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CLINICAL RESEARCH

Patient-Reported Gastrointestinal Symptoms and the Association With Quality of Life Following Kidney Transplantation

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Background: There has been limited study of the prevalence of gastrointestinal symptoms and their impact on the quality of life (QOL) in kidney transplant recipients. The aim of this study was to examine the prevalence and predictors of gastrointestinal symptoms and the association with QOL in kidney transplant recipients.

Methods: All chronic kidney transplant recipients at the Princess Alexandra Hospital were provided with 3 questionnaires, the Gastrointestinal Quality of Life Index (GIQLI), the Gastrointestinal Symptoms Rating Scale (GSRS), and Structured Assessment of Gastrointestinal Symptoms (SAGIS) scale, to ascertain QOL impairment and to screen gastrointestinal symptom severity. Linear regression was used to determine the predictors of gastrointestinal QOL and gastrointestinal symptom severity.

Results: Of the 343 participants, the median age was 47 (interquartile range [IQR] 36–55) years, 58% were men, 79% were white, 39% had chronic glomerulonephritis, 83% had received their first graft, and median time since transplant was 6.3 (IQR 1.8–13.1) years. Using GSRS, 88% of participants reported at least 1 gastrointestinal symptom, most commonly indigestion (57%) and diarrhea (54%). Using GIQLI, 42% and 38% of participants reported mild and moderate QOL impairment, respectively. Gastrointestinal symptoms were predicted by female sex (coefficient −0.11, 95% CI −0.21 to −0.02) and mycophenolate (coefficient 0.0001, 95% CI 0.0001 to 0.0002), and were associated with poorer QOL (coefficient −0.38, 95% CI −0.45 to −0.30). Similar findings were observed using SAGIS for gastrointestinal symptoms.

Conclusions: Gastrointestinal symptoms are frequent in kidney transplant recipients, particularly in women and those receiving mycophenolate, and are strongly associated with poorer QOL.

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Transplantation is the optimal form of replacement therapy for most patients with kidney failure[1]; however, this treatment may be complicated by gastrointestinal adverse effects, such as reflux and diarrhea, which may be due to a number of factors, including infection, altered gut microbiota, and immunosuppressive agents. In a multicenter cross-sectional study involving 1788 solid organ transplant recipients, of whom 1132 were kidney transplant recipients, 53% reported gastrointestinal symptoms, particularly diarrhea (53%).[2] Another retrospective single-center cross-sectional study involving 1445 kidney transplant recipients undertaken in Finland between 1990 and 1999 reported that 10% experienced a severe gastrointestinal complication (defined as gastroduodenal ulceration,

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perforation, infection or malignancy, pancreatitis, or cholecystitis) over a median follow-up time of 6.2 years.[3] Ten percent of these gastrointestinal complications were fatal. Furthermore, in a single-center, open-label, non-randomized, prospective study involving 236 kidney transplant recipients, gastrointestinal symptoms were prevalent, with abdominal pain (30%), reflux (37%), indigestion (50%), constipation (58%), and diarrhea (33%) commonly reported.[4]

Although the occurrence of gastrointestinal symptoms in kidney transplant recipients and their association with immunosuppressive therapies are well-documented,[2–4] little is known about the impact these symptoms have on patients' QOL. The few reports that are available[5,6] have been limited by small sample sizes, heterogeneity, use of different assessment instruments, and underrepresentation of centers from the Asia-Pacific region.

The aim of this study was therefore to evaluate the prevalence and predictors of gastrointestinal symptoms in kidney transplant recipients and the association of these symptoms with QOL using 3 separate, validated instruments of gastrointestinal symptoms and QOL.

METHODS

Study Design

This was a cross-sectional observational study of kidney transplant recipients attending outpatient clinics at the Princess Alexandra Hospital in Brisbane, Queensland, Australia. Ethics approval was granted through the Metro South Human and Research Ethics Committee (HREC/18/QPAH/399) and The University of Queensland Human Research Ethics Committee, and each patient gave written informed consent.[7]

Study Population

The study included all kidney transplant patients who were both willing and able to provide informed consent to participate, and whose transplanted kidney survived for at least 2 months. There were no language restrictions or any other exclusions applied for this study.

