GASTROINTESTINAL SYMPTOMS AND GASTROINTESTINAL QUALITY OF LIFE IN RENAL TRANSPLANT PATIENTS:

A DESCRIPTIVE CROSS SECTIONAL STUDY

A DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE (INTERNAL MEDICINE), SCHOOL OF MEDICINE, UNIVERSITY OF NAIROBI.

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I dedicate this to my parents. I hope to be half the people they are.

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LIST OF ABBREVIATIONS

AZA	Azathioprine
AcMPAG	Mycophenolic acid acyl glucuronide
ATPase/ATP	synthase adenosine triphosphatase/synthase
CAPD	Continuous ambulatory peritoneal haemodialysis
CHD	Center haemodialysis
CMV	Cytomegalovirus
CsA	Cyclosporine
ECMPs	Enteric coated mycophenalate sodium
ESRDSC-TM	End stage renal disease symptom checklist transplantion module
ESRD	End Stage Renal Disease
FK506	Tacrolimus
GI	Gastrointestinal
GIQLI	Gastrointestinal Quality of Life Index
GSRS	Gastrointestinal Symptom Rating Scale
HRQL	Health related quality of life
HSV	Herpes Simplex Virus
IBS	Irritable bowel syndrome
IMPDH	Ionsine monophosphate dehydrogenase
KNH	Kenyatta National Hospital
KPT	Kidney /Pancreas transplantation

KTQ   Kidney transplant questionnaire

KDQOL   Kidney disease quality of life

MMF   Mycophenolate mofetil

MPA   Mycophenolic acid

MPAG   7-O-Mycophenolic acid glucuronide

NHP   Nottingham health profile

NSAIDs   Non-steroidal anti-inflammatory drugs

NTPR   USA National transplantation pregnancy registry

QOL   Quality of Life

ABSTRACT

Background

Renal transplant recipients are a special group with specific needs in their care, overall care is centered on the graft function and bodily functioning. The immunosuppressive state and immunosuppression affect them greatly. The immunosuppressive state and immunosuppression affects ones ability to function in this new acquired state of being. Gastrointestinal symptoms impact their quality of life over several Qol domains that can be evaluated to improve patients commonly overlooked areas of patient care.

Objectives

The aim of this study was to establish the gastrointestinal symptoms and their gastrointestinal quality of life by identifying the prevalent symptoms and the quality of life at the time of interview.

Methods

A total of 83 patients were recruited from the renal transplant clinic that runs at the Kenyatta National Hospital renal unit on Tuesdays. This was a cross-sectional study with consecutive sampling. All patients who gave consent were recruited. The data was collected over eight weeks. Patients records were used to collect data on prescribed medication. Demographic data was collected using pre-structured questionnaires. The validated tools used for this study were the Gastrointestinal Symptom Rating Scale (GSRS) and Gastrointestinal Quality of Life(GIQLI).Renal transplant patients with a stable graft were recruited to fill the self - administered GSRS .The GIQLI was filled by the interviewer during the same clinic visit.

Results

Of the 83 patients enrolled during the study period, 57% were males. The mean age was 41.3 years with a median of 52 years.

Using the GSRS score 96% of patients reporting at least one gastrointestinal symptom (defined as a score>1) When considering individual GSRS symptoms across all five domains four symptoms most frequently reported by patients were, in order of prevalence, abdominal pain (57%), boborygmus (55%), heartburn (55%) and regurgitation (53%).

The mean reported GSRS total score was 3.364. Combining individual symptoms into the five domains of the GSRS scores gave of 3.42 for diarrhea, 4.29 for indigestion, 3.46 for constipation, 3.18 for abdominal pain and 2.29 for reflux syndrome.

For the patients who ever experienced gastrointestinal symptom, the mean reported GIQLI total score was 2.326. Combining individual symptoms into the five domains of the GIQLI scores gave of 1.89 for GI symptoms, 0.83 for emotional function, 1.12 for physical function, 1.65 for social function and 6.14 for medical treatment.

Conclusion

The presence of GSRS score of >1 was reported at 96% most symptoms reported as mild. This has an impact in the HRQol in renal transplant patients. Immunosuppressants may not be singled out to be the only contributor yet the high burden does necessitate considerations when choosing the best suited immunosuppressive therapy.

CHAPTER ONE: INTRODUCTION

1.0 BACKGROUND

Renal transplantation offers a superior approach in treatment of chronic renal failure patients. The health-related quality of life improvement is marked in comparison to hemodialysis. The symptomatology occurring in chronic renal failure improves with improved graft functioning. Graft functioning is important to maintain these benefits post -transplant.

Gastrointestinal symptoms are recurring in renal transplant recipients and may involve any segment of the gastrointestinal tract. These manifestations may be related to stress, infections and/or aggravation of pre-existing gastrointestinal diseases. In inclusion to immunosuppressive agents may cause gastrointestinal side effects such as reflux, diarrhea, and constipation either directly or by favoring the development of bacterial and/ or viral infection [1].

In one study it was reported that up to 90 % of renal patients on immunosuppressive therapy reported gastrointestinal (GI) symptoms [2].Though majority of these symptoms may be trivial,10 % of renal transplant patients may progress to having serious gastrointestinal complications, leading to loss of graft or death of the patient.[3] Minor gastrointestinal symptoms may impair Quality of Life (QOL) in renal transplant recipients and this could threaten long-term transplant stability through reduced adherence to immunosuppressant drug therapy.[4] Ponticelli et al in a study in Italy reported that quality of life was significantly worse in patients with gastrointestinal symptoms than in patients without. [5]

While the effects of gastrointestinal symptoms are well understood on a clinical level, little is known about the patient perspective. There is evidence to suggest that patients on different immunosuppressant regimens may feel less bothered by GI side effects or report better health related quality of life (HRQL) depending on the regimen they are taking.[6] Therefore, patient reports of these GI complications and related QOL are important. This study aims to estimate the prevalence of gastrointestinal symptoms from a patient's perspective and how it affects the patients perceived quality of life using the Gastrointestinal Symptom Rating Scale (GSRS) and the Gastrointestinal Quality of Life Index (GIQLI). These are two patient reported outcomes instruments with demonstrated reliability and validity for use among renal transplant populations [2].

1.1 LITERATURE REVIEW

1.1.1 Gastrointestinal(GI) Symptoms in Kidney Transplant Patients

Gastrointestinal (GI) symptoms are common in patients with chronic renal failure (CRF) especially in patients having continuous ambulatory peritoneal dialysis (CAPD) and those who have undergone a renal transplant [7,8,9]. Dong et al reported a prevalence of GI symptoms of 43 % to 58% in patients who had undergone organ transplantation.[10] While there is paucity of data from studies involving renal transplant patients, a variety of GI symptoms in CAPD patients have been reported of which, functional disorders like gastroesophageal reflux symptoms (GERS), dyspepsia and eating dysfunction seem to be the most common ones[4]. Other symptoms may include oral ulcers, odynophagia, diarrhoea, fever, nausea, vomiting among others.

1.1.2 Pathogenesis of Gastrointestinal Symptoms in Kidney Transplant Patients

2.1.1 Functional Disorders Gastrointestinal (GI) adverse events are common following renal transplantation and all immunosuppressive regimens have been associated with such events. Mycophenolate mofetil (MMF) or enteric coated mycophenolate sodium (EC-MPS) are commonly prescribed in most immunosuppression regimens, and are associated with the good outcomes in kidney transplantation [11]. The effects of MMF and EC-MPS are likely mediated via the active metabolite mycophenolic acid (MPA). The GI events caused by both MMF and EC-MPS may partly, be related to MPA, independent of the formulation or route of administration. MPA may produce GI events either via its direct action or through the action of it metabolites [12].

The forthright action of MPA is linked to its anti-proliferative properties, as it is a selective inhibitor of inosine monophosphate dehydrogenase (IMPDH) an enzyme key to the *de novo* production of purines for T and B cells [13] and other cells in the body, including GI epithelial cells. MPA thus may inhibit the replication of GI epithelial cells leading to villous atrophy leading to diarrhoea and fluid absorption affecting fluid balance[11]. The same mechanism is also thought to induce oral ulcers and erosion of the oesophagus leading to odynophagia.

MPA is primarily metabolized to 7-O-MPA-bglucuronide (MPAG) and mycophenolic acid acyl glucuronide (AcMPAG) [14]. MPAG is thought to be pharmacologically inactive, but acyl glucuronides are generally toxic molecules and thus do display pro-inflammatory effects. AcMPAG forms adducts to plasma proteins and inturn activates the release of cytokines both

in vitro and in vivo [14,15].The inflammatory symptoms observed in renal transplant patients are linked to these effects. AcMPAG may also be generated within the GI tract, produced from MPA by intestinal and hepatic glucuronidases [12,13]. In the GI tract, AcMPAG inhibits IMPDH II and this affects the GI epithelial cells directly promoting diarrhoea by affecting replication as described previously.[14] However, it should also be noted that epithelial cells in the GI tract may not be wholly dependent on *de novo* purine synthesis, and may be permeable to purines that are released into the intestine during digestion thus bypassing the IMPDH dependent pathway.[15] Therefore, while IMPDH inhibition may play a role, additional processes may be involved in mediation of the GI effects.

AcMPAG also forms protein adducts that can directly interfere with cell function or trigger the immune system, leading to hypersensitivity and autoimmune reactions, or cause glutathione depletion [14, 15]. A recent preclinical study identified proteins from rat liver and colonic homogenates that react with AcMPAG. The alpha (α) and beta (β) chains of ATPase/ATP synthase, selenium-binding protein 2 and protein disulphide isomerase from liver homogenates formed adducts with AcMPAG [15]. However, while ATPase/ATP synthase and protein disulphide isomerase are known to be involved in the control of the energy and redox states of cells, the role of selenium-binding protein 2 is not yet understood.

1.1.3 Role of Immunosuppression

With the suppression of the body's defensive immune functions, all immunosuppressive regimens can lead to increased rates of systemic or localized infections including those of the GI tract. These infections may be bacterial, viral, fungal, or parasitic and may infect one or more gut segments between the mouth and anus [11]. The common viruses with GI involvement in patients on immunosuppressive regimen included cytomegalovirus (CMV) and herpes simplex virus (HSV). The incidence of enteric and/or gastric infection is remarkably high, affecting a substantial portion of patients, especially during the first 6 to 12 months after organ transplantation [1]. *Sarkio et.al* demonstrated the incidence of CMV enteritis post-transplant to be 27.7% in the cyclosporine (CsA)–treated group and 20% in the tacrolimus-treated group.[3] The symptoms and signs depend on the affected gut segment and may include dysphagia, odynophagia, nausea, vomiting, abdominal pain, GI bleeding, perforation, or Diarrhoea [21]. CMV infection can also mimic many other entities such as ischemic colitis, intestinal pseudo obstruction, toxic megacolon, and colon carcinoma [9].

An association has also been suggested between the type of immunosuppressive therapy and the incidence of invasive CMV of the GI in renal transplant patients. Several studies suggest that there is an association between mycophenolate mofetil (MMF) and tissue-invasive CMV, especially of the GI tract [12, 13]. In one study in the US, tissue-invasive CMV disease was more common in the MMF groups, with rates of 7% for azathioprine (AZA) group, 11% for MMF 2 g/d, and 12% for MMF 3 g/d [13]. In one study, 57% of patients treated with MMF had either dose reductions or interruptions due to adverse events, especially diarrhoea, nausea, vomiting, and leucopenia [12]. In addition, 6.5% were diagnosed with tissue-invasive CMV of the GI tract, compared with 0% for the AZA group. In another study, CMV infections were diagnosed in 16.6% of CsA patients and 13.5% of Tacrolimus (FK506) patients [14].

Any patient, especially in the early post-transplantation setting or during intensive immunosuppression for rejection, presenting with fever, nausea, vomiting, diarrhoea, and laboratory findings of leucopenia as well as increased liver enzymes should warrant need for endoscopy and biopsy to assess the possibility of CMV enteritis [11].

Herpes simplex virus (HSV) is next in order to CMV among viral agents that cause clinical infection in transplant patients. It usually presents as a reactivation of the latent virus mostly within the first 6 weeks following transplantation. HSV can affect many parts of the GI tract. In addition to mild, ulcer-like muco-cutaneous lesions in the oral cavity and pharynx, another common site for infection is the esophagus. In one study, HSV oesophagitis was reported in 2.2% renal transplant patients over an 8-yr period [14]. All cases developed during the treatment of acute rejection with high-dose steroids and anti-lymphocyte preparations.

Patients with HSV infection after transplantation usually present with odynophagia or dysphagia as well as oro-cutaneous HSV lesions, although the oro-cutaneous complaints in some patients may develop after the appearance of oesophagitis. It is a common belief that symptoms of odynophagia or dysphagia in the setting of intensive immunosuppression must be investigated through endoscopy without delay as untreated herpetic ulcers can progress to hemorrhage, which may even be fatal, or to esophageal perforation.

Candida infection most typically presents in the immunosuppressed transplant patient as oesophagitis with or without oral thrush and is the most comfortable fungal infection. The responsible species is most commonly either *Candida albicans* or *Candida tropicalis* [15]. Determinants associated with invasive candida infections include administration of broad

spectrum antibiotics, recent treatment for acute rejection with high dose steroids or antibodies [11]. Candida esophagitis usually presents with odynophagia or dysphagia. Less commonly, patients may present with fever, heartburn, epigastric pain, or GI bleeding. Lesions may include superficial erosions, ulcers, and white nodules or plaques. Identification of lesions is important because the infection may be severe and necrotizing, which may result in perforation [16]. Perforation with formation of tracheo-esophageal fistulas has also been reported [17].

Bacterial infections of the GI tract are not uncommon in transplant recipients. Examples include *Yersinia enterocolitica* and *Clostridium difficile* colitis. Such infections may be more prevalent in patients with systemic CMV infection [18]. Patients usually present with GI symptoms such as diarrhea, and abdominal tenderness, and rarely with erythema nodosum, arthritis, myocarditis, meningitis, and acute renal failure. Antibiotic treatment is efficient to cure the disease. The true incidence of *Clostridium difficile* colitis among renal transplant is not known [11].West et al reported an overall incidence of *C. difficile* colitis as 8%, with 16% in the pediatric kidney transplant group, 15.5% in the combined kidney-pancreas group, and 3.5% in the adult kidney only group[19] Transplant recipients can be asymptomatic carriers of *C. difficile* but can also develop diarrhea, intestinal obstruction, abscess, and toxic megacolon [11]. Treatment with oral metronidazole in less severe cases and vancomycin in severe *C. difficile* colitis is very effective.

