;1591-99.
3. Locatelli F, Marielli D, Comelli I, et all. Proteinuria and Blood Pressure as cause components of progression to End Stage Renal Disease. *Nephrol Dial Transplant .1996;461-67*
4. Walker WG, Neaton JD, Culter JA, et al. Renal function change in hypertensive members of the multiple risk factor intervention trial. *J Am Med Ass.1992;260;3085-91*
5. Buck K, Fechally J, Diabetes and Renal failure in Indo-Asians in the UK-A paradigrim of disease susceptibility. *Nephrol Dial Trans 1997;12;1555-57*
6. Klahr S, Brever JA, Beck GJ,et al. Dietary protein restriction, Blood pressure control and progression of polycystic kidney disease, modification of diet in renal disease study group. *J Am Soc Nephrol 1995; 5; 2037-47.*
7. Nakamura T,Fukui M,Ebihara I,et al ,Low protein diety blunts the rise in glomerular gene expression in focal glomerulosclerosis. *Kidney Int 1994; 45; 1593.*
8. Apperloo AJ, de Zeeuw D, de Long PE, et al. Short term antiproteinuric response to antihypertensive treatment predicts long term GFR decline in patients with non diabetic renal disease. Kidney Int 1999;147-78
9. Attman PO. Progression of renal failure and lipids-is there evidence of a link in humans. *Nephrol Dial Transplant.1998; 13.545-47.*
10. Orth SR, Stein IH,Smoking :Arisk factor for progression of chronic kidney disease

and for cardiovascular morbidity and mortality in renal patients-absence of evidence or evidence of absence .*Clin J Am Soc Nephrol 2008;3:226-236.*

11. Barsoum RS, Chronic Kidney Disease in the Developing world. *NEJ Med 2006; 354; 997-99*
12. Barsoum RS, Rihaz ZE, Ibrahim AS, et al. Long term intermittent haemodialysis in Egypt. *Bull World Health Organ, 1974; 51; 647-654.*
13. Combined Report on Maintenance dialysis and Transplantation , Regisrtry report 1994;Edited by Du Toit ED, Pascoe M, Mac Gregor K, PAGE
14. Mabayoje MO, Bamgboye EL, Odutala TA et al. Chronic renal failure at the Lagos university teaching Hospital. A 10 years review. *Transplant Proc 1992; 24; 1851-52.*
15. Anochic I, Eke F, Chronic renal failure in children. A report from Port Harcourt Nigeria. *Ped Neph 2003; 18; 692-695.*
16. Naiker S, End stage renal disease in Sub Sahara and South Africa. *Kidney Int (2003)63; S119-22.*
17. Basinda SL, Maro EE, Mc Larty DG,et al.Ten Tanzanian transplants; problems and perspectives. *Postgraduate Medical Journal; 1988; 64; 778-82.*
18. Maro E, Ammur A, Chale S, Medical complications in twenty six Tanzanian transplant patients .*TMJ; 2002; 17; 31-35.*
19. Mc Kenzie JK, Moss AH, Feest TG, et al. Dialysis decision making in Canada, The United Kingdom, and United States. *Am J Kidney Dis1998; 31; 12; 18.*
20. Parry RG, Crowe A, Stevens JM, et al. Referral of elderly patients with severe renal failure, questionnaire survey of Physicians. *BMJ 1996; 313; 466.*
21. Singer PA, Nephrologists' experience with and attitudes towards decision to forego dialysis. *J. Am Soc Neph; 1992; 2; 1235-40.*
22. Moss AH, Dialysis decisions and the elderly .*Clin Geriatric Med 1994; 10; 463-473.*
23. Barret BJ, Parfrey PS, Morgan J. et al. Prediction of elderly death in end stage renal disease starting dialysis. *Am J Kidney Dis 1997; 29; 214-22.*

24. Nissenson AR,Prichard SS,Cheng IKP,et al.Non medical factors that impact on ESRD Modality selection. *Kidney Int, 1993; 43(suppl 40); S120-127.*

25. Hashmi S, Poommpanit N, Kahwaj J, et al. Overview of renal transplantation. *Minerva Med 2007; 98(6)713-729.*

26. Kenny LC, Barker PN, Venmrg M, et al. Successful renal transplant during first trimester of pregnancy. *Transplant International, 20(4); 390-391.*

27. United Network for Organ Sharing (UNOS),Division of Organ Transplantation USD.*1993 An*nual report of the US scietific Registry for Transplant Recipients and the Organ Procurement and Transplantation Network-*Tranplant Data 1988-1991 Richmond, VA: UNOS, 1993.*

28. Robollo P,Ortega T,Ortega F,et al. Spanish validation 'Kidney Transplant Questionnaire' a successful Instrument for assessing health related quality of life in kidney transplant patients. *BMC Mol Biol ;20031;56-62.*

29. Fleck M, Louzada S, Xavier M, et al. Quality of life in end stage renal disease. *Rev Saude Publica; 2004; 38; 732-34.*

30. Evans R, Manninen D, Garrison L et al. Health Related Quality of Life assessment in end stage renal failure. *NEMJ* 1985;312: 553-59.