Data Collection

Three questionnaires, the GSRS,[8] GIQLI,[9] and SAGIS,[10,11] were administered to patients when they attended their routine kidney transplant outpatient appointment between September 2019 and January 2020. The questionnaires were administered in English and for non–English-speaking participants consenting to participate, an on-site interpreter was available. Participants were provided with a pen and clipboard and were asked to complete the questionnaires independently. Questionnaires were identified and recorded by a unique patient study identification number that was different from their hospital identification number but associated with the patient name to allow clinical and demographic data to be extracted from the Princess Alexandra Hospital Nephrology Database. Participants consented to this extraction and took approximately 20 minutes to complete the 3 questionnaires.

Demographic characteristics extracted from the Princess Alexandra Hospital Nephrology Database were age, sex, and ethnicity; and the clinical information comprised primary kidney disease, graft number, cytomegalovirus serology, time since transplant, H_2 receptor antagonist and proton pump inhibitor use, immunosuppressant use, and immunosuppressant combination.

Survey Instruments

GSRS

The GSRS questionnaire evaluated gastrointestinal symptoms in kidney transplant recipients. It consists of 15 questions designed to assess the impact of upper and lower gastrointestinal symptoms. There are 5 subscales, specifically reflux, diarrhea, constipation, abdominal pain, and indigestion. Each question produced a mean subscale score ranging from 0 (no discomfort) to 3 (very severe discomfort). Higher scores indicated worse symptom impact. A total score (0 to 45) also was calculated. Higher scores represented worse gastrointestinal symptoms. The presence of gastrointestinal symptoms was defined if the GSRS score was $\geq$1.

GIQLI

The GIQLI questionnaire focused on the impact gastrointestinal complaints may have on a patient's QOL. This questionnaire consisted of 36 questions and primarily assessed the impact of gastrointestinal symptoms and disease on daily life. The GIQLI had 4 domains: gastrointestinal symptoms, emotional status, physical function, and social function. Subscale scores ranged from 0 to 4 and a total score (0 to 144) was also calculated. Higher scores represented better QOL.

SAGIS

The SAGIS scale was developed as a tool assessing the impact of gastrointestinal symptoms in the routine clinical setting.[10,11] Questions were graded on a 5-point scale from no problem, mild (can be ignored when one does not think about it), moderate (cannot be ignored but does not influence daily activities), severe (influencing concentration on daily activities), and very severe (markedly influences daily activities and/ or requires rest) problem. Higher scores indicated greater severity of symptoms. The survey also gave participants the opportunity to describe in free text their first and second most important "health concern/problem."

Statistical Analyses

Results were expressed as frequencies (percentages) for categorical data, mean $\pm$ SD for continuous normally

distributed data, or median (interquartile range [IQR]) for continuous non-normally distributed data. Predictors of QOL (mean GIQLI score) and gastrointestinal symptoms (mean GSRS and mean SAGIS scores) in kidney transplant recipients were estimated using linear regression models. Models for the mean QOL score, the mean GSRS and mean SAGIS scores, as well as for each mean gastrointestinal symptom score (i.e., abdominal pain, reflux, indigestion, constipation, and diarrhea) included as predictor variables participant age at transplant, sex, ethnicity, primary cause of kidney disease, time following kidney transplantation, H_2 receptor antagonist use, proton pump inhibitor use, graft number, cytomegalovirus serology, and immunosuppressive therapy (specifically tacrolimus, mycophenolate and prednisolone). Variables with P values less than 0.2 in univariable models were included in the multivariable model. Data were analyzed using Stata/SE version 14.0 (StataCorp. College Station, TX). P values <0.05 were considered statistically significant.

RESULTS

Study Population

Overall, 365 (89%) of 409 eligible patients who were approached consented to the study. A summary of participant flow through the study is shown in Figure 1