Another consequence of immunosuppression is susceptibility to infection by protozoan or metazoan parasites. GI infection due to microsporidia is the most notable cause of diarrhea in patients with HIV infection. Gumbo *et al* described four cases in which microsporidia infection led to unexplained chronic diarrhea, fatigue, and weight loss in solid organ transplant recipients. [20]The authors speculated that microsporidia infection is under diagnosed because suspicion is low and the organism is not detected by routine stool examination. Since patients can remain carriers for several years, with intermittent symptomatic periods, it has been suggested that transplant recipients with chronic, unexplained diarrhea in the late post-transplantation period should have stools examined with a modified trichrome stain, which can detect microsporidia. Infection with the nematode *Strongyloides stercoralis* has been reported to lead to fever, abdominal pain, bloody diarrhea, abdominal distension, nausea, and vomiting in renal transplant recipients [21]. Microsporidia infections respond well to treatment with metronidazole.

1.1.4 Side Effects of Drug Therapy

In addition to infectious causes, diarrhea can be caused by certain immunosuppressive drugs. Three large trials involving tacrolimus, comprising a total of almost 1500 patients, suggest that GI side effects are more common with tacrolimus than CsA [14. 22]. All three trials show increased rates of tacrolimus-associated GI side effects; in two of the three, the difference was substantial (2.2 times and 1.5 times, respectively) [12,17] Two large trials with MMF demonstrated rates of diarrhea in the MMF groups to be between 1.3 and 1.9 times those in the AZA groups [12, 18]. In many event categories, the highest rates were found in the MMF 3-g/d group, which suggests a dose dependent effect. A number of possible mechanisms for MMF-associated diarrhea have been proposed, such as inhibition of colonic crypt cell division possibly due to immune-mediated mechanism as well as loss of normal villous structure in the duodenum. Dose manipulation, reduction of total dosage, and/or dose splitting (e.g., changing two times daily dosing to four times daily) of particular immunosuppressive drugs, such as MMF and tacrolimus, is an important strategy to manage GI toxicities, particularly diarrhea, in transplant recipients.

Multiple factors contribute to ulcer formation in transplant patients. Examples include the stress of surgery, the use of non-steroidal anti-inflammatory drugs (NSAIDs), the use of steroids, and the possible impairment of native gastro-duodenal cytoprotection due to an AZA- or MMF-induced slowing of intestinal cell turnover [11]. In kidney transplantation, a number of additional ulcer-producing factors may come into play, such as increased gastric acid secretion during post-transplantation dialysis, the possible ulcer-causing effect of heparin used during dialysis, and elevated postoperative histamine and gastrin levels [11].

The role of steroids in peptic ulcer is still controversial. A meta-analysis of a large number of patients on steroids by *Conn et al* revealed that peptic ulcer was a rare complication of corticosteroid therapy. [29] On the other hand, another study by *Steger et al* demonstrated that there were certain trends for those patients treated with methylprednisolone for rejection to develop more ulcers or inflammatory lesions. [23] It is most likely that the development of peptic ulcer in transplant recipients is multi-factorial. Further complicating diagnosis is the fact that steroids frequently mask the clinical symptoms of ulcers (and other GI disorders) and thereby delay diagnosis and treatment. Many ulcers in transplant recipients are entirely asymptomatic as was demonstrated by one study where only 39% of patients with endoscopic proven ulcers had symptoms [23]. Cyclosporine therapy has been shown to be associated with increased incidence of gallstones due to an increased cholestasis and reduced bile flow

in animals [24, 25]. Cholelithiasis was also reported more frequently in a group of renal transplant recipients using cyclosporine/ prednisone compared to a group of patients treated with AZA/ prednisone [25]. These will present with symptoms of obstructive jaundice with or without flank pains.

1.1.5 Quality Of Life (QoL)

In the medical field, interest in QoL has steadily increased since 1948, when the World Health Organization defined health as being not only the absence of disease and infirmity, but also the presence of physical, mental and social well-being [26]. The term QoL refers to the physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions [27]. This definition reflects two fundamental concepts: (i) that health has multiple dimensions (physical, mental and social) and (ii) that health is more than the absence of disease. There has been an increasing consensus regarding the centrality of a patient's feelings in the assessment of health status. The conventional outcomes considered as important endpoints by clinicians need to be integrated with patients' opinions of their health, reflecting how they really feel, and how much their disease affects their way of life. As expectations regarding health and the ability to cope with limitations and disability can greatly affect a person's perception of health and satisfaction with life, two people with the same objective health status may have a very different QoL.

1.1.6 QoL and Kidney Transplant

Overall QoL has markedly improved after kidney transplantation [28-32]. With particular note this has been focused on QoL in dialyzed patients because dialysis represents an alternative to kidney transplantation, which is not always a life-saving procedure.

*Cameron et al.*compared emotional distress and psychological well-being across renal replacement therapies, i.e. continuous ambulatory peritoneal dialysis (CAPD), home- and in-center hemodialysis (CHD) and transplantation. In this study less distress was noted with successful renal transplatation and more well-being than either type of dialysis. CAPD was associated with more wellbeing than CHD; and CHD was associated with more distress than home hemodialysis.[33]

Hathaway et al. showed a significant improvement in all QoL domains in a group of 68 patients evaluated while on the waiting list and again 6 and 12 months after transplantation [34]This amelioration occurred early (within the first 6 months after surgery) and continued to

be stable during the follow-up. When predictors were analyzed, three parameters influenced 20–54% of the variability in QoL, i.e. social support ,number of hospital admissions (representing early morbidity after transplantation) and work (representing economic autonomy).[34]

Tsuji et al in a study done in Japan reported that the improved QoL after transplantation was mainly related to the social and physical domains, although it did not reach the same level as in the healthy population, particularly in relation to the perception of overall health [35] Although transplantation dramatically improves QoL, there are racial, gender and socio cultural differences in how it is perceived after surgery. Afro-Americans achieved a less marked improvement than Caucasian-Americans in the affective and functional measures of QoL [36]; women scored consistently lower than men and reported improvements mainly in functional ability, while perceptions of self-image remained low [37, 38]; higher economic and educational levels were associated with a higher perception of overall QoL after transplantation [39].

1.1.7 Measurement of QoL after Kidney Transplant

1.1.7.1 Disease Specific Tools
To evaluate the impact of a specific disease on health related quality of life (HRQL), specific evaluation tools have to be utilised. These tools are sensitive enough to determine longitudinal changes of a disease but they are not appropriate to compare different diseases. Disease-specific tools in HRQL evaluation after renal transplantation include the Kidney Transplant Questionnaire (KTQ) [40], the Kidney Disease-Quality of Life (KDQOL) [26] and the End Stage Renal Disease Symptom Checklist Transplantation Module (ESRDSC-TM) [27].

The KTQ as the first cited examples contains 26 questions in five domains (physical symptoms, depression, fatigue, relationship with others, frustration) each of which can be scored on a scale from 1 to 7, where the lowest score represents the lowest QOL. For the final analysis all points are summed up, thus the maximum score is 182 and the minimum 26 points. As others, these questionnaire need to be evaluated in the native language of the patient.

The KDQOL was initially developed for patients with chronic renal disease and dialysis patients. However, recent papers used this tool for the evaluation of transplant patients as

well in order to compare them to patients on hemodialysis and peritoneal dialysis [28]. The original KDQOL covers eleven dimensions with a different number of items. The dimension symptoms/problems include 34 items, effects of kidney disease on daily life 20 items, burden of kidney disease 4 items, cognitive function 6 items, work status 4 items, sexual functions 4 items, quality of social interaction 4 items, sleep 9 items, social support 4 items and patient satisfaction 2 items. In case of dialysis patients the domains dialysis staff encouragement with 6 items completes the list. The response options are a Likert scale whereas higher scores denote better QOL.

The ESRDSC-TM was specifically developed to evaluate the effects of immunosuppressant medication on QOL. The distributed questions are scored on a five-point Likert scale, again where higher scores represent better QOL. The authors tested over 400 transplant patients and evaluated the test-retest correlation in a subset of 88 patients at an interval of one year and found adequate validity.

Until now no single method has been shown to be ideal for measure HRQL under all circumstances. By comparing HRQL results from studies using different measuring tools, it is possible to get similar numerical results but a discrepancy in meaning. It has been shown that very different HRQL results can be obtained in the same population if different tools are used [39].

1.7.1 .2Generic Tools

Generic tools are useful for comparisons among groups and studies and for evaluating the impact of different diseases on QOL. These tools are used in HRQL research and include tests such as the Sickness Impact Profile (SIP), the 36-item short-form of Medical Outcomes Survey (SF-36) also known as the Gastro-intestinal Quality of Life Index (GIQLI), and the Nottingham Health Profile (NHP).With more than 2000 publications, the SF-36 is one of the most widely used quality of life instruments worldwide [30, 31].

The SF-36 questionnaire (GIQLI)

The SF-36 questionnaire is a self administered survey and contains 36 items that take a few minutes to complete. It includes one multi-item scale that assesses eight health domains: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of

physical health problems; 4) bodily pain; 5) general mental health; 6) limitations in usual role activities because of emotional problems; 7) vitality; 8) general health perceptions.

The evaluations of the instruments are based on reliability and validity, and of particular pertinence for use in clinical trials, responsiveness to change. Reliability refers to the precision or the reproducibility of a measure (i.e. if it is free from random error). This is usually expressed by a coefficient ranging from 0 to 1, with 1 indicating maximum reliability. A common estimate used is internal consistency, which should usually range from 0.5 to 0.7 for group comparisons and 0.85–0.95 for individual comparisons.[47–50.] *Brazier et al* obtained data from 25 consecutive clinically stable patients with gastrointestinal disease, assessed and reassessed them within 48 hours to estimate the stability of GIQLI scores. The mean (S.D) score of the first test was 90.1(22.9) and the retest score was 93.6(22.8). The Intra-class Correlation Coefficient was reported as (0.92) which denote a high level of reliability.[28]

The second variable is validity, which expresses to what degree an instrument measures what it is supposed to. Results from the preliminary validation studies, conducted during phase 11 as reported by *Brazier et al* based on 204 patients completing 44 items of the questionnaire, reported the Pearson product moment correlations of the GIQLI with the QL Index and the Affect Balance Scale of 0.53 and 0.42 respectively.[28] The moderately strong correlations suggest that the measures have a common, underlying dimension. The GIQLI is therefore an appropriate, validated and potentially useful tool to assess health-related quality of life in clinical studies of patients with gastrointestinal disease and in daily clinical practice.

1.2 Gastrointestinal Symptom Rating Scale (GSRS)

The GSRS is a disease-specific instrument of 15 items combined into five symptom clusters depicting Abdominal pain, Indigestion, Reflux, Diarrhoea and Constipation. The GSRS has a seven-point graded Likert-type scale where 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms. The reliability and validity of the GSRS are well-documented [54], and norm values for a general population are accessible[45].The GSRS is used as a basis to evaluate gastrointestinal symptoms and as a clinical evaluation tool in patients with Gastrointestinal symptoms.

1.3 Studies evaluating QoL after renal transplantation

The pioneers to study the long-term quality of life after kidney and simultaneous kidney and pancreas transplantation were colleagues from Minnesota. In 1998 Matas and co-workers

described the QOL assessed by using the SF-36 form [33]. The authors managed to have 446 patients evaluated once, 632 twice and 53 three times. The patients were between one and ten years after transplantation. The SF-36 scores remained unchanged significantly over the years after transplantation and remained consistently lower compared to the normal US population. Curiously of note was that the diabetic and non-diabetic subjects scored similarly on the mental health scales whereas non-diabetic patients scored better on physical functioning and on general health.

The same authors published a longitudinal relationship between adverse effects particular of immunosuppressive drugs in renal transplant recipients and QOL [34]. In this study, 4247 self-selected patients were enrolled and assessed by a QOL questionnaire. The authors conducted a multivariate analysis which showed that emotional problems, reduced sexual interest and headache were the main factors that negatively influenced QOL in these patients.

Gross et al also from the University of Minnesota, evaluated the impact of transplantation on QOL in diabetic patients with ESRD. Specifically, the authors addressed the question whether simultaneous kidney/pancreas transplantation (KPT) confers a better QOL than kidney transplantation alone with subcutaneous insulin therapy[35] Most QOL readings improved after transplantation in both groups. After adjustment for co-morbidities, the authors found higher SF-36 scores in KPT in the domains of physical functioning, bodily pain, general health and the physical component.

Johnson and colleagues published the first study that evaluated changes in QOL in the first year after renal transplantation split by gender and race [36]. The authors used three questionnaires to assess HRQL, the Sickness Impact Profile, Ferrans and Powers' Quality of life index, and the adult self -image scales. African-American patients observed less QOL improvement compared to Caucasian patients, and women scored consistently lower than men. This study demonstrates that although all participants improved their QOL, considerable racial and gender differences exist and these differences may affect care requirements.

Reimer et al compared the HRQL among 63 cyclosporine and an equal number of tacrolimus treated renal transplant recipients between 1997 and 1999 [48]. HRQL was assessed using the SF-36 and a disease-specific QOL instrument, the End-Stage Renal Disease Symptom Checklist – Transplantation Module (ESDR-SCL). The measurements were performed at transplantation and one year thereafter, time after transplantation and the type of

immunosuppression were included into the regression model as independent variables. Patients with tacrolimus based immunosuppression reported significantly better global and disease specific HRQL than those receiving cyclosporine micro-emulsion.

Franke et al. evaluated the HRQL in patients with end stage renal failure [39]. The trial explored the differences in HRQL among patients on the waiting list for kidney transplantation while maintained on haemodialysis and recipients of renal transplants. The outcome was measured with generic (SF-36) and disease specific tools (End Stage Renal Disease Symptom Checklist-Transplantation Module). In that trial the group of 80 dialysis patients on the transplant waiting list experienced a decreased satisfaction with social support, while the 222 patients after successful renal transplantation exhibited an increase of social support. Similarly, psychological distress was higher among patients on maintenance haemodialysis compared to the transplanted subjects.