31. Theofanis A,Quality of life in the elderly patients on dialysis,*2007;39:679683.Int Urol and Nephrol.*

32. Sayag R, Kaplan de Nour A, Shapira Z,et al.Comparison of psychosocial adjustment of male non diabetic kidney transplant and hospital hemodialysis patients. *Nephron 1990;54(3): 214-18*

33. Fraglora J. Multi centre study of physical activity and employment status of CAPD patients in USA. *Proceedings of European Dialysis and Transplantation 1983.*

34. Cameron J, Whiteside C, Katz J et al. Differences in Quality of Life accross renal replacement therapies, a Meta analysis comparison. *Am J Kidney Dis 2000;35: 929.*

35. Russel J, Beecroft M, Ludwin D et al. The Quality of Life in renal

tranplantation.Aprospective study.*Transplantation; 1993:54; 656.*

36. Witzike O, Becker G, Frank G et al. Kidney transplantation improves Quality of Life.*Transplant proc 1997;29: 1569*
37. Evans R. Quality of Life assessment and the treatment of end stage renal disease. *Transplant rev1990; 4(1) 28-51.*
38. Salifu M, Tedla F, Markell M. Managment of well renal transplant recipient: Outpatient survilance and treatment recommendation. *Semin Dial. 2005;18 (6) 520-28.*
39. Guyat G, Feeny D, Patrick D et al. Measuring Health Related Quality of Life. *Ann Int Med 1993; 118: 622-24.*
40. Testar M, Simson D. Assesment of Quality of Life outcomes. *NEJM; 2005: 335-35*
41. Broyer M. Combined report on regular dialysis and transplantation of children in Europe. *Proceeding of European Dialysis and Transplantation Association.1981; 19: 4-58.*
42. Stewart C, Alex M, Jean Pierre G, Eberhard R. Oxford *textbook of Clinical Nephrology;* Oxford University Press,1st edition;1992;1591
43. Gautrrez M, Acebedo-Ribo M, Garcia-Donaire J et al. Pregnancy in kidney transplant recipients. *Transaplant proc 2005; 37:*
44. Ware J, Snow K Gandek B et al. SF-36 health survey.Manual and interpretation guide.Boston,MA: The Health Institute, New England Medical Center 1993.
45. Hathaway.D, Hartwig M, Milstead J et al. Improvement in Quality of Life reported by diabetic recipients of kidney only and pancreatic-kidney allografts. *Transplantation proc 1994; 26: 512-514.*
46. Littlefield C, Abbey S, Fiducia D et al. Quality of life following transplant of heart, liver and lung .*General hospital Psychiatry 1996; 18; 36-47.*
47. Ogutmen B,Yildim M,Sever S et al. HRQoL after kidney transplantation. *Transplant proc 2006; 38:419-421.*
48. Balaske A. Changes in health related quality of life in Greece patients 1 year after

successful renal transplant. *Exp Clin Transplant; 2000; 4:521-524.*

49. Jofre R,Moreno F,Sanz-Guajardo D et al. Quality of Life after Renal Transplantation. *Am J Kidney Dis 1998; 32:93-100.*
50. United Network for Organ Sharing (UNOS).Available from URL:http://www.unos.org
51. Wolfe R. Comparison of mortality in all patients on dialysis, patient on dialysis awaiting transplantation and recipients of a first cadaveric transplant. *NEJM 1999; 341:1725-1730.*
52. Taylor L. Living kidney donation: experience of spousal support of donors. *J Clin Nurs 2008; 17:232-241.*
53. Rebollo P,Ortega F,Ortega T et al. Health Related Quality of Life of Kidney Transplant patients in Spain: Variables that influence it. *Cl. Transplantation 2000; 14:199-207.*
54. Chen Wan-Chin. Quality of Life, symptom distress and social support among renal transplant recipients in Southern Taiwan: A correlational study. *J Nurs Res 2007;15: 312-329.*
55. Ministry of Health and Social Welfare United Republic of Tanzania.Trainer guides. Laboratory course for laboratory staff.Haematology module 2006
56. Vincenti F. A long term comparison of Tacrolimus (FK5060 and cyclosporine in Kidney Transplantation: Evidence for improved allograft survival at 5 years. *Transplantation 2000; 73:775-782.*
57. Olpez G, Wujciak T, Ritz. Association of Chronic Kidney Graft Failure with recipient blood pressure: Collaborative Transplant Study: *Kidney Int 1998; 53: 217-222.*
58. Chobanian A. The Seventh Report of the Joint National Committee on prevention, detection and treatment of high blood pressure. The JNC 7 report. *JAMA 2003; 289:2560-2572.*
59. Hariharan S. Improved graft survival after renal transplantation in the United States; 1988 to 1996. *NEJM 2000; 342: 605-612.*