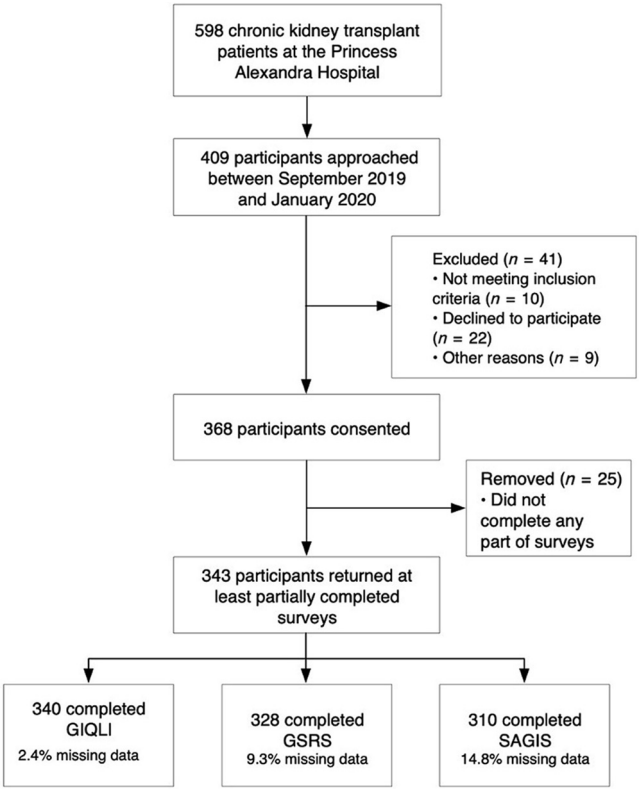

Figure 1. Summary of patient flow through the study. GIQLI, Gastrointestinal Quality of Life Index; GSRS, Gastrointestinal Symptoms Rating Scale; SAGIS, Structured Assessment of Gastrointestinal Symptoms.

and the missing figures for each survey is shown in Supplementary Table S1. The baseline demographic and clinical characteristics of the kidney transplant recipients are outlined in Table 1. The median (IQR) age of the cohort was 47 (36–55) years, 58% were men, and 79% were white. The most common etiology of kidney failure was chronic glomerulonephritis (39%). The

Table 1. Baseline characteristics of the kidney transplant recipient cohort

Characteristics	$N = 343$
Age	
Median (IQR), yr	47 (36–55)
Sex, *n* (%)	
Male	200 (58)
Primary kidney disease, *n* (%)	
Glomerulonephritis	134 (39)
Genetic renal disease	57 (17)
Reflux nephropathy	23 (7)
Renovascular disease	53 (15)
Diabetic nephropathy	23 (7)
Other	53 (15)
Ethnicity, *n* (%)	
Caucasian	271 (79)
Aboriginal or Torres Strait Islander	8 (2)
Asian	26 (8)
Other	38 (11)
Graft number, *n* (%)	
1	286 (83)
2	50 (15)
≥3	7 (2)
Time elapsed since kidney transplant, *n* (%)	
2–6 mo	38 (11)
6 to <12 mo	15 (4)
1 to <2 yr	27 (8)
2 to <5 yr	63 (18)
≥5 y	200 (58)
Cytomegalovirus serology, *n* (%)	
Donor-positive/recipient-negative	62 (18)
Donor-positive/recipient-positive	170 (50)
Donor-negative/recipient-negative	35 (10)
Acid-suppressing therapy, *n* (%)	
H_2 receptor antagonist use	64 (19)
Proton pump inhibitor use	180 (52)
Immunosuppressant use, *n* (%)	
Cyclosporin	42 (12)
Tacrolimus	279 (81)
Mycophenolate	268 (78)
Prednisolone	326 (95)
Everolimus	7 (2)
Sirolimus	10 (3)
Azathioprine	37 (11)
Immunosuppressant combination, *n* (%)	
Tacrolimus+mycophenolate+prednisolone	227 (66)
Tacrolimus+azathioprine+prednisolone	23 (7)
Cyclosporin+mycophenolate+prednisolone	22 (6)
Tacrolimus+prednisolone	21 (6)
Tacrolimus+mycophenolate	3 (1)
Other combination	47 (14)

IQR, interquartile range.

Table 2. Frequency and severity of gastrointestinal symptoms (measured by the Gastrointestinal Symptom Rating Score) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia)

Domain	Frequency (%)	Severity (IQR)
Abdominal pain ($n = 317$)	143 (45)	0.33 (0 to 0.67)
Constipation ($n = 289$)	106 (37)	0 (0 to 0.67)
Diarrhea ($n = 301$)	162 (54)	0.33 (0 to 1)
Indigestion ($n = 321$)	182 (57)	0.5 (0 to 0.75)
Reflux ($n = 321$)	145 (45)	0.5 (0 to 1)

IQR, interquartile range.

median (IQR) time following transplantation was 6.3 (1.8–13.1) years and 83% of patients had received only 1 kidney transplant. The most common immunosuppressant combination was tacrolimus, mycophenolate, and prednisolone (66%), and 18% of the cohort had cytomegalovirus seromismatch (donor IgG–positive, recipient IgG–negative).