1.4 Health-Related Quality Of Life in Gastrointestinal Disease

Health-related quality of life has been evaluated in a number of gastrointestinal conditions, including cancer

1.4.1 Gastroesophageal reflux disease

Gastroesophageal reflux is symptomatic in most patients and affects a large proportion of the population. Reflux may affect patients in several activities of their daily living such as work, bending forward, eating, and sleeping [50]. Several studies of reflux patients show an impaired HRQL compared with a healthy reference population [51, 52]. Coincidentally, Kaplan et al in a rural primary care population with GERD symptoms, with or without comorbidity, reported compelling deviations compared to healthy reference values in terms of impairment in emotional and physical role functioning, pain, health perceptions vitality and mental health [53]. Patients with gastrointestinal conditions have generally been shown to be considerably more overtly impaired than those with other conditions such as arthritis, hypertension and myocardial infarction [52]. This can partly be ascribed to the fact that gastrointestinal conditions considerably affect most of the domains measured. Lack of vitality, emotional distress, pain, limitations in physical and social activities have been found in reflux patients [53]. Sleep disturbance has also been found in patients with heartburn and regurgitation [54]. The difference between symptomatic GERD and reflux esophagitis is seen on endoscopy. In symptomatic terms no differences can generally be found. Nor have the

effects on quality of life been correlated to esophagitis [55, 56] the level of anxiety and pain in heartburn patients has been found to be a factor in predicting effect of treatment [57].

1.5 Dyspepsia

Dyspepsia or pain refers to discomfort in the upper abdomen and can include ulcer and reflux disease, while functional dyspepsia involves similar symptoms but without any organic findings on examination with, for example, an endoscopy. The HRQL in these groups has been defined as low and at the same level with or without investigational findings of reflux disease or duodenal ulcer, and the values reflected the intensity of symptoms well [58] Another factor of importance was the increased pain and anxiety level found in patients with negative endoscopy [59].

1.6 Irritable bowel syndrome

Irritable bowel syndrome (IBS) has many similarities to dyspepsia, which explains why some questionnaires have been developed for both areas. The SF-36 has shown that HRQL is low in patients with IBS. Values have been found lower than other groups such as diabetes and GERD. Irritable bowel syndrome patients disclose a diversity of HRQL impacts such as pain, poor health, sleep disturbances and a pronounced impact on social functioning and mental health. Dimensions affected are particularly energy/fatigue, role limitation, physical pain and health perceptions [61, 62].

CHAPTER TWO: STUDY RATIONALE

2.0 PROBLEM STATEMENT

The increase in the number of transplanted patients has given rise to a new socio-medical community of transplanted people, characterized by specific psychopathological and clinical features. The goal of transplantation is not only to ensure their survival and graft functioning, but also to offer patients much the same state of health as they enjoyed before the disease, achieving a balance between the functional efficacy of the graft and patient's psychological and physical integrity. That is why a change has been seen in the evaluation of medical intervention in the field of organ transplantation, as in other medical fields [12]. Previously used parameters, such as clinical judgment, biochemical and instrumental tests and survival rates, have been integrated with new indicators evaluating the relationship between the costs (both human and economic) and benefits of any intervention in terms of quality of life (QoL) [17].

There are no local studies on record that have estimated the burden of gastro intestinal symptoms in renal transplant patients at Kenyatta National Hospital (KNH) and how it affects the QoL of patients seen at its renal unit. Moreover, the use of existing hospital records to estimate the burden of GI symptoms in renal patients may not accurately estimate the burden of the problem. Studies have shown that there is discrepancy between patient reported and doctor elicited symptoms. Ponticelli *et al* [5] in a study in Italy reported that doctors underreported gastrointestinal symptoms while they tend to overestimate the QoL compared to the patient's perceived outcomes.

2.1 JUSTIFICATION

Currently at KNH, there are 140 patients who are recipients of a renal transplant. Graft survival in renal transplant patients has improved steadily over the last decades as a result of improved immunosuppressive therapies. Immunosuppressive regimens continue to have side effects which patients find burdensome and which may lead to sub-therapeutic dosing and non-compliance by the patient. Although patient and graft survival are remarkably high, opportunities to improve transplant outcomes exist particularly as they relate to patient self-reported indicators of QoL. Health-related QoL has become a frequently used outcome in clinical and health policy settings in the last two decades, as expression of the centrality of patients' point of view in the assessment of health status. The role of QoL evaluation is

crucial particularly with respect to therapies involving the allocation of scarce resources, such as organ transplantation.

Organ transplantation represents the treatment of choice for many patients with end-stage organ diseases, with good outcome from a technical standpoint. Individual variability in post-transplant QoL has been observed in the PORTEL study and may limit ability to come up with recommendations to improve outcomes globally and uniformly.[56] However, identification of individual patterns and any relationship that may exist between the GI symptoms and patient factors may assist in tailoring treatment regimen and changing hospital policy towards improving the QoL of post renal patients seen at KNH. It is the aim of this study to quantify the burden of GI symptoms and perceived quality of life and establish any patterns in patient variables that may be associated with the GI symptoms.

2.2 RESEARCH QUESTIONS

1. What is the burden of gastro-intestinal symptoms among renal transplant patients receiving care at Kenya National Hospital?

2.What is the gastrointestinal quality of life in renal transplant patients?

2.3 STUDY OBJECTIVES

2.3.1 General Objective

To assess the prevalence of gastrointestinal symptoms and gastrointestinal QOL in renal transplant patients receiving care at the Kenyatta National Hospital

2.3.2 Specific Objective

1. To study the type and prevalence of the gastrointestinal symptoms using the gastrointestinal symptom rating scale questionnaire
2. To determine patient's gastrointestinal quality of life (QOL) using the GIQLI questionnaire

CHAPTER THREE:METHODOLOGY

3.0 STUDY SETTINGS

The study was conducted at the renal transplant clinic within the renal unit of Kenyatta National Hospital .Kenyatta National Hospital is a tertiary and referral teaching hospital situated in Nairobi, Kenya. It is the largest hospital in East and Central Africa, with a bed capacity of 2000. It is the only public hospital with a specialized renal transplant programme that has a transplant clinic offering care to post-transplant patients. The programme has been successful with the Inter-life programme that subsidised the cost of transplant. Novartis Pharmaceuticals are funding this programme. The clinic is held on a weekly basis every Tuesday with the exception of public holidays.

The Transplant clinic has about a total number of 140 patients that underwent renal transplant. The average patients attended to per week in the clinic was 12 patients.

3.1 STUDY PARTICIPANTS

The study population comprised of all adult medical patients who have previously undergone a renal transplant procedure and are receiving care at KNH renal unit and have given consent. In this study all patients above 18 years of age were classified as adults as per Legal age in Kenya.

3.2 Inclusion Criteria

The eligibility criteria used to include participants into the study were

1. Patients having undergone kidney transplant at least six weeks prior to recruitment.
2. Patients who showed willingness to participate in the study and document this by means of a written informed consent form.

3.3 Exclusion Criteria

The exclusion criteria were

1. Patients requiring in patient hospitalization or admitted two weeks prior to recruitment.
2. No consent.
3. Patient with cognitive impairment

3.4 Study Design

This was a prospective cross-sectional observational study. Over a period of two months eligible patients were interviewed using validated self- administered questionnaire on their gastrointestinal symptoms and perceived impact on their QOL.

3.5 Sample Size

Currently there are 140 patients who are recipients of a renal transplant and are on active follow up at KNH renal clinics. All patients meeting the inclusion criteria and gave consent were included in the study.

3.6 Sample size calculation

According to KNH data from hospital records, an estimated number of 140 renal transplant recipients are on follow up. Therefore, out of this population a representative sample will be drawn and the sample size calculation will be obtained using the formula for finite population (Daniel, 1999). The calculation was as follows:

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where

n' = sample size with finite population correction,

N = size of the target population = 140,

Z = Z statistic for 95% level of confidence = 1.96,

P = Estimated proportion of with gastrointestinal symptoms= 88.3%

d = margin of error = 5%

$$= \frac{140 \times 1.96^2 \times 0.883 \times 0.117}{0.05^2 (140\text{-}1) + 1.96^2 \times 0.883 \times 0.117}$$

= **75** renal transplant patients needed sampling for analysis

96 patients attended the clinic only 83 met eligibility.

3.7 STUDY PROCEDURES

Eligible participants were approached in any one of the clinical settings described above. Informed consent was obtained; demographic data was captured using the study proforma after which the GSRS and GIQLI questionnaires were administered. Patients requiring assistance to understand the questions without bias were assisted by the trained research assistant.

3.8 DATA MANAGEMENT

3.8.1 Data Collection
The demographic data was collected using the study proforma (Appendix IV)

A self-administered Gastrointestinal Symptom Rating Scale (GSRS Section 2) was used to assess the baseline presence and severity of gastrointestinal symptoms in the renal transplant patients. Patients who were unable to understand the questions were assisted by the research assistant(clinical officer) a diploma holder from the Kenya Medical training College.

 The assistant was trained to collect the data and how to record the study findings for this study. A pilot run was done before the commencement of the study to ensure the assistant was able to capture the demographic data. The relationship between gastrointestinal symptoms and ongoing treatments as well as the impact on gastrointestinal symptoms on QOL was to be measured with the Gastrointestinal Quality of Life Index (GIQLI). These two instruments were validated for the measurement of gastrointestinal symptoms in renal patients[2,63]The GIQLI is a 36-item GI-specific HRQL instrument designed to assess health related quality of life (HRQL) in clinical practice and clinical trials of patients with GI disorders. The GIQLI has five subscales (GI Symptoms, emotion, physical function, social Function, and medical treatment) as well as a Total Score. Higher scores represent better HRQL and sub-scores range from 0–4 while the total score range from 0–144.

3.8.2 Data Analysis
The outcomes of interest are analysed as gastrointestinal symptoms as categorised in the GSRS questionnaire. The symptoms are grouped under any of the following main categories: reflux syndrome (heartburn and acid regurgitation), abdominal pain syndrome,(abdominal pains, hunger pains and nausea) constipation syndrome (constipation, hard stools and feeling of incomplete evacuation), indigestion syndrome (boborygmus, abdominal distension, eructation and increased flatus), and diarrhoea syndrome(diarrhoea, loose stools and urgent

need for defecation). If the symptom does not match any of the above groups then it will be categorised under eating dysfunction.

Gastrointestinal symptom domains as per severity score distribution in the study population

Table 1.Severity score distribution

Severity score	symptoms
0-1.0	No symptoms
1.1-2.0	Minor
2.1-3.0	Mild
3.1-4.0	Moderate
4.1-5.0	Moderately severe
5.1-6.0	severe
6.1-7.0	Very severe

Quality of life as determined by the GIQLI questionnaire mean score range in healthy population was 125+/- 13 or no symptoms 126,score of 65.00 or less is severe symptoms reflective of poor quality of life, moderate symptoms score of 95.00-65.00 with average quality of life mild symptoms at 126-96,GIQLI scores for all domains ,any score less than 4 is in keeping with worse symptoms in the GI symptoms ,emotional, social, physical and medical treatment.

Table 2-GIQLI Scores

GIQLI score	Interpretation
125 +/- 13	No impairment
125-96	Mild impairment
95-65	Moderate impairment
65 0r less	Severe impairment

GIQLI mean score in each of the five sub-scale domains (GI symptoms, emotion, physical, social and medical).A GIQLI score of less than 4 is indicative of worse symptoms therefore poor quality of life.

Even though this is a descriptive study, explanatory variables were collected to determine if there is an association between these variables and gastrointestinal symptoms. To explore participant factors that impact on the intensity of gastrointestinal symptoms the following data was collected: age and gender of the patient, disease leading to renal failure, height, weight, serum urea and creatinine, duration of dialysis pre- renal transplant, duration of graft tolerance, the cytotoxic drugs used by the patient and consumption of drugs used for GI disorders, the serum creatinine results were noted at the time of interview,

The estimated GFR was calculated using the MDRD equation i.e. (GFR (mL/min/1.73 m2) = $175 \times$ (Serum Creatinine)-1.154 $\times$ (Age)-0.203 $\times$ (0.742 if female) $\times$ (1.212 if African American)

Data analysis was done using Stata version 10 (Stata-Corp , College Station, Texas, United States). Demographic variables and clinical conditions was evaluated by descriptive analysis. For the descriptive analysis, a Chi-square (χ2) test was used to evaluate categorical data; Mann-Whitney test and   Kruskall-Wallis test was used to analyse the data.

The results of data analysed is presented using frequency distribution tables, charts and graphs**.**

STUDY VARIABLES

The independent variables such as

    a) Age – It was recorded as the nearest number of years from reported date of birth.

    b) Gender– It was determined by the phenotypical sexual appearance of the subjects. That is, the secondary sexual characteristics.

    c) Disease duration from diagnosis – This was determined to the nearest year by documented date of when the disease was diagnosed for the first time.

    d) Treatment modality – This was defined as drug therapy used and the duration of use. It was obtained from the subjects records.

    e) Level of education – It was reported as the highest level of education the patient has acquired as reported by the patient.

f) Marital status – This was categorized as single, married, divorced or widowed and was documented as reported by the patient.

The dependant variables that is

i.GSRS calculated Chi-square test

ii.GIQLI calculated using Chi-square test and Kruskall –Wallis test

3.9 DATA PRESENTATION

Data was entered into a password protected Microsoft Access database managed by the statistician. Once data entry was complete, entries in the database were compared to the hard copies to ensure accurateness. Inconsistencies were detected by use of simple frequencies and correlations and those identified were rectified before data analysis began, then analysed using SPSS software version 20 for windows.

3.10 ETHICAL CONSIDERATIONS

Permission and ethical approval was obtained from the Department of Clinical Medicine and Therapeutics of the University of Nairobi and Kenyatta National hospital -UON Research and Ethics Committee before data collection.

Before study on participants the study purpose was explained to all subjects and informed the written consent was obtained.

Patients with severe GI symptoms from assessment were informed and referred to the gastroenterologist for review. Baseline evaluation as routine standard care practice was carried out prior to referral and emergent treatment put in place.