60. Sung R. Excess risk of renal allograft loss associated with cigarette smoking. *Transplantation 2001; 71: 1752-1757.*

61. Matas A. Immunological and non immunological factors: Different risks for cadaver and living donor transplantation. *Transplantation 2000; 69: 54-58.*

62. Gross C,Kreitzer M,Russas V et al. Impact of transplantation in patients with diabetes mellitus and renal dysfunction. *Transplantation 2000; 70:1736-1746.*

63. Kasiske B,Anjum S,Shah R et al. Independent risk factors for Post transplant Diabetes Mellitus.*Am J Transplant 2000; 3: 178- 185.*

64. Jonson C. Racial and gender differences in Quality of Life following Kidney transplantation. *Image J Nurs Sch 1998; 30: 125- 130.*

65. Ponto P,Rupollo G,Feltrin A et al. Quality of Life changes after kidney transplantation. *Transplant Proc 2001;33: 1887-1889.*

66. Neipp M, Karavul B,Jackobs S et al. Quality of Life in Adult Transplant recipients more than 15 years after kidney transplantation. *Transplantation 2006; 81: 1640-1644*

67. ANONYMOUS:K/DOQI Clinical practice for CKD,Evaluation,Classification and stratification. K/DOQI. *Am J Kidney Dis 2002; 39: 1- 246.*

68. Iseki Y. Protenuria and the risk of development of ESRD.*Kidney Int 2003; 63: 1468-1473.*

69. Zoja L. How to fully protect the kidney in a severe model of progressive nephropathy: A multi drug approach. *J Am Soc Nephrol 2002; 13; 2898-2902.*

70. Ritz E, Mc Clellan W. Overview Increased cardiovascular risk in renal dysfunction: An emerging issue with far reaching consequences. *J Am Soc Nephrol 2004;15:513-516.*

71. Schera F. Epidemiology of ESRD: International comparison. *Kidney Int 2000; 74: 539-544.*

72. De Vecchi A, Drativa M, Wiedmon M. Health care system and ESRD. An International Review: Costs and reimbursement of ESRD therapies. *NEJM 1999;14: 31-41.*

73. Xue J. Forecast of the number of patients with ESRF in the US to the year 2010.*J Am Soc Nephrol 2001; 12: 2753-2758.*

74. Lysagat M. Maintenance Dialysis population dynamics: Current trends and long-term complications.*J Am Soc Nephrol 2002; 1:37-40.*

75. Agarwal S, Dash S: Spectrum of renal diseases in India in adults. *J Assoc Physicians India 2000; 48: 594-600.*

76. Wilds S.. Global prevalence of Diabetes mellitus: Estimates for the year 2000 and projections for the year 2030.*Diabetic Care 2004; 27; 1047-1053.*

77. WHO: Global burden of disease estimate. Available at :http://www3.who.int/whois/menu.cfm?path=evidence,burden&language=english

78. Joint United Nations Programe on HIV/AIDS/WHO.UNAIDS/WHO. Annual report: Epidemic Uptodate, December 2003.

79. WHO; WHO/United nations Global Population Hepatitis C Prevalence Report 2000.

80. Wellems T, Miller L: Two worlds of malaria. *NEJM 2003; 349: 1496-1498.*

81. Chitsulo L. The global status of Schistosomiasis and its control. *Acta Trop 2000; 77: 41-51.*

82. Drobniewski F. Modern laboratory diagnosis of Tuberculosis. *Lancet Infect Dis 2003; 3: 142- 147.*

83. Mani M. Prevention of chronic renal failure at the community level.*Kidney Int.2003; 63: 86- 89.*

84. Mani M. Chronic Renal Failure in India.*Nephrol Dial Transplant 1993; 8: 684-689.*

85. Sakhuja V. Chronic renal Failure in India. *Nephrol Dial Transplant 1994;9: 871-872.*

86. Al- Nuaim A, Bagnigboye E, Al-Herbish. A pattern of growth and obesity in Saudi Arabian school children. *Int J Obes Relat Metb Disord 1996; 20: 1000- 1005.*