Gastrointestinal Symptoms

The median (IQR) total GSRS score was 15.6 (6.7–24.4); 303 (88%) participants reported at least 1 gastrointestinal symptom (defined as GSRS≥1). The most common reported symptoms were indigestion (57%) and diarrhea (54%) (Table 2). In relation to gastrointestinal symptom severity, the median (IQR) score for abdominal pain was 0.33 (0–0.67), for constipation was 0 (0–0.67), for diarrhea was 0.33 (0–1), for indigestion was 0.5 (0–0.75), and reflux was 0.5 (0–1) (Supplementary Figure S1A). These findings from the GSRS survey are consistent with the SAGIS scale (Supplementary Figure S1B). Gastrointestinal disturbances were rated as the most important and second most important priorities in 16% and 17% of participants, respectively (Supplementary Table S2).

Quality of Life

The median (IQR) total GIQLI score was 71.5 (59.0–83.3). The median (IQR) GIQLI score was 2.86 (2.36–3.33), 2.74 (2.21–3.21) for gastrointestinal symptoms, 3.20 (2.80–3.80) for emotional function, 2.57 (2.00–3.29)

Table 3. Factors associated with gastrointestinal symptoms (measured by the Gastrointestinal Symptom Rating Score) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia

	Univariable analysis		Multivariable analysis	
Demographics	Coefficient (95% CI)	*P* value	Coefficient (95% CI)	*P* value
Quality of life (GIQLI)	−0.40 (−0.45 to −0.35)	<0.001	−0.38 (−0.45 to −0.30)	<0.001
Age (per 10 yr)	−0.009 (−0.02 to 0.0008)	0.07	−0.02 (−0.07 to 0.02)	0.25
Sex	−0.14 (−0.22 to −0.06)	0.001	−0.11 (−0.21 to −0.02)	0.02
Ethnicity		0.84		0.50
Caucasian	1		1	
Indigenous	0.10 (−0.19 to 0.38)	0.51	0.05 (−0.24 to 0.33)	0.78
Asian	−0.07 (−0.23 to 0.09)	0.38	−0.14 (−0.34 to 0.07)	0.19
Other	−0.03 (−0.17 to 0.10)	0.61	0.02 (−0.13 to 0.17)	0.80
Primary cause of kidney failure		0.35		0.27
Glomerulonephritis	1		1	
Cystic kidney disease	0.07 (−0.05 to 0.19)	0.27	0.008 (−0.14 to 0.15)	0.91
Reflux nephropathy	0.12 (−0.05 to 0.29)	0.18	−0.01 (−0.21 to 0.19)	0.92
Renovascular	0.05 (−0.07 to 0.17)	0.40	0.05 (−0.09 to 0.20	0.45
Diabetic kidney disease	0.06 (−0.12 to 0.24)	0.52	−0.10 (−0.30 to 0.10)	0.32
Other	0.06 (−0.06 to 0.19)	0.31	0.0005 (−0.13 to 0.13)	0.99
Time post-transplant (per 10 yr)	−0.0004 (−0.005 to 0.004)	0.84	0.005 (−0.003 to 0.01)	0.23
Acid-suppressing therapy	0.12 (0.03 to 0.20)	0.008	0.04 (−0.07 to 0.15)	0.48
Graft number	0.15 (−0.04 to 0.35)	0.12	0.09 (−0.11 to 0.29)	0.38
Cytomegalovirus serology		0.87		0.64
Positive/negative	1		1	
Positive/positive	0.32 (−1.45 to 2.10)	0.72	−0.08 (−0.49 to 0.35)	0.71
Negative/negative	0.06 (−0.55 to 0.68)	0.82	−0.08 (−0.54 to 0.38)	0.74
Immunosuppression		0.08		0.04
Tacrolimus	0.006 (0.0003 to 0.01)	0.04	0.005 (−0.002 to 0.01)	0.15
Mycophenolate	0.00005 (−0.00007 to 0.0002)	0.40	0.0001 (0.0001 to 0.0002)	0.03
Prednisolone	0.008 (−0.004 to 0.02)	0.20	0.01 (−0.0001 to 0.03)	0.07
Immunosuppression combination		0.80		0.24
Tacrolimus/ mycophenolate/ prednisolone	1		1	
Other	−0.01 (−0.10 to 0.07)	0.80	0.05 (−0.35 to 0.44)	0.24

CI, confidence interval; GIQLI, Gastrointestinal Quality of Life Index.