CHAPTER FOUR: RESULTS

RECRUITMENT PROCESS

The process to recruit participants is shown below in Figure 1.
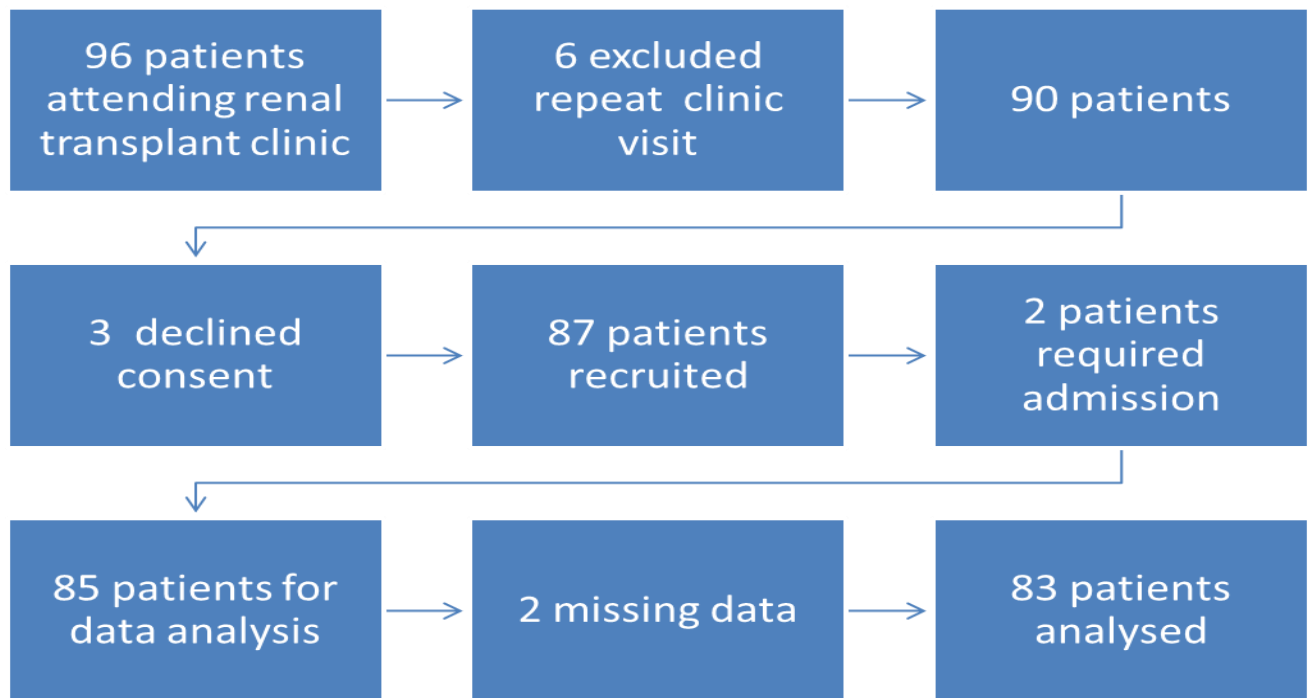
Figure 1: Recruitment process

A UNIVARIATE ANALYSIS

4.0 Socio-demographic characteristics

A total of 36 females and 47 males were interviewed Kenyatta National Hospital, Renal Unit in the period August 2015 to September 2015 .Their mean age was 41.3 years. The youngest patient was 18 years old whereas the oldest was 65 years old. Majority of the patients (67.1%) were married. The level of education noted in this study that 94%. Of the patients had attended school up to primary school level these characteristics are outlined in Table.1

Table 3: Socio-demographic characteristics

Demographic characteristics		n=83
Age (years)	Mean	41.3±2.7
	Median	52 (21.5)
	Range	22-65
Marital status	Divorced	6.4%
	Married	67.1%
	Single	22.8%
	Widowed	2.5%
	Not classified	1.3%
Employment status	No formal employment	38.0%
	Employed	62.0%
Education	No formal education	5.1%
	Primary level	11.4%
	Secondary level and above	60.9%
Number of pills	Mean	5.45±0.4
	Median	5(3)
Number of immunosuppressants	Mean	2.80±0.1
	Median (mode)	3(3)

4.2 Years elapsed since diagnosis of kidney disease

About 50% of the patients were diagnosed with kidney disease more that 5 years prior to the interview while only 4% were diagnosed less than one year prior as illustrated in Figure 2 below,
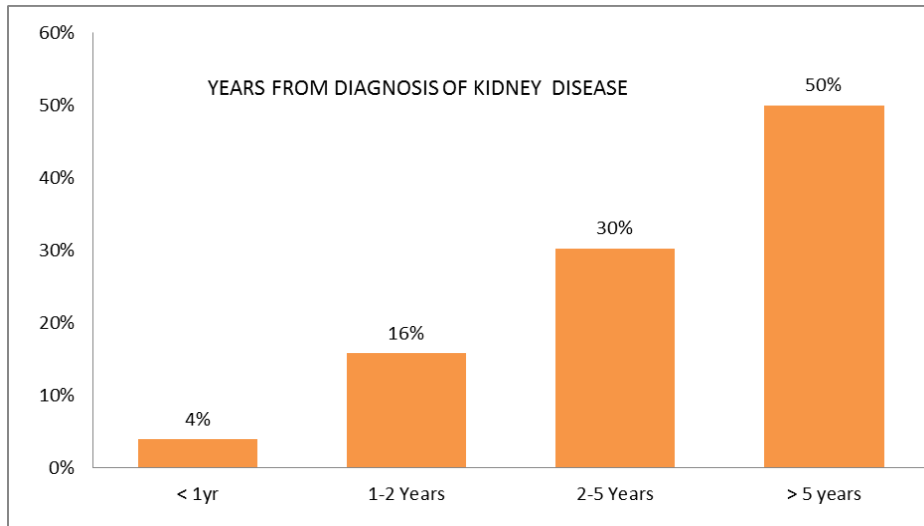
Figure 2:Years from diagnosis of kidney disease.

4.3: Time elapsed since Kidney Transplant.

76.3% of the patients had a kidney transplant less than five years prior to interview. The rest of the times are shown as in the figure below,
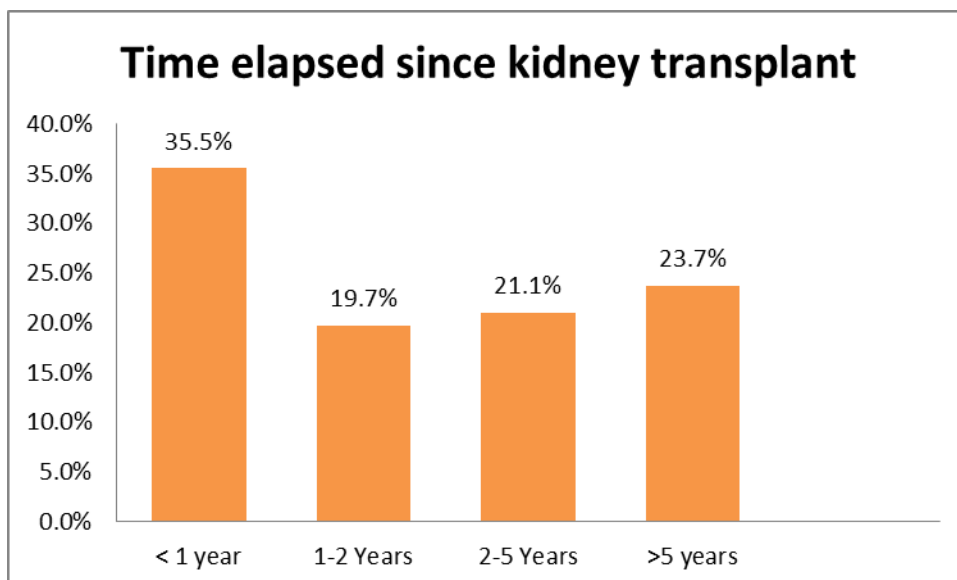
Figure 3: Time elapsed since kidney transplant

4.4 Immunosuppressive drug distribution .

Most patients were on three types of immunosuppressant drugs. Prednisone and mycophenolate sodium drugs were the most widely used drugs. Ciclosporin and tacrolimus were in use at 44% and 54% as shown belowFig.4
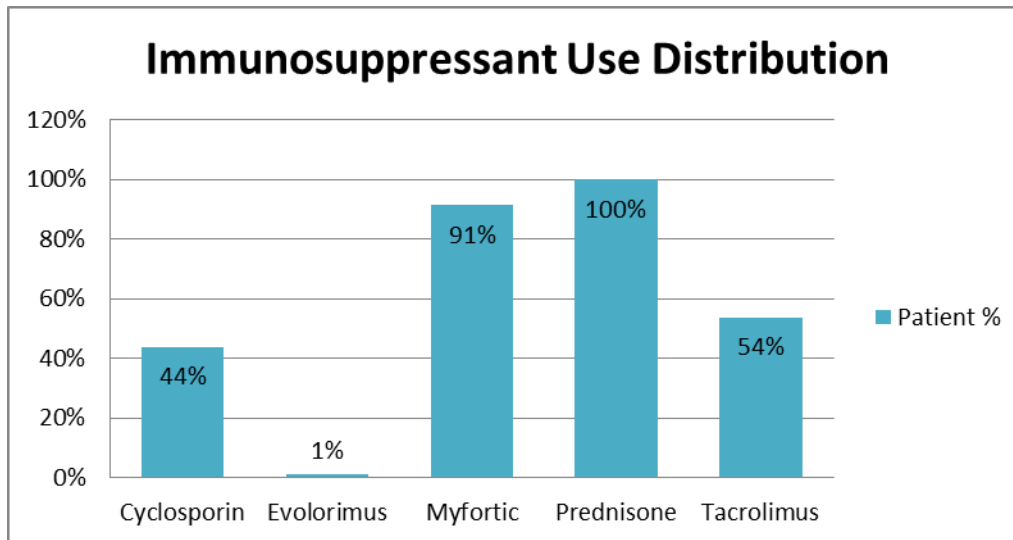
Figure 4: Number and Type of immunosuppressant drugs.

Immunosuppressant drug combinations

The commonest combination in the study group was myfortic, prednisone and tacrolimus at 49% followed closely by cyclosporine, prednisone and myfortic at 41%
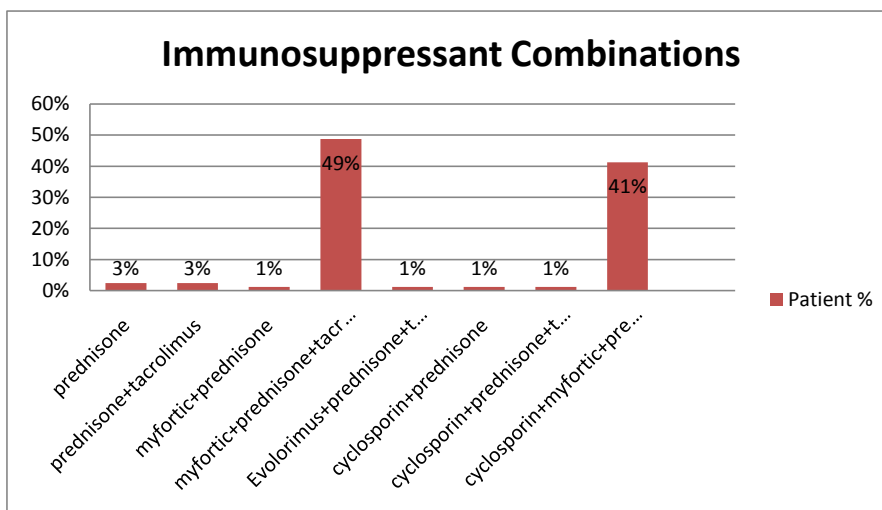
Figure 5: Immunosuppressant Drug combination distribution.

4.5 Type and Prevalence of the gastrointestinal symptoms

4.5.1: Type of the gastrointestinal symptoms

Only 5 out of 81 Patients (7%) reported that they had oral ulcers while none had odynophagia and dysphasia.

When the GSRS score was used, the number of patients reporting at least one gastrointestinal symptom (defined as a score>1) was 96%. When considering individual GSRS symptoms across all five domains four symptoms most frequently reported by patients were, in order of prevalence, abdominal pain (57%), boborygmus (55%), heartburn (55%) and regurgitation (53%).The rest of the individual scores are represented as in the figure below
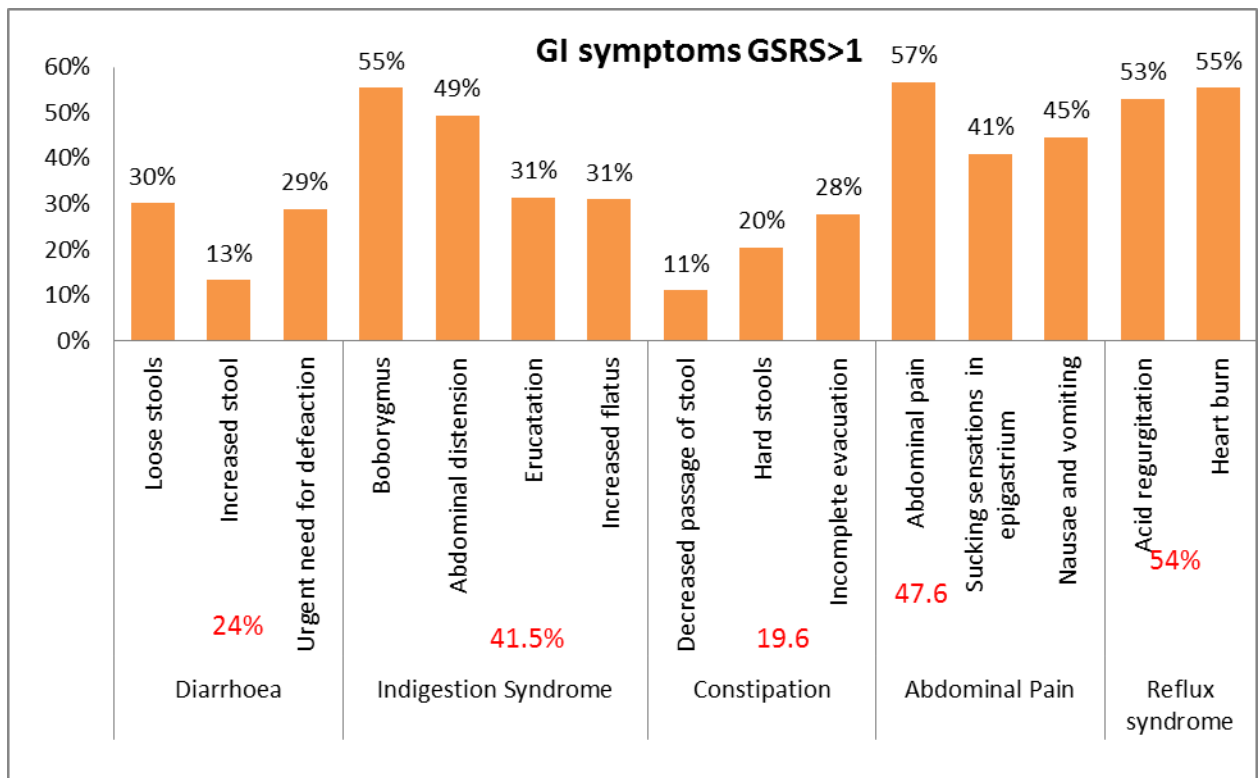
FIGURE 6: Gastrointestinal symptom GSRS >1