87. Al- Mahroos F, Rooni K. Overweight and obesity in Arabian Peninsula: an Overview. *J. R. Health 1999;119: 251- 253.*

88. Lindistorm J. Prevention of Diabetes mellitus in subjects with impaired Glucose tolerance in the Finnish Diabetic Prevention Study: Results of a randomized clinical trial. *J Am Soc Nephrol 2003; 14: 108- 113.*

89. Molich M. The Diabetes Mellitus Prevention Programe at its global implication. *J Am Soc Nephrol 2003; 14: 103- 107.*

90. Appel L. Life style modification as a mean to prevent and treatment of raised blood pressure. *J Am Soc Nephrol 2003; 14: 99- 102*

91. Oberzanek E, Proschan M, Vollmer M. Individual Blood Pressure responses to changes in salt intake: results from the DASH- Sodium trial.*Hypertension 2003; 42: 459- 467.*

92. ANONYMOUS: K/DOQI clinical practice guidelines on Hypertension and antihypertensive agents in CKD. *Am J Kidney Dis 2004; 43: 1-290.*

93. Parving H. Diabetic Nephropathy: Prevention and treatment. *Kidney Int 2001; 60: 2042-2055.*

94. UNITED KINGDOM PROSPECTIVE DIABETES STUDY GROUP: Tight blood sugar control and risk of microvascular complication in type 2 Diabetes (UKPDS 38).*BMJ 1998; 317: 703- 713.*

95. THE DIABETES CONTROL AND COMPLICATION TRIAL (DCCT) RESEARCH GROUP: Effect of intensive therapy on development and progression of Diabetic Nephropathy in the DCCT trial. *Kidney Int 1995; 47: 1703-1720.*

96. The ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *NEJM 2009; 358: 2545- 2559.*

97. The Action to Control Cardiovascular Risk in Diabetes Study Group: Effects of intensive Glucose lowering in type 2 Diabetes. *NEJM 2008; 358: 2545- 2449.*

98. Rossing P. Reduction in albuminuria predicts diminished progression in Diabetic Nephropathy. *Kidney Int 1994, 32: 145- 149.*

99. Ruggenenti P. Urinary Protein Excretion Rate is the best independent predictor to ESRF in non Diabetic chronic nephropathies. *Kidney Int 1998; 53:1209- 1216.*

100. Ruggenenti P. Progression, Remission and Regression of Chronic Renal Disease.

Lancet 2001; 357: 1601- 1608.

101. Wald NJ, Law MR. Strategy to reduce cardiovascular disease by more than 80%. *BMJ 2003; 326:1499- 1422.*
102. Fried L. Effects of lipid reduction on the progression of renal disease: A Meta analysis. *Kidney Int 2001; 59:260- 269*
103. Weiner D. CKD as a risk factor for CVD and all cause Mortality Rate: A pooled analysis of community based studies.*J Am. Soc Nephrol 2004; 15: 1307- 1315.*
104. Iseki Y. Proteinuria and the risk of developing ESRD. Kidney Int 2003; 63: 1468- 1473.
105. Klag G. ESRD in African- American and Whiteman : MRIFT FINDINGS. *JAMA 1997; 277: 1293- 1298.*
106. Available at www.pkids.org/hbvglobal
107. Available at www.pkids.org/hcvglobal
108. Hsiao-Cheng H,Po-Liang L,Yen-Hsu C et al.Genitourinary tuberculosis in a medical centre in southern Taiwan:an eleven year experience. *J Microbiol Immunol Infect 2006:39; 408-413.*
109. Park H, Kim S,Yong J et al. Clinical Outcomes of Tuberculosis in renal Transolant recipients. *Yousei Med J 2004; 45: 865- 862*
110. Gracia- Rundrigez J. Genitalurinary tuberculosis in Spain: Review of 81 cases. *Cl. Infect Dis 1994; 18: 557- 567.*
111. Kher V. End stage renal disease in India. *Kidney Int 2002 62: 350- 362.*
112. Rebeca J, Bryan N. Life after Transplantation in QoL and psychological Distress. *Seminars in Dialysis 2008; 18: 124- 131.*