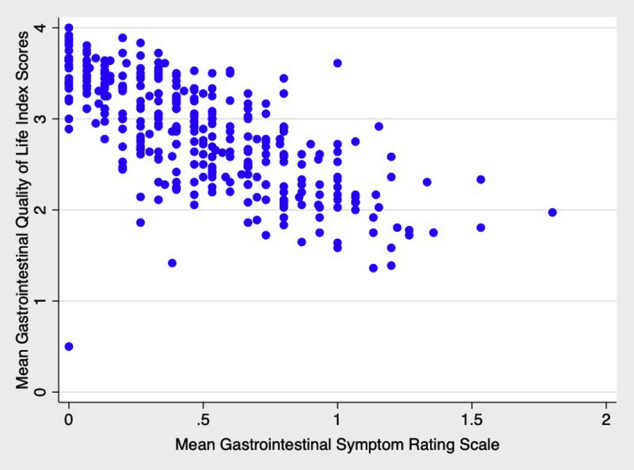

Figure 2. Association between mean gastrointestinal QOL scores and the mean gastrointestinal symptom rating scores ($r^2 = 0.69$).

for physical function, and 3.29 (2.86–3.71) for social function. Approximately 44% and 38% of the participants reported mild and moderate QOL impairment, respectively (Supplementary Figure S2). Participants reported significantly greater gastrointestinal complaints and physical dysfunction compared with complaints relating to emotional and social function (Supplementary Figure S3).

Factors Associated With Gastrointestinal Symptoms

Using multivariable linear regression, gastrointestinal symptoms (GSRS) were inversely associated with QOL (GIQLI) (coefficient −0.38, 95% CI −0.45 to −0.30) (Table 3). The correlation between gastrointestinal symptoms and QOL was 0.69 (Figure 2). Gastrointestinal symptoms were independently associated with female participants (coefficient −0.11, 95% CI −0.21 to −0.02) and mycophenolate (coefficient 0.0001, 95% CI 0.0001 to 0.0002) (Table 3). There were no significant differences in gastrointestinal symptoms between mycophenolate mofetil users and mycophenolate sodium users. Patient-reported abdominal pain was associated with tacrolimus therapy (coefficient 0.01, 95% CI 0.003–0.02) (Supplementary Table S3) and patient-reported diarrhea was associated with mycophenolate (coefficient 0.0003, 95% CI 0.0001–0.0006) (Supplementary Table S4). Similar findings were observed using the SAGIS scale compared with the GSRS survey (Supplementary Tables S5–S7).

DISCUSSION

This cross-sectional study of chronic kidney transplant recipients performed in a single center in Queensland, Australia, found that gastrointestinal symptoms were reported by 88% of participants, and that gastrointestinal symptoms were associated with significantly impaired QOL, affecting patients for many years following transplantation. This study also showed that women were more likely to report gastrointestinal symptoms compared with men, and that gastrointestinal symptoms, such as abdominal pain and diarrhea, were associated with tacrolimus and mycophenolate use, respectively.

The findings that 88% of kidney transplant recipients in the present study reported gastrointestinal symptoms are in keeping with previous studies in the literature. For example, in a multicenter study involving 23 Italian transplant centers comprising 1130 participants, 88.3% of kidney transplant patients reported at least 1 gastrointestinal symptom with a higher prevalence in flatulence, abdominal distension, borborygmi, and the sensation of incomplete bowel emptying.[12] Another important study involving 4232 kidney transplant recipients from Denmark, Finland, Norway, and Sweden, reported that 92% of participants reported gastrointestinal symptoms, including indigestion (83%), abdominal pain (69%), constipation (58%), and reflux (47%).[13] Furthermore, a study consisting of 85 kidney transplant recipients from Greece reported that 82% suffered from gastrointestinal symptoms with the most frequent and severe symptoms recorded as indigestion and diarrhea.[14] Thus, gastrointestinal symptoms are prevalent in the kidney transplant population and should be routinely evaluated and addressed in the outpatient setting.