4.5.1.1 Abdominal pain

Individual score distribution was as described most patients scored 2 reflective of mild symptoms.
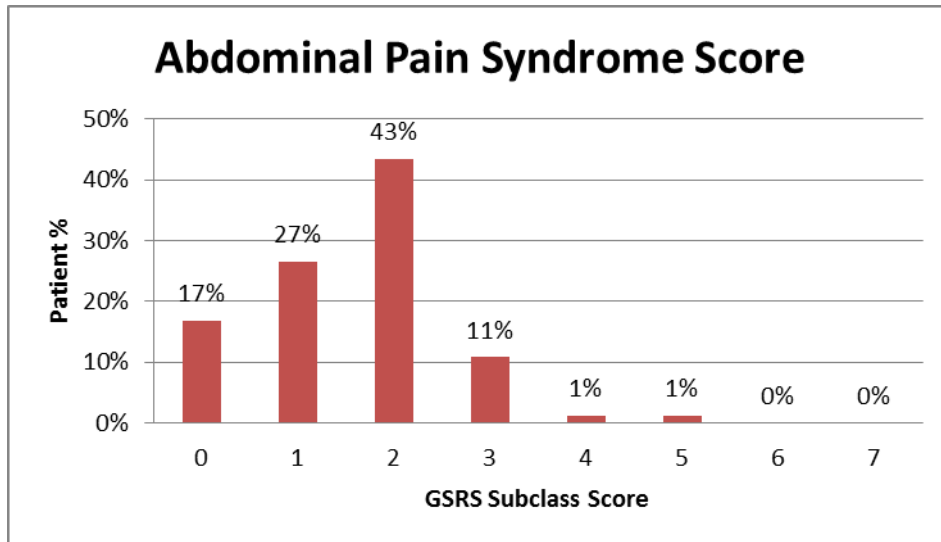
Figure 7: Abdominal pain syndrome score

4.5.1.2 Constipation syndrome

In this sub category most patients had a score of zero at 56% reflects that most patients had no symptoms.
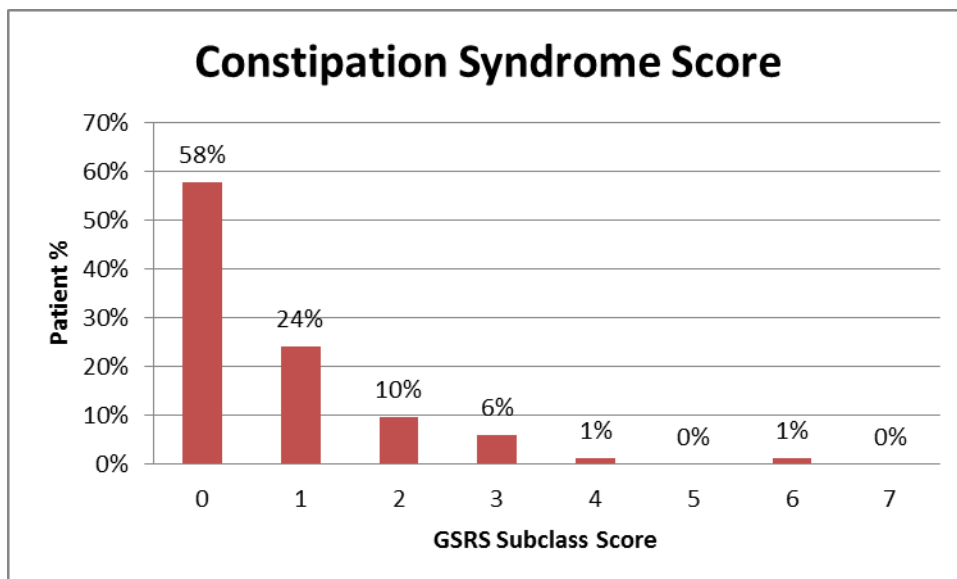
Figure 8: Constipation syndrome score

4.5.1.3 Diarrhea syndrome

The distribution here was still in the mild symptom category with 4% scoring with moderately severe symptoms.
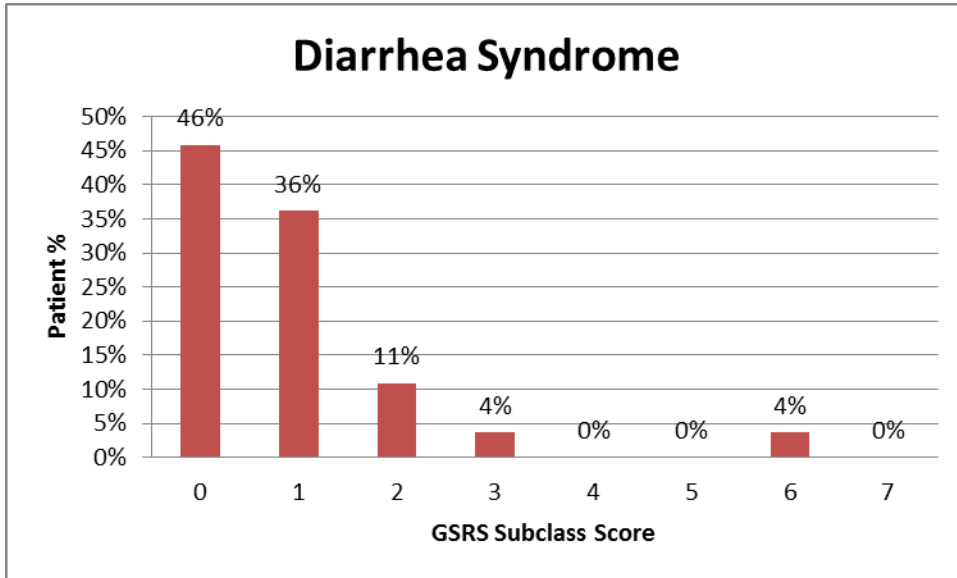
Figure 9: Diarrhea syndrome

4.5.1.4 Indigestion syndrome

In this indigestion syndrome sub- group noted variable individual scores from 19% with no symptoms and 1% with severe symptoms.
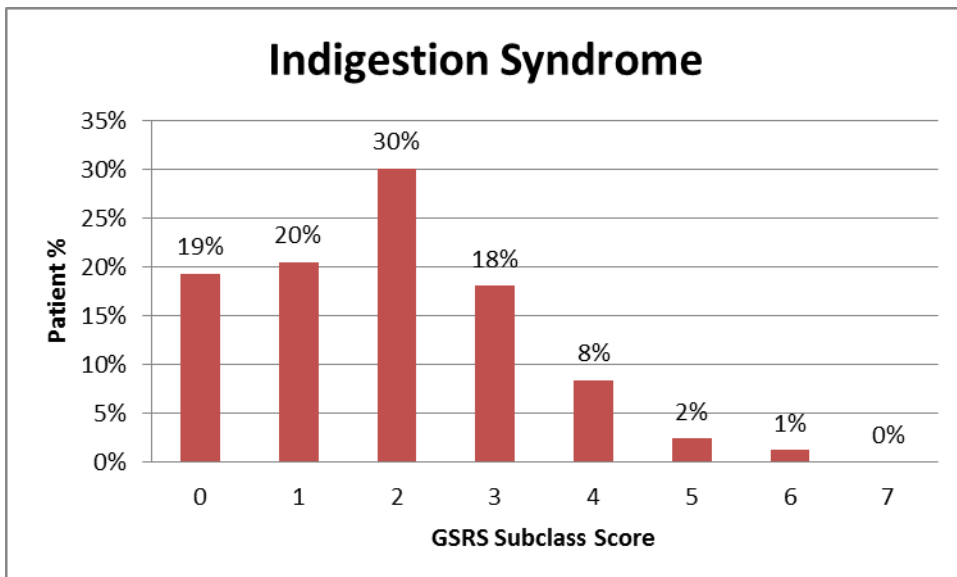
Figure 10: Indigestion syndrome score

4.5.1.5 Reflux syndrome

Most patients in this sub group had no or minor symptoms and 40% had mild to moderate symptoms.
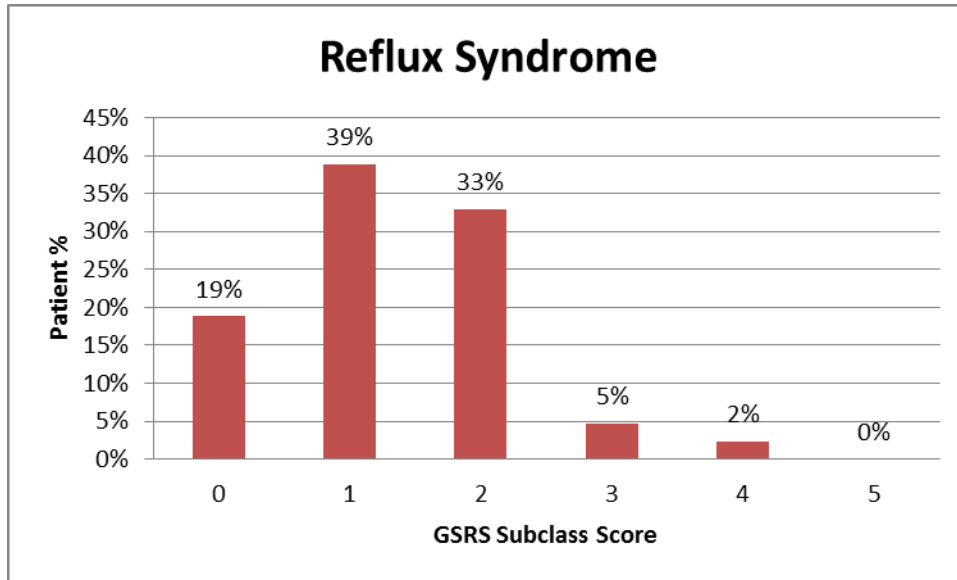
Figure 11: Reflux syndrome subclass scores

4.6 Prevalence of the gastrointestinal symptoms

Abdominal pain (upper) was the most prevalent (58%) of all the GI symptoms.57% of the abdominal pain symptoms were mild. Of all patients with loose stool, 4% of the cases were severe than in any other lower GI symptom category

The prevalence and severity of individual upper and lower gastrointestinal symptoms reported are shown in Fig.12 below.
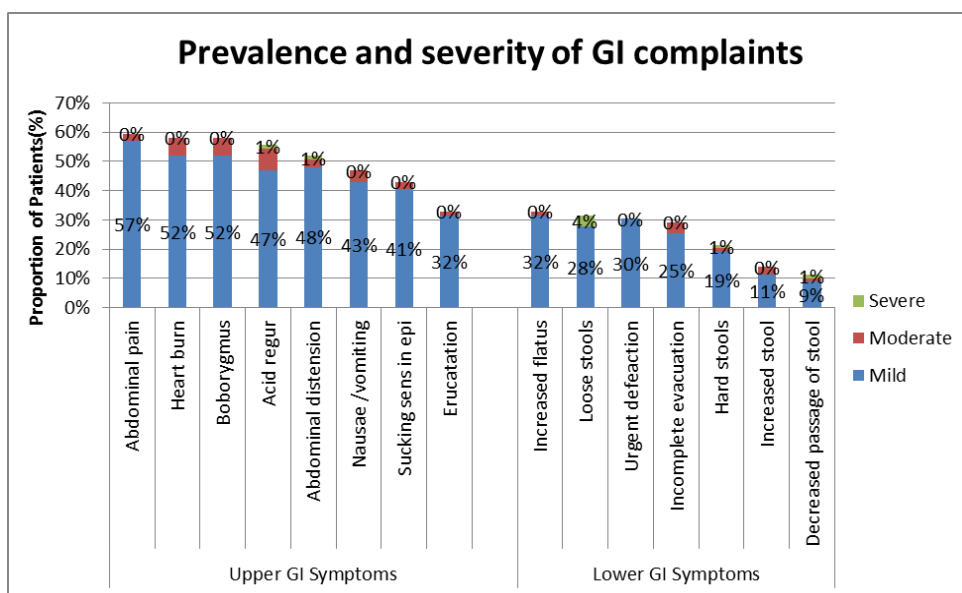
Figure12: Prevalence and severity of GI complaints.

4.7 Patient's gastrointestinal quality of life.

4.7.1: GSRS Subscales Scores for GI Complaints.

The mean reported GSRS total score was 3.364. Combining individual symptoms into the five domains of the GSRS gave scores of 3.42 for Diarrhoea, 4.29 for Indigestion, 3.46 for constipation, 3.18 for abdominal pain and 2.29 for reflux syndrome as shown in Fig 13.
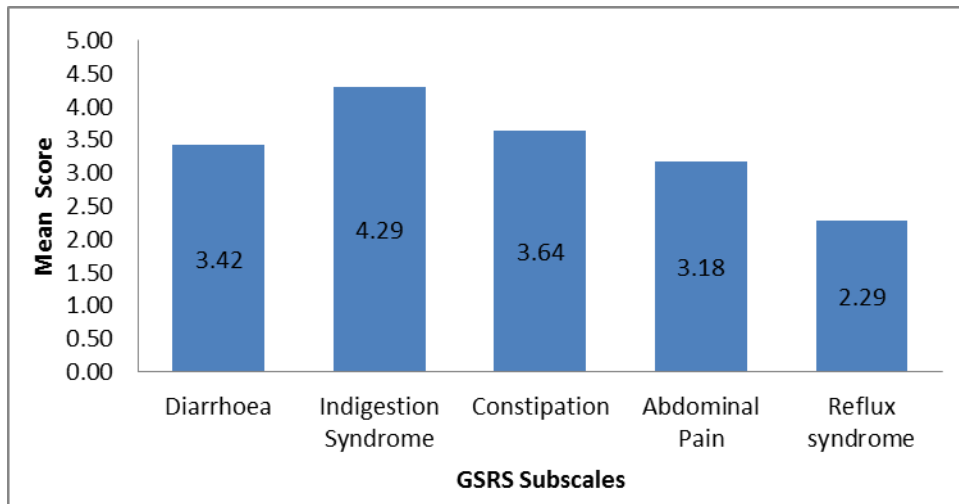
Figure 13: GSRS subscales for GI complaints.

*Higher scores indicate worse symptoms

4.7.2 GIQLI symptom severity score

49% of patients reported symptoms ranging from mild to severe symptoms. The severe symptoms noted at 5%
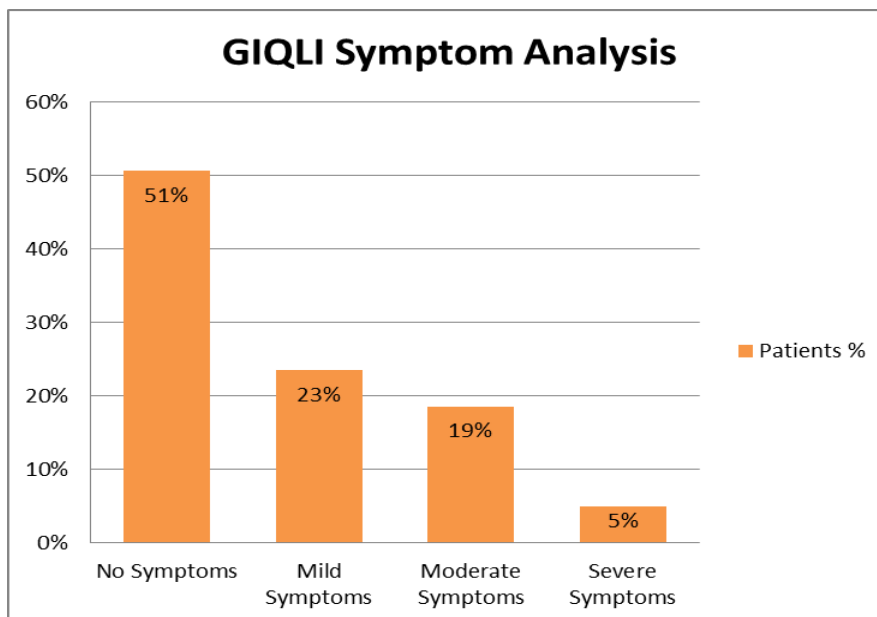
Figure 14: GIQLI symptom analysis

4.7.3 GIQLI Subscales Scores for GI Complaints.

For the patients who ever experienced a gastrointestinal symptom, the mean reported GIQLI total score was 2.326. Combining individual symptoms into the five domains of the GIQLI gave scores of 1.89 for GI Symptoms, 0.83 for Emotional Function, 1.12 for physical function, 1.65 for   social function and 6.14 for medical treatment. A score less(<)4 is indicative of worse symptoms. All domains were affected except medical treatment as shown in Figure 15 below.
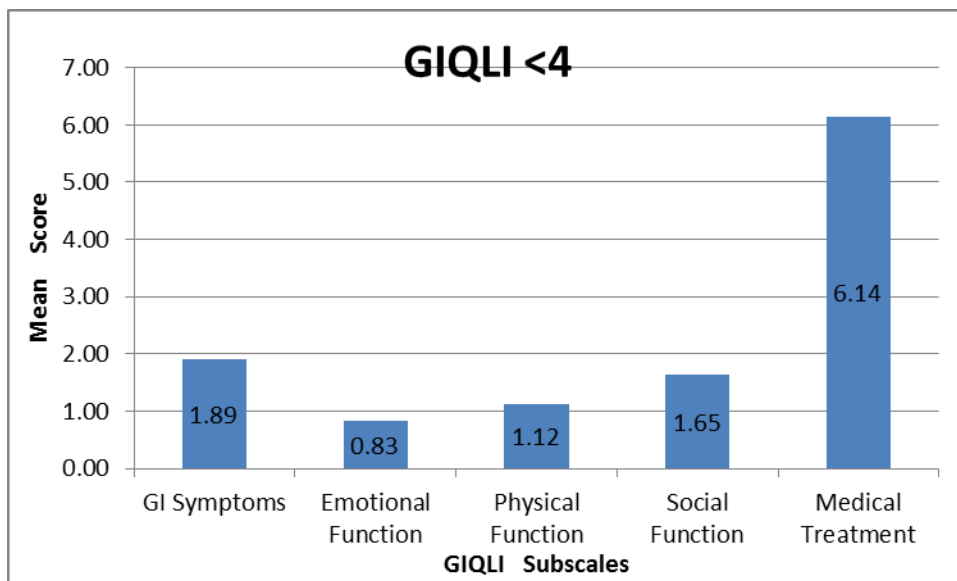
Figure 15: GIQLI SUBSCALES

*Lower scores indicate worse symptom

CHAPTER FIVE: DISCUSSION

This cross-sectional study in post-renal transplant patients captured patients who had gastrointestinal symptoms, with a GSRS score of more than 1(GSRS>1) which accounted for 96% of the study subjects. Similar observations were made in cohort studies in the Italian and Scandinavian renal transplant patients who had a point prevalence GSRS scores of 90% and 92%[4,5]

Upper gastrointestinal symptoms in the study subjects who scored GSRS>1 comprised mainly: abdominal pain - 47.6%, reflux - 54% and indigestion at 41.5%. In the Scandinavian study, their subjects had frequencies of: abdominal pain at 69%, reflux at 47% and indigestion at 83%, which was relatively higher than those of this study. These findings may be attributable to the time from kidney transplant in this study, where 23.7% were transplanted more than five years ago similar results to the Scandinavian population transplanted more than 6 years prior to study[4]. Importantly, however *Ponticelli et al.* reported comparable lower gastrointestinal symptoms in the Italian study group where frequency of constipation was 28.9% versus 19.6% in this study, but diarrhea at 22.8% versus to 24%.[5] This study population was comparable to the Italian population in terms of male predominance, at 56.6% versus 63.5%. However, the mean age of that we found in this study was 41.3±2.7years whereas 29±12years in the Italian study subjects was lower [5]. In contrast however Ekberg and colleagues demonstrated a higher proportion of lower GI symptoms GSRS >1,diarrhea was at 53% ,constipation at 56% whereas upper GI symptoms indigestion at 83% abdominal pain 28.8% and reflux 22.7% were comparable to the general population in the Scandinavian population that comprised of an older age group .[4]

These findings may be as a consequence of the non-selective gastrointestinal manifestations during the early post-transplant period which may be as a consequence of exposure to high dose steroids or as a continuum of symptomatology from chronic kidney disease [5]

Most patients were on a higher dose in the early transplant period, mainly Prednisone, to prevent rejection, but slowly tapered off over a year. The dose variation may over time have improved or worsened some gastrointestinal symptoms but this being a cross-sectional study it limited us to the information captured. Recall bias does affect one's ability to capture all symptoms as one experiences them. The GSRS and GIQLI are able to capture symptoms experienced in the last two weeks. [4,5]

Gastrointestinal symptom evaluation becomes important in this group both pre and post-transplant, because this can help one to identify symptoms and complications that may arise from both the drugs and opportunistic infections or that may affect the patient's compliance with medication. Variation or changes in symptomatology would help in decision-making as well. Serious complications leading to poor adherence with medications and potential for graft loss can be recognized earlier and measures to prevent loss can be actively implemented

Most patients reported mild symptoms in all categories. Severe symptoms were noted as acid regurgitation at 1%, hard stools at 1%, constipation at 1% and loose stools at 4%. The severity may have also been further masked in the acid regurgitation group as up to 7% of patients at the time of interview were on proton pump inhibitors. 50% of the populations at the time of study had been diagnosed to have kidney disease 5 years prior to interview and yet 35.5% transplanted only one year before the interview. This could notably contribute to the severity in gastrointestinal symptoms and the presence of symptoms post- transplant having been in a state of long standing uremia as well as the effects of the chronic disease state to the gastrointestinal system.[7,67] Other co-morbidities known to worsen or improve symptoms were not looked in this study, for example, Helicobacter Pylori infection, smoking status and upper gastrointestinal symptoms. In one study, it had been noted that GI symptoms were more prevalent in those who are unemployed as it was a psychological stressor and in any other stressful situations.[62,] In our study most of patients were in formal employment. Even though the numbers studied were small, it would effect on overall graft and patient function, loss of graft impacts largely on a patients confidence and the choice of treatment. Therefore these symptoms that are presented can easily be ignored as trivial but may be indirectly impacting on the graft function as well as the patient's overall HRQoL [4].

Loose stool was reported as severe in 4% of this study group whereas in the Italian study it was noted at 17%. In the Italian study three quarters of the patients were notably on MMF at doses of less than 1.5gm/day or lower, and in half of them, less than 1gm/day thus devoid of the GI effects of MMF which causes GI symptoms at doses of 2g/day or larger. In this study the preferred combination in all patients was with Mycophenolate sodium (Myfortic), an agent which has been shown in other studies to have less GI side effects[4,12,18]This finding does highlight the need to further evaluate the patients at consecutive visits to compare the severity of GI symptoms as well as establish drug-associated GI side effects.

The mean GSRS scores in the five syndrome groups were noted in diarrhea as 3.42, indigestion 4.29, constipation at 3.64, abdominal pain 3.18, reflux syndrome 2.29. In the study by *Ponticelli.et al,* they noted mean GSRS scores on the syndromes as; diarrhea 1.44±0.88, reflux 1.31±0.61, abdominal pain 1.49±0.72, constipation 1.49±0.67, indigestion 1.77±0.79.[5] The higher mean scores in each domain did highlight the burden of disease in this group, however no associations could be evaluated with immunosuppressive drug combinations which were the only medications captured in this study. Use of other drugs, both over the counter and prescribed drugs to relieve gastrointestinal symptoms were not documented.

The presence of oral ulcers at 7% did highlight manifestation of both immunosuppression or immunosuppressant drug therapy, though in a relatively small proportion. This made it difficult to ascertain the cause of the oral ulcers in our study population, but some known causes are CMV disease and mycophenolate without prednisone combination.[58] Sirolimus emulsion use has been attributed to presence of oral ulcers, but only one participant in the study population was on everolimus.[68]

The immunosuppressive drug combination most commonly used in our study subjects were prednisone, enteric coated mycophenolate sodium, tacrolimus at 49%, followed closely at 41% by prednisone, enteric coated mycophenolate sodium and cyclosporine combination. The severe lower gastrointestinal symptoms noted as loose stools cannot be attributed to any one drug as this was a cross-sectional study. Though other studies have shown that Mycophenolate causes more diarrhea than Azathioprine and Tacrolimus more than cyclosporine.[11,14] No conclusion could be made as this was based on one interview and recall bias as well as other drugs or food choices could attribute to these findings. In this study such factors were not investigated.

The most common drug combinations of mycophenolate sodium, tacrolimus and prednisone and mycophenolate sodium, cyclosporine and prednisone are widely used drug combinations with good effects on graft functioning and maintenance.(4,5) In this study we were not powered to compare drug combinations to presence of gastrointestinal symptoms or impact on gastrointestinal quality of life.

Azathioprine was not prescribed in the transplant patients in this study, further reflecting on the good practice of drug choices that were followed to maintain graft function. Azathioprine though is devoid of GI symptoms of MMF but is associated with graft loss and has to be

handled carefuly.Several studies done previously had shown that patients even before being investigated as to the cause of their GI symptoms were changed to other immunosuppressive regimens with loss of graft. Mycophenolate mofetil can be dose adjusted to reduce the GI symptom and prevent graft loss as has been noted in two studies. [12,18] However care should be exercised in adjusting immunosuppressant medication to balance the adverse events on the gastrointestinal tract with optimal immunosuppression.

The HRQoL overall scores for GI symptoms 1.89, emotional function 0.83 and social function 1.65 were low, i.e. GIQLI < 4, representing a poor QoL in this study population. The GI symptom seems to have serious burden to the patients functioning both socially and emotionally. The need to identify these symptoms as they present is important and helps in early identification of what may be considered trivial but may contributing to negatively affect both the patient directly and transplanted organ functioning indirectly. Elsewhere in the Italian study group presence of any GI symptoms whether patient or physician reported showed statistical significance and affected HRQoL with an overall score GSRS >4, where the domains most affected were physical function and bodily function[5]

Post-transplant patients with major troublesome GI symptoms have been found to be affected in terms of regularity and choice of food/diet. Catabolic states impair graft functioning.[66] Graft function remains critical, yet severe GI symptoms impair one's ability to comply to drugs. Co-administration of cyclosporine with mycophenolate does reduce the body's exposure to mycophenolate mofetil. [30, 32] this observation emphasizes the balance of drug interactions, the gastrointestinal effects and the all-important immunosuppression for graft survival. Reduction in mycophenolate mofetil dose and discontinuation has reduced graft function by more than 50%. [61]

Drug compliance is also affected with the presence of GI symptoms and increases the likelihood of graft rejection [67] In this study in the GIQLI subscale ,medical treatment mean score was 6.14 indicative of good HRQol in this domain. Other than just taking medical treatment, pill burden is also attributed to the presence of GI symptoms than to the individual drugs itself . Drug compliance is also based on how the patient feels ,the relationship with his physician and patients perspective with a higher social functioning had better drug compliance[69],in this study social functioning was impaired score of 1.65 (GIQLI score <4)indicative of worse symptoms.

GI symptoms are under-rated by physicians and most clinic interview are focused on the graft function, overall functioning are not detailed enough.[5] Incorporation of the GSRS as a standard care and practice tool can improve and facilitate communication between patients and physicians. This in turn helps patients to benefit holistically. Gastrointestinal conditions affect drug compliance and using tailored regimens does benefit and helps in maximizing compliance and avoiding graft rejection. [70]

In this cross-sectional survey using the GSRS as a tool did add some value in terms of sensitization to the significance of and standardization in measurements of the GI symptoms in these study patients. .However, the tools were unable to distinguish GI symptoms due to or attributable to immunosuppressive regimens that maximizes patient's quality of life.

5.1 Conclusion
In this study it was noted that gastrointestinal symptoms are prevalent and were affecting the HRQoL in emotional, physical, social functions this is in corroboration with studies done in Italy and Scandinavain counrties. Severe gastroinstestinal symptoms may impact ones ability to function wholly after renal transplant and impacts negatively in all domains related to HRQol. Patient care should aim to closely monitor these symptoms and manage these symptoms effectively to improve HRQol in these patients.

5.2 Limitations
The limitations in this study was that it was a cross-sectional study and both gastrointestinal symptoms and quality of life are continuously varying in nature and are influenced by several factors such as immunosuppressive drugs ,co-morbid conditions ,the burden of disease itself to the patient and family as well as the immunosuppressive state.

Recall bias may have influenced ones ability to report the symptoms presence and severity, possibly also overlook it as trivial and not of concern at the time of interview having a significance to patient care and physician approach to patient care.

Presence of gastrointestinal symptoms prior to transplant was not documented nor could symptoms prior to the study, whether they are due to disease state prior or immunosuppressant's not be established. Inclusion may have added benefit.

5.3 Recommendations.

The inclusion of the GSRS and GIQLI tools for renal transplant patients in the routine clinics as a standard of care and practice tool   .

 A longitudinal study is also recommended to determine relationship between GI symptoms over time with nutritional status, adherence to drugs and overall outcomes.

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APPENDICES

APPENDIX I: INFORMATION SHEET

Research Title: The Prevalence of Gastrointestinal Symptoms and Associated Quality of Life in Renal Transplant Patients at Kenyatta National Hospital

You are being invited to take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the purpose of the study?

Dr. Rupal Maru who is currently studying for a Masters degree in Medicine (Internal Medicine) at University of Nairobi is carrying out a survey to assess how common the problems of gastro-intestinal system are in patients who have received a kidney transplant and are followed up at Kenyatta Hospital Renal Clinic. This survey also seeks to understand how these problems affect the quality of their life.