The inverse association between gastrointestinal symptoms and QOL is consistent with the findings of previous studies.[5,6,12] For example, in a single-center cross-sectional study involving 96 patients in the United States, there was a significant association between all GSRS subscales and the total GIQLI score between patients with and without significant gastrointestinal complications ($P < 0.05$).[15] Another cross-sectional study conducted within 5 clinical centers across 4 countries involving 92 patients showed a significant association between all GSRS domains and overall GIQLI score, and was also able to differentiate between patients with and without gastrointestinal symptoms ($P < 0.05$).[6] Furthermore, an observational survey based on postal questionnaires of GSRS and GIQLI study involving 4232 Scandinavian kidney transplant recipients showed that gastrointestinal symptoms were associated with impaired QOL.[13] This study also interestingly showed that nephrologists frequently underestimated gastrointestinal symptoms and overestimated the QOL of their patients.[13] Possible explanations for the association between gastrointestinal symptoms and impaired QOL include patients' embarrassment when using or locating public toilets, fecal incontinence, and their perception that they are

incapable of returning to work.[16] These potential barriers have been borne out in patients suffering from irritable bowel syndrome who often report a constellation of gastrointestinal symptoms to their physicians, which may mirror the symptoms reported by kidney transplant recipients.[16]

Immunosuppressive therapy, such as tacrolimus and mycophenolate, may be a possible contributor to the patient-reported gastrointestinal symptoms found in the present study. There are some studies in the literature that support this. For example, 3 open-label randomized controlled trials, which comprised 1521 patients, showed that tacrolimus was associated with increased frequency of nausea and vomiting, and abdominal pain, compared with cyclosporine.[17–19] Another 2 double-blind, multicenter trials comprising 1002 patients, showed that patients who were taking mycophenolate were approximately 1.5 to 2.0 times more likely to experience diarrhea.[20,21] Yet, some studies have refuted the association between immunosuppressive therapy with gastrointestinal symptoms. For example, in an open, nonrandomized, multicenter study involving 108 patients from 16 Belgian transplant centers, it was proposed that diarrhea was mitigated through antimicrobial therapy, changes to certain medications, and other empirical therapy.[22] Another single-center study undertaken in Canada involving 36 kidney transplant recipients who reported a 2-week history of diarrhea showed that in 30 of the 36 cases, an infectious agent was found.[23] Thus, other mechanisms such as the role of the gastrointestinal microbiota[24–26] may explain the gastrointestinal symptoms reported in kidney transplant recipients.

Another finding in the present study was the observed sex disparity in patient-reported gastrointestinal symptoms, with female kidney transplant recipients reporting more gastrointestinal symptoms compared with men. This association may be due to differences in immune responses, hormonal levels, or the composition and diversity of the gastrointestinal microbiota.[27,28] In addition, alterations in the pharmacokinetic and pharmacodynamic immunosuppressive responses as well as a greater frequency of HLA sensitisation in women leading to different immunosuppression approaches, selection bias, and sex-specific differences in the propensity for infection (e.g., greater incidence of urinary tract infections in women) may explain the sex differences.[27,29] Women have also been shown to report more gastrointestinal symptoms to health care professionals compared with men.[30,31]

The association between acid-suppressing therapy and gastrointestinal symptoms is unclear. For example, in a cross-sectional study of 100 kidney transplant recipients, mean GSRS score was higher in patients who used proton pump inhibitors (7.8 ± 5.5 vs. 4.6 ± 3.0; $P = 0.013$), with diarrhea reported as the primary symptom (mean score 2.3 ± 2.2 vs. 1.3 ± 1.9, $P = 0.04$).[32] The mechanism behind this may be that proton pump inhibitors inhibit active magnesium absorption in the small intestines, thus generating gastrointestinal symptoms.[33] In contrast, the present study did not find a significant association between acid-suppressing therapy (both histamine antagonists and proton pump inhibitor therapy) and gastrointestinal symptoms (Table 3), and thus further studies may be warranted to evaluate this.