Why have I been invited to take part?

We are asking all adults and children above 15 years who have received a kidney transplant and are on regular treatment at Kenyatta Hospital to participate in the study. We are also asking healthy adults who are not sick to participate to enable us compare the results.

Do I have to take part?

It is up to you to decide whether or not to take part, taking part is voluntary. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. You will still receive all treatment that you should get even without participating in the study.

What would I have to do?

If you decide to take part, the survey will take approximately 60 minutes to complete. You will be given two blank questionnaires and you will be asked to complete these.

Confidentiality

All the information that is collected will be anonymous and kept strictly confidential. Your personal data will be held in accordance with the applicable laws of the land.

What happens to the information that is collected?

All details that can identify you will be removed before storing the data. The data will then be analysed to help us build an understanding of public awareness of the burden of gastrointestinal symptoms in patients with kidney transplant and help the doctors at Kenyatta Hospital improve on the treatment of these patients. The data will be destroyed after successful completion of her studies.

Thank you for taking the time to read this information sheet.

CONSENT FORM

Please tick the appropriate boxes

I have read and understood the project
information sheet.   ☐

I have been given the opportunity to ask
questions about the project.   ☐

I agree to take part in the project. Taking part   ☐
in the project will include completing a
survey/being interviewed.

I understand that my taking part is voluntary;   ☐
I can withdraw from the study at any time
and I will not be asked any questions about
why I no longer want to take part.

I understand my personal details such as   ☐
phone number and address will not be
revealed to people outside the project.

I understand that my words may be quoted in   ☐
publications, reports, web pages, and other
research outputs but my name will not be
used unless I requested it above.

I agree for the data I provide to be archived at   ☐

the Investigator

I understand that other researchers will have ☐
access to this data only if they agree to
preserve the confidentiality of that data and
if they agree to the terms I have specified in
this form.

I understand that other researchers may use ☐
my words in publications, reports, web
pages, and other research outputs according
to the terms I have specified in this form.

Signing this consent form indicates that you have read this consent form (or have had it read
to you), that your questions have been answered to your satisfaction, and that you voluntarily
agree to participate in this research study. You will receive a copy of this signed consent
form.

If you agree to participate in this study, please sign your name below

_____

Participant's Signature

Date:_____

_____

Investigator or Designee Obtaining Consent

Signature

Date:_____

_____

Witness Signature

Date:_____

For further information please contact:

Dr. Rupal Maru   Kenyatta National Hospital/UoN Ethics Committee

 Tel: +254722342236   OR   P.O Box 20723 - 00202

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APPENDIX II: INFORMATION SHEET FOR PARENTS/GUARDIAN

Research Title: The Prevalence of Gastrointestinal Symptoms and Associated Quality of Life in Renal Transplant Patients at Kenyatta National Hospital.

Your child is being invited to take part in a research study. Before you decide whether or not to allow him/her to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the purpose of the study?

Dr. Rupal Maru who is currently studying at University of Nairobi is carrying out a survey to assess how common problems of the digestive system are in patients who have had a kidney transplant. The results will help doctors at Kenyatta Hospital improve treatment policies for these patients.

Why is my child invited to take part?

We are asking children who are 15 years and above who have had a kidney transplant to take part in the study. Children under the legal age of 18 years will require the consent of their legal guardians or parents to participate.

Does my child have to take part?

It is up to you to decide whether or not your child will take part, taking part is voluntary. If you do decide your child to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw him/her at any time and without giving a reason. He will not be refused treatment because you decide not to participate.

What would I have to do?

If you decide to take part, the survey will take approximately 60 minutes to complete. Your child will be asked several questions by use of 2 questionnaires. You may assist him/her in completing the questionnaires.

Confidentiality

All the information that is collected will be anonymous and kept strictly confidential. Your personal data will be held in accordance with the applicable laws of the land.

What happens to the information that is collected?

All details that can identify you will be removed before storing the data. The data will be destroyed after successful completion of her studies. The results will help doctors at Kenyatta Hospital improve treatment policies for these patients.

Thank you for taking the time to read this information sheet.

CONSENT FORM

Please tick the appropriate boxes

I have read and understood the project
information sheet.   ☐

I have been given the opportunity to ask
questions about the project.   ☐

I agree to my child taking part in the project.   ☐
Taking part in the project will include
completing a survey/being interviewed.

I understand that my child's taking part is   ☐
voluntary; I can withdraw her from the study
at any time and I will not be asked any
questions about why I no longer want her to
take part.

I understand my child's personal details such   ☐
as phone number and address will not be
revealed to people outside the project.

I understand that my child's words may be   ☐
quoted in publications, reports, web pages,
and other research outputs but her name will
not be used unless I requested it above.

I agree for the data I provide to be archived at the Investigator ☐

I understand that other researchers will have access to this data only if they agree to preserve the confidentiality of that data and if they agree to the terms I have specified in this form. ☐

I understand that other researchers may use my words in publications, reports, web pages, and other research outputs according to the terms I have specified in this form. ☐

Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree for your child to participate in this research study. You will receive a copy of this signed consent form.

If you agree to your child participating in this study, please sign your name below.

_____ _____

Participant's Signature   Signature of Parent/Guardian

Date:_____ Relationship:_____

Date:_____

_____ _____

Investigator or Designee Obtaining Consent   Signature of Parent/Guardian #2
Signature
                                                Relationship:_____

Date:_____ Date:_____

_____

Witness Signature

Date:_____

For further information please contact:

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APPENDIX III:RESEARCH ASSENT FORM

Protocol Title: The Prevalence of Gastrointestinal Symptoms and Associated Quality of Life in Renal Transplant Patients at Kenyatta National Hospital.

Principal Investigator: Dr. Rupal Maru

Phone: 0722342236

Email: rupalmaru@hotmail.com

We want to tell you about a research study we are doing. A research study is a way to learn information about something. We would like to find out more about how common problems of the digestive tract are and how they affect the patient's life. You are being asked to join the study because you are within the age group we want to know about and have had a kidney transplant.

If you agree to join this study, you will be asked to provide some information about yourself by use of a form. Some of the questions may need you to give private information about yourself. Your parent may assist you in answering some questions if you wish.

It will take about 60 minutes to answer all questions. Some of the questions may be uncomfortable to answer.

We do not know if you will benefit directly by being in this study. We may learn something that will help other children with kidney transplant some day to improve on their treatment.

You do not have to join this study. It is up to you. You can say okay now, and you can change your mind later. All you have to do is tell us. No one will be mad at you if you change your mind.

Anything we learn about you from this study will be kept as secret as possible.

Before you say yes to be in this study, we will answer any questions you have.

If you want to be in this study, please sign your name. You will get a copy of this form to keep for yourself.

_____   _____

(Sign your name here)   **(Date)**

_____   _____

(Investigator's sign/name)   **(Date)**

APPENDIX IV: QUESTIONNAIRE

Study Title: The Prevalence of Gastrointestinal Symptoms and Associated Quality of Life in Renal Transplant Patients at Kenyatta National Hospital.

Study ID No ☐☐☐

SECTION I: DEMOGRAPHICS

Instructions to complete: Please tick the relevant box to indicate your answer for the question.

1. What is your age?　　　Years ☐　　　　　prefer not to say ☐

2. What is your gender?　Male ☐　　　　Female ☐

3. What is your marital status?

Single/never married	Married/living with partner	Married separated	Divorced	Widowed	Civil partnership	Prefer not to say
☐	☐	☐	☐	☐	☐	☐

4. What is the highest level of education qualification you have obtained?

☐	Degree or higher degree	☐	O Level or GCSE equivalent (Grade A - C)
☐	Higher education qualification below degree level	☐	O Level or GCSE (Grade D - G)
☐	A-levels or higher	☐	No formal qualifications
☐	Primary School	☐	Other ………………………….
☐	Still studying	☐	Prefer not to say

4. Are you currently:

☐   Employed full-time   ☐   Full-time homemaker

☐   Employed part-time   ☐   Retired

☐   Unemployed   ☐   Still studying

☐   Self-employed   ☐   Disabled or too ill to work

☐   Prefer not to say

5. When were you diagnosed with advanced kidney disease?

Less than 1 year ago ☐   1- 2 years ago ☐

2-5 years ago ☐   more than 5years ☐

6. When did you have the kidney transplant done?

Less than 1 year ago ☐   1-2 years ago ☐

2-5 years ago ☐   more than 5years ☐

7. a) Are you currently taking any drugs to suppress immunity?

Yes ☐   No ☐

7. b) If Yes, please indicate the names or number of drugs you are taking below.

1..   Number of drugs   ☐☐

2..

3..

61

4..

5…………………………………

6…………………………………….

7…………………………………

8…………………………………..

9…………………………………..

10……………………………………..

8. Except for kidneys disease, do you have any other major condition?

Yes   ☐   No   ☐

If yes, which one?   ………………………………………………………….

9.Do you any particular complaints other than what you have asked?

Yes   ☐   No   ☐

If yes, please specify………………………….

10.Do you have any of these symptoms

☐ oral ulcers   Yes   ☐   No   ☐

☐ odynophagia   Yes   ☐   No   ☐

☐ dysphagia   Yes   ☐   No   ☐

SECTION II: GASTROINTESTINAL SYMPTOM RATING SCALE (GSRS)

This is a rating scale for gastrointestinal symptoms in patients with kidney transplant. **Circle the number** which best represents the current severity of the symptom you are experiencing.

1. **Abdominal pains**. Representing subjectively experienced bodily discomfort, aches and pains.

The type of pain may be classified according to the patient's description of the appearance and quality of the pain as epigastric (upper abdominal pain), on the basis of typical location, association with acid-related symptoms, and relief of pain by food or antacids; as colicky when occurring in bouts, usually with a high intensity, and located in the lower abdomen; and as dull when continuous, often for several hours, with moderate intensity.

Rate the symptom according to intensity, frequency, duration, request for relief, and impact on social performance.

0 No or transient pain

1 Occasional aches and pains interfering with some social activities

2 Prolonged and troublesome aches and pains causing requests for relief and interfering with many social activities

3 Severe or crippling pains with impact on all social activities

2. **Heartburn**. Representing retro-sternal discomfort or burning sensations. Rate the symptom according to intensity, frequency, duration, and request for relief.

0 No or transient heartburn

1 Occasional discomfort of short duration

2 Frequent episodes of prolonged discomfort; requests for relief

3 Continuous discomfort with only transient relief by antacids

3. Acid regurgitation. Representing sudden regurgitation of acid gastric (stomach) content. Rate the symptom according to intensity, frequency, and request for relief.

0 No or transient regurgitation

1 Occasional troublesome regurgitation

2 Regurgitation once or twice a day; requests for relief

3 Regurgitation several times a day; only transient and insignificant relief by antacids

4. Sucking sensations in the epigastrium. Representing a sucking sensation in the epigastrium with relief by food or antacids. If food or antacids are not available, the sucking sensations progress to ache, and pains. Rate the symptom according to intensity, frequency, duration, and request for relief.

0 No or transient sucking sensation

1 Occasional discomfort of short duration; no requests for food or antacids between meals

2 Frequent episodes of prolonged discomfort, requests for food and antacids between meals

3 Continuous discomfort; frequent requests for food or antacids between meals

5. Nausea and vomiting. Representing nausea which may increase to vomiting. Rate the symptom according to intensity, frequency, and duration.

0 No nausea

1 Occasional episodes of short duration

2 Frequent and prolonged nausea; no vomiting

3 Continuous nausea; frequent vomiting

6. Borborygmus. Representing reports of abdominal rumbling. Rate the symptom according to intensity, frequency, duration, and impact on social performance

0 No or transient borborygmus

1 Occasional troublesome borborygmus of short duration

2 Frequent and prolonged episodes which can be mastered by moving without impairing social performance

3 Continuous borborygmus severely interfering with social performance

7. Abdominal distension. Representing bloating with abdominal gas. Rate the symptom according to intensity, frequency, duration, and impact on social performance.

0 No or transient distension

1 Occasional discomfort of short duration

2 Frequent and prolonged episodes which can be mastered by adjusting the clothing

3 Continuous discomfort seriously interfering with social performance

8. Eructation. Representing reports of belching. Rate the symptom according to intensity, frequency, and impact on social performance.

0 No or transient eructation

1 Occasional troublesome eructation

2 Frequent episodes interfering with some social activities

3 Frequent episodes seriously interfering with social performance

9. Increased flatus. Representing reports of excessive wind. Rate the symptom according to intensity, frequency, duration, and impact on social performance

0 No increased flatus

1 Occasional discomfort of short duration

2 Frequent and prolonged episodes interfering with some social activities

3 Frequent episodes seriously interfering with social performance

10. Decreased passage of stools. Representing reported reduced defecation. Rate the symptom according to frequency. Distinguish from consistency.

0 Once a day

1 Every third day

2 Every fifth day

3 Every seventh day or less frequently

11. Increased passage of stools. Representing reported increased defecation. Rate the symptom according to frequency. Distinguish from consistency.

0 Once a day

1 Three times a day

2 Five times a day

3 Seven times a day or more frequently

12. Loose stools. Representing reported loose stools. Rate the symptom according to consistency independent of frequency and feelings of incomplete evacuation.

0 Normal consistency

1 Somewhat loose

2 Runny

3 Watery

13. Hard Stools. Representing reported hard stools. Rate the symptom according to consistency independent of frequency and feelings of incomplete evacuation.

0 Normal consistency

1 Somewhat hard

2 Hard

3 Hard and fragmented, sometimes in combination with diarrhoea

14. Urgent need for defecation. Representing reports of urgent need for defecation, feelings of incomplete control, and inability to control defecation. Rate the symptom according to intensity, frequency, and impact on social performance.

0 Normal control

1 Occasional feelings of urgent need for defecation

2 Frequent feelings of urgent need for defecation with sudden need for a toilet interfering with social performance

3 Inability to control defecation

15. Feeling of incomplete evacuation. Representing reports of defecation with straining and a feeling of incomplete evacuation of stools. Rate the symptom according to intensity and frequency.

0 Feeling of complete evacuation without straining

1 Defecation somewhat difficult; occasional feelings of incomplete evacuation

2 Defecation definitely difficult; often feelings of incomplete evacuation

3 Defecation extremely difficult; regular feelings of incomplete evacuation

KISWAHILI TRANSLATION OF THE GSRS

Kiambatisho M

Gastrointestinal Symptom Rating Scale (GSRS) (Mizani ya Kukadilia dalili Ugonjwa wa gesi ya utumbo)

Jina: _____

Mizani ya kukadilia dalili za gesi ya tumbo kwa wagonjwa walio na dalili nyeti za kutambulika za utumbona ugonjwa wa banguzi (vidonda vya tumbo). Weka mduara kwenye nambari ambayo inawakilisha bora zaidi ukali wa sasa wa dalili.

1. **Maumivu ya tumbo.** Inayowakilisha vyema zaidi usumbufu wa mwili unaihisiwa, kuumwa na

   maumivu.

Aina ya maumivu inaweza kuwengwa katika viwango kulingana na maelezo ya mgonjwa ya kuonekana na ukali wa maumivu kama epigastric, kwa misingi ya kawaida ya eneo, kwa uhusiano na dalili za gesi ya tumbo, na kutulizwa kwa maumivu kutokamana na chakula au dawa za kupunguza gesi ya tumbo; kama maumivu makali ya tumbo ya msimu fulani; kwa kawaida kwa ukali haswa katika sehemu za chini za tumbo; na wakati mwingine ni uchungu wastani mara nyingi masaa kadhaa kwa kiwango cha wastani.

Chagua Kiwango cha kulingana na ukali, marudiorudio, muda, ombi kwa ajili ya misaada, na athari katika masuala ya utatendaji kazi kijamii

0 Hakuna au muda mfupi wa maumivu

1 Uchungu wa hapa na pale na maumivu yayosababisha kuathirika kwa baadhi ya shughuli za kijamii

2 kuumwa kunako tatisa kwa muda mrefu na maumivu yanayosababisa kilio cha msaada nakuathiri shughuli ya kawaida za kijamii

3 Maumivu makali au yanayolemaza na kuwa na athari juu ya shughuli zote za kijamii

2. Heartburn. Kiungulia:

Inayowakilisha usumbufu wa ndani au kijihisi kuchomeka. kadilia kulingana na kiwango cha ukali, marudiorudio , muda, na kuomba kwa ajili ya misaada.

0 Hakuna au muda mfupi wa kiungulia

1 usumbufu wa hapa na pale wa muda mfupi

2 Matukio ya mara kwa mara ya usumbufu wa muda mrefu; maombi kwa ajili ya misaada

3 usumbufu unao tatisa kwa muda mrefu na kupungua maumivu kidogo kwa muda kutokana na dawa za kupunguza gesi

3. **kutabika Asidi:** inayowakilisha kucheua; kutabika ghafla asidi ya tumbo. kadilia kulingana na kiwango cha ukali, marudiorudio , muda, na kuomba kwa ajili ya misaada

1.Hakuna au kutabika gesi kwa nadira

2.Kutabika gesi kunakotatisa ila kwa hapa na pale, sio sana

3.Kutabika gesi mara moja au mbili kwa siku; maombi kwa ajili ya misaada

4.Kutabika gesi mara kadaa kwa siku moja; kunakopunguka kidogo tu kwa msaada wa tembe za kupunguza ukali wa asidi

4.Hisia za Msisimuko, za kufyonza kwenye sehemu ya kati ya juu ya tumbo:

Inayowakiliza hisia za msisimko za kufyonza au kunyonya kwenye sehemu ya kati ya juu ya tumbo, inayopunguzwa na chakula au dawa za dhidi ya asidi. Kama hakuna chakula au dawa kunakuwa na kuwazwa au hisia za kunyonywa zinaendelea hadi kuumwa, na kuwa na maumivu. Kadilia kulingana na kiwango cha uchungu, muda, marudiorudio, na kuombwa kwa msaada.

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0 Hakuna au hisia chache za msisimko zinazokunyonya

1 Usumbufu wa hapa na pale wa muda mfupi; hakuna itaji ya chakula wala dawa za kutuliza makali

  ya asidi wakati wa kula

2. Usumbufu wa muda mrefu, hamu ya chakula mara kwa mara na hitaji la dawa za kupunguza makali ya asidi unapo kula.

3.Usumbufu usio koma, hamu ya chakula mara kwa mara na hitaji la dawa za kupunguza makali ya asidi unapo kula.

5.Kichefuchefu na kutapika. Inawakilisha kichefuchefu ambacho kinaweza kuongeza hadi kufikia kutapika. kadilia kulingana na ukali,marudiorudio na muda.

0 Hakuna kichefuchefu
1 matukio ya muda mfupi ya mara moja moja
2 Kichefuchefu cha mara kwa mara na cha muda mrefu ; hakuna kutapika
3 kichefuchefu cha kudumu muda mrefu Kuendelea; kutapika mara kwa mara

6. **Tumbo kutoa sauti ya ukelele**. Inawakilisha taarifa za ukelele tumboni. kadilia kulingana na ukubwa,
marudiorudio, muda, na athari juu ya utendaji katika jamii

 0 Hakuna au ukelele tumboni kwa muda mfupi
1 milio ya yenye kutatisa ya hapa na pale ya tumbo ila kwa muda mfupi ara

2 matukio ya kudumu ya mara kwa mara ambayo yanaweza kabiliwa na kuendelea bila kutatisa au kuharibika kwa shughuli katika jamii
3 makalele ya tumbo yanayoendelea kwa muda mrefu yanayoweza kutatisa utendaji kazi katika jami

7. uvimbe wa tumbo. Inawakilisha kufura na gesi tumboni. kadilia kulingana na kiwango, marudiorudio, muda, na athari juu ya utendaji ya kijamii

0 Hakuna au kufura kwa wa tumbo kidogo

1 usumbufu wa hapa na pale na wa muda mfupi

2 milio ya mara kwa mara ya tumbo na ya muda mrefu matukio ambayo yanaweza

kukabiliwa kwa kurekebisha mavazi

3 Usumbufu wa kudumu unaoweza kuathiri umakini na utendaji katika jamii

8. **Eructation.** (**kuchafya gesi kupitia mdomoni**) Inawakilisha taarifa ya kuchafya. kadilia
kulingana na ukali,marudiorudio na athari juu ya utendaji kazi katika jamii

0 Hakuna au kuchafya gesi ya tumboni kupitia mdomoni kwa muda mfupi

1 matatizo ya kuchafya gesi mara moja moja

2 matukio ya mara kwa mara yanayoathiri na baadhi ya shughuli za kijamii

3 matukio ya mara kwa mara yanayoathiri mno umakini na utendaji kazi katika jamii

9. Kuongezeka kwa kunyamba. Inawakilisha taarifa ya upepo mwingi. Kadilia kulingana na
ukubwa,

marudiorudio, muda, na athari juu ya utendaji kazi ya kijamii

 0 Hakuna kuongezeka kunyamba

 1. usumbufu wa nadhira na wa muda mfupi

 2. Matukio ya mara kwa mara na ya muda mrefu yanayoingilia na kuathiri baadhi ya
shughuli za

   kijamii

 3. Matukio ya mara kwa mara yanayoingilia na kuathiri mno umakini na utendaji shughuli
za

   kawaida katika kijamii

10. Kupungua kwa kuendesha . Inawakilisha taarifa kupunguka kwa hamu ya kutaka kujisaidia haja kubwa. Kadilia kulingana na

marudiorudio Tofautisha na uthabiti au kawaida

0 Mara moja kwa siku

1 Kila baada ya siku tatu

2 Kila baada ya siku tano

3 Kila baada ya siku ya saba au kwa uchache mara moja moja

11. **Kuongezeka kwa kuendesha** . Inawakilisha taarifa za kuongezeka kwa haja kubwa. Kadilia kulingana

na marudiorudio. Tofautisha na uthabiti au kawaida

0 Mara moja kwa siku

1 mara tatu kwa siku

2 Mara Tano kwa siku

3 mara saba kwa siku au mara kwa mara

12. Kinyesi legevu au laini.. Inawakilisha ripoti au taarifa za kinyesi laini au legevu. Kadiria kulingana na hali ya kawaida bila ya kuzingatia marudiorudio na hisia za kutokamilika uokoaji.

0 Msimamo wa Kawaida

1 legevu au laini kwa kiasi fulani

2 inayokimbia

3 majimaji

13. Kinyesi kigumu.. Inawakilisha taarifa za Kinyesi kigumu. Kadiria kulingana na hali ya kawaida bila kuzingatia ni mara ngapi inatokea na hisia za kutokamilika kwa uokoaji.

0 Msimamo au hali ya Kawaida

1 Kwa kiasi fulani ngumu

2 ngumu

3 ngumu na ya kugawanyika vipande vipande, wakati mwingine pamoja na kuharisha/kuendesha

14. Haja ya haraka kwa ajili ya kujisaidia haja kubwa. Inawakilisha ripoti za haja ya haraka ya kuenda haja kubwa, hisia kutokudhibiti au kukosa uwezo wa kudhibiti kwenda haja kubwa. Kadiria kulingana na ukubwa wa haja, marudiorudio, na athari juu ya utendaji shughuli za kijamii.

0 kudhibiti kwa Kawaida

1 Hisia za hapa na pale za haja ya haraka kuenda haja kubwa

2 Hisia za mara kwa mara za kuenda haraka kwa haja kubwa na haja za ghafla kwenda choo na

   ili linaathiri utendaji shughuli za kijamii

3 Kutokuwa na uwezo wa kudhibiti haja kubwa

15. Hisia ya kutokamilika kutoa haja kubwa. Inawakilisha ripoti za haja kubwa na kujikaza na
hisia ya kutokamilika ya kutoa kinyesi. Kadiria kulingana na ukubwa au ukali na marudiorudio.

0 Hisia za kutokwa kamili haja bila ya kujikaza au kuhangaika

1 ugumu kutoa Haja Kubwa ; hisia za hapa na pale za kutokamilika kutoa haja

2 kwenda Haja Kubwa dhahiri ni ngumu; mara nyingi hisia za kutokamilika kutokwa na haja

3 kwenda Haja Kubwa kuwa vigumu sana; hisia za mara kwa mara za kutokamilika kutokwa na haja

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SECTION III: GASTROINTESTINAL SYMPTOMS QUALITY OF LIFE INDEX (GIQLI)

Instructions: Please circle the answer that best describes your symptom.

1. During the last 15 days, you have had a stomach ache?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

2. During the last 15 days, you had the feeling of having bloated stomach

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

3. During the last 15 days, you had the feeling of having a lot of gas in the stomach

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

4. During the last 15 days, have you been bothered the issue of "winds"

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

5. During the last 15 days, have you been bothered by belching or referrals

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

6. During the 15 days were you embarrassed by noises "gurgling" in the belly?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

7. During the last 15 days, you've been bothered by frequent bowel movements

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

8. During the last 15 days, you ate with pleasure and appetite?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

9. Because of your illness, you are required to remove certain foods?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

10. During the last 15 days, you have been able to overcome daily problems?

 Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

11. During the last 15 days, how many times your illness made you sad?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

12. During the last 15 days, how many times have you been anxious because of your illness?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

13. During the last 15 days, how many times have you felt joy of living?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

14. During the last 15 days, how many times have you been frustrated because of your illness?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

15. During the last 15 days, how often did you felt tired?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

16. During the last 15 days, how many times have you been painful?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

17. During the last week, did you awake during the night?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

18. Since you are sick, have you been chagrined changes in your appearance?

For a very large part (0),   for an important part (1),   a little (2),   a few (3),   not at all (4)

19. To what extent is that it has reduced your requirement physics in general?

Enormously (0),   a lot (1),   some (2),   a little (3),   not at all (4)

20. Because of your health, you have lost your endurance?

For a very large part (0), for an important part (1),   a little (2), a few (3),   not at all (4)

21. By your illness you feel the loss of your tone?

Major (0),   moderate (1),   small (2),   insignificant (3),   none, you feel well (4)

22. During the last 15 days, how many times have you been able to do your usual activities (work, school, cleaning, etc.) ?

Never (0),   rarely (1),   sometimes (2),   most of the time (3),   always (4)

23. During the last 15 days, you have been able to attend your usual leisure or new activities

Never (0),   rarely (1),   sometimes (2),   most of the time (3),   always (4)

24. During the last 15 days, have you been bothered by medical treatment?

Enormously (0),   a lot (1),   some (2),   a little (3),   not at all (4)

25. To what extent your illness she disrupts your relationships with others (family or friends)?

For a very large part (0),   for an important part   (1),   a little (2),   a few (3), not at all (4)

26. To what extent has your illness harmed your sex life?

For a very large part (0),   for an important part (1),   a little (2),   a few (3), not at all (4)

27. During the last 15 days, how many times have you been inconvenienced by liquid or food in the mouth (regurgitation)?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

28. During the last 15 days, have you felt forced to decrease the speed with which you eat?

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

29. During the last 15 days, you had problems to swallow

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

30. During the last 15 days, you have felt the need urgent need to defecate

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

31. During the last 15 days, you have been inconvenienced by Diarrhoea

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

32. During the last 15 days, you have been inconvenienced by constipation

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

33. During the last 15 days, you have been inconvenienced by nausea

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

34. During the last 15 days, you were worried by presence of blood in stool

Always (0),   most of the time (1),   sometimes (2),   rarely (3),   never (4)

35. During the last 15 days, you have been inconvenienced by burn or acidity back in the chest

Always (0), most of the time (1), sometimes (2), rarely (3), never (4)
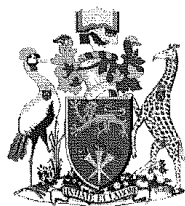
36. During the last 15 days, you have been inconvenienced by incontinence for stool?

Always (0), most of the time (1), sometimes (2), rarely (3), never (4)

END

Thank you for taking your time to participate in this study.

APPENDIX V:KNH/UON-ERC LETTER OF APPROVAL

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Ref: KNH-ERC/A/300

7th July 2015

Dr. Rupal Mahindra Maru
H58/79216/12
Dept.of Clinical Medicine & Therapeutics
School of Medicine
University of Nairobi

Dear Dr. Maru

Research proposal – Gastrointestinal symptoms and associated quality of life in renal transplant patients: a descriptive cross sectional study (P349/05/2015)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 7th July 2015 6th July 2016.
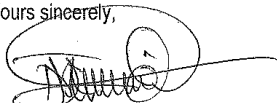
This approval is subject to compliance with the following requirements:

    a)   Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
    b)   All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
    c)   Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
    d)   Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
    e)   Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
    f)   Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
    g)   Submission of an *executive summary* report within 90 days upon completion of the study
        This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

Protect to discover

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY,   KNH/UON-ERC

c.c.   The Principal, College of Health Sciences, UoN
        The Deputy Director CS, KNH
        The Chair, KNH/UoN-ERC
        The Assistant Director, Health Information, KNH
        The Dean, School of Medicine, UoN
        The Chairman, Dept.of Clinical Medicine & Therapeutics,UoN
        Supervisors: Prof. Elly Ogutu, Prof. Joshua Kayima, Dr.A.J.O. Were, Dr. Edna Kamau

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