The major strength of this study is the comprehensive analysis of the prevalence of gastrointestinal symptoms and QOL of a large sample size of participants from a single center. This needs to be balanced against the limitations of this study. Response bias, including social desirability bias, cannot be excluded, as the response rate was 62%. A study by Galea and Tracy[34] reported that a low response rate does not necessarily lead to significant changes in clinical outcomes. The response rate in this study is still within an acceptable response rate according to the study of Galea and Tracy.[34] A further limitation of the present study is the provision of 2 gastrointestinal symptom surveys to participants, which may bias participants to report gastrointestinal symptoms rather than reporting other symptoms that may be more relevant to them.

In conclusion, this study has found that gastrointestinal symptoms are highly prevalent and are associated with significantly impaired QOL in kidney transplant recipients. It also highlighted that gastrointestinal symptoms are more frequently reported by women and that these symptoms may be associated with immunosuppressive use, such as tacrolimus and mycophenolate. Further studies will need to explore interventions to alleviate gastrointestinal symptoms, which may in turn improve the overall QOL of patients with a kidney transplant.

DISCLOSURE

SC is supported by the Australian National Health and Medical Research Council (NHMRC) Postgraduate Scholarship, the Microba recipient grant, the Metro South Research Support Scheme, and the Royal Australasian College of Physicians NHMRC Research Excellence top-up award. Furthermore, SC is a current recipient of the 2018 Sir Gustav Nossal NHMRC Postgraduate Scholarship award. CMH is the recipient of research grants paid to her institution from Baxter Healthcare and Fresenius Medical Care and from Otsuka, Janssen, and GlaxoSmithKline for trial steering committee activities, paid to her institution. DWJ has received consultancy fees, research grants, speaker's honoraria and

travel sponsorships from Baxter Healthcare and Fresenius Medical Care. He has received consultancy fees from Astra Zeneca and travel sponsorships from Amgen. He is a current recipient of an Australian NHMRC Practitioner Fellowship. NMI has received consultancy fees and speaker's honoraria from Alexion Pharmaceuticals, Novo Nordisk, and Amgen. All the other authors declared no competing interests.

AUTHOR CONTRIBUTIONS

SC drafted the manuscript. CC, EMP, DWJ, AS, GAH, RSF, SBC, NMI, and CMH provided critical analysis to the paper. All authors read and approved the final manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. (A) Severity distribution of overall gastrointestinal symptom rating scores. (B) Severity distribution of overall structured assessment in gastrointestinal symptom scale.

Figure S2. Mean gastrointestinal quality of life index scores as measured by the Gastrointestinal Quality of Life Index Survey.

Figure S3. Severity distribution of the overall gastrointestinal quality of life index scores.

Table S1A. Gastrointestinal Quality of Life Index missing figures.

Table S1B. Gastrointestinal Symptom Rating Score missing figures.

Table S1C. Assessment in Gastrointestinal Symptoms scale missing figures.

Table S2. Self-reported most and second most important health concern (as per the Structured Assessment in Gastrointestinal Symptoms scale).

Table S3. Factors associated with abdominal pain (as measured by the Gastrointestinal Symptom Rating Score) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia.

Table S4. Factors associated with diarrhea (as measured by the Gastrointestinal Symptom Rating Score) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia.

Table S5. Factors associated with gastrointestinal symptoms (as measured by the Structured Assessment in Gastrointestinal Symptom scale) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia.

Table S6. Factors associated with abdominal pain (as measured by the Structured Assessment in Gastrointestinal Symptom scale) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia.

Table S7. Factors associated with diarrhea (as measured by the Structured Assessment in Gastrointestinal Symptom scale) among chronic kidney transplant recipients at the Princess Alexandra Hospital in Queensland, Australia.

DATA SHARING STATEMENT

De-identified individual participant data that underlie the results reported in this publication can be requested by any qualified researchers. Medicare and all other administrative data will not be available. Methodologically sound proposals should be directed to aktn@uq.edu.au. The Australasian Kidney Trials network Data Sharing Committee will assess proposals based on the following criteria: sound science, benefit-risk balancing, and research team expertise. The data will be available in a digital repository supported by The University of Queensland but without investigator support other than deposited metadata. To gain access, data requestors will need to sign a data access agreement. Data will be available beginning 2 years after the publication of all prespecified analyses.

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