CASE STUDIES

Gastric bypass oxalosis in renal transplant: clinicopathologic correlates

Maria Nieva A. Salazar *[1], Dave J. Taber[2], Tiffany O'neill[3], Beje S. Thomas[1], Prince Mohan[1], Maria Aurora Posadas[1], Sally E. Self[3], Prabhakar K. Baliga[2], Titte R. Srinivas[1]

[1] *Department of Medicine, Division of Transplant Nephrology, Medical University of South Carolina, Charleston, South Carolina, USA*
[2] *Department of Surgery, Division of Transplant Surgery, Medical University of South Carolina, Charleston, South Carolina, USA*
[3] *Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, South Carolina, USA*

Received: November 29, 2015 **Accepted:** December 8, 2015 **Online Published:** January 5, 2016
DOI: 10.5430/crcp.v3n1p47 **URL:** http://dx.doi.org/10.5430/crcp.v3n1p47

ABSTRACT

Background: Reports of oxalate nephropathy after gastric bypass (GB) leading to graft loss of kidneys causes concern for transplant professionals. We examined the clinical phenotype of GB related oxalate nephropathy (ON), its contribution to graft loss and propose a management strategy to mitigate graft loss in renal transplant recipients.
Methods: Retrospective case series of patients who had GB surgery prior to renal transplant at a single institution were studied. Oxalate burden in renal transplant biopsies was quantified by intratubular calcium/glomeruli (Ca T/G) ratio and correlated with other clinical covariates.
Results: We identified 16 GB patients; the mean BMI pre-GB was 52.5 kg/m^2 (range 42-80), with a follow-up BMI of 30.9 kg/m^2 (range 22-36.5) at transplant evaluation. Among 11 patients who had for cause biopsies, 3 patients had significant intra tubular allograft calcium oxalate deposition with a median time from graft to failure of 9 months. Among patients with functioning grafts, follow up creatinine averaged 1.6 mg/dl (0.9-3.4 mg/dl); median follow up was 4 years (0.5-7 years).
Conclusions: The relationship between GB and ON post renal transplant is variable. The expression of ON after acute kidney injury (AKI) suggests that mitigating strategies should be directed at preventing alloimmune and other forms of AKI in addition to managing oxalate intake.

Key Words: Gastric bypass, Oxalate nephropathy, Oxalosis, Renal transplant, Roux en Y

1. INTRODUCTION

Obesity is increasingly prevalent among patients with End Stage Renal Disease (ESRD) and kidney transplant candidates.[1] As obesity associates with increased cardiovascular mortality and post operative complications, transplant centers often set an upper limit for BMI before listing potential transplant recipients.[2] Despite outcomes that are inferior to those among the non obese transplant recipients, obese recipients accrue benefit from a renal transplant when compared to wait listed patients.[3–5] Bariatric surgery confers greater weight loss than conservative measures; and among obese patients with uncontrolled diabetes, bariatric surgery is associated with better glucose control and decreased use of glucose lowering medications.[6,7] Increasing awareness of enteric hyperoxaluria complicating jejunoileal bypass surgery and Roux-en-Y gastric bypass progressing to oxalate nephropa-

*Correspondence: Maria Nieva A. Salazar; Email: salazarm@musc.edu; Address: Division of Nephrology, 96 Jonathan Lucas Street, Clinical Science Building Suite 629, Charleston, South Carolina 29425-6290, USA.

thy (ON) and renal failure offers reason for pause and concern.[8–14]

An index case of oxalate nephropathy occurring in the transplanted kidney in a recipient that had received jejunoileal gastric bypass (GB) prior to transplantation at our center prompted us to examine outcomes among our post-gastric bypass renal transplant recipients.

We describe the clinical expression of oxalate nephropathy, the pathologic findings and the renal outcomes in 16 patients who had bariatric surgery for morbid obesity prior to renal transplant. We propose a pathophysiologic schema for ON leading to graft dysfunction and outline a preventive strategy that could be of utility in this unique population.

2. MATERIALS AND METHODS

We identified patients who had bariatric surgery for obesity prior to renal transplant at our center. As concern for oxalate nephropathy is restricted to those who have had malabsorptive bariatric surgery, we excluded patients who had restrictive bariatric surgery alone including laparoscopic gastric banding and sleeve gastrectomies. Adult patients who had a solitary renal transplant at the Medical University of South Carolina between 2000 and 2012 were reviewed. Recipients who had malabsorptive bariatric surgery including jejunoileal bypass, Roux en Y gastric bypass and gastroplasty with duodenal switch for obesity prior to transplant were included. Medical records were reviewed for demographics, medical history, date and type of bariatric surgery, BMI before bariatric surgery, BMI at time of renal transplant evaluation and weight lost from bariatric surgery to time of evaluation. Data collected include cause of ESRD, type of organ donor, HLA matching, donor age and sex, BK virus associated nephropathy (BKVAN) and episodes of rejection. The etiology of ESRD was recorded from review of records during transplant evaluation. The outcome measures were graft loss and serum creatinine.

At the time of study, all biopsies were re-examined by two pathologists including the renal pathologist who initially signed out the case. Biopsy specimens were processed according to standard techniques for light microscopy and immunofluorescence. All slides stained with hematoxylin and eosin, were re-examined under both light microscopy and polarized light. The degree of tubulitis, glomerulitis, arteriolar hyalinosis, fibrosis and tubular atrophy were classified based on Banff '97 criteria in the original biopsy reports and remained unchanged after reexamination of the biopsies. We quantified the degree of oxalate nephropathy by recording the number of tubules with intraluminal or intracellular calcium oxalate deposits in the biopsy core and corrected for the size of the biopsy sample by relating tubular oxalate deposits to the numbers of glomeruli in the biopsy thereby deriving a ratio of intratubular calcium oxalate deposits to glomeruli in the biopsy. The study was approved by the Institutional Review Board of Medical University of South Carolina.

3. RESULTS

3.1 Clinical features

We summarize key demographic and clinical features in Table 1. The cohort included 9 (56%) females and 7 (44%) males with a mean age of 56 years old (range 45 to 68). Twelve were Caucasian (75%) and four (25%) were African Americans. Three of sixteen (18%) had diabetes, and all patients were hypertensive and receiving antihypertensives at the time of transplant. The mean BMI prior to bariatric surgery was 52.5 kg/m^2 (range 42 to 80), the mean weight lost after bariatric surgery was 66 kg and the mean BMI at the time of transplant evaluation was 30.9 kg/m^2 (range 22 to 36.5).

The indication for bariatric surgery was obesity in all patients. The mean dialysis duration was 54 months (range 9 to 216 months). Four of the sixteen patients had long segments of the intestinal tract bypassed while the remaining patients had proximal Roux en Y procedures. Three patients in the cohort had jejunoileal bypass done in the 1970's, and one had gastroplasty with duodenal switch.

Serum oxalate level was checked in only one patient and was elevated. None of the patients had BKVAN. Only one patient, case 8, who received a standard criteria deceased donor kidney from a 43-year-old female had delayed graft function which was attributed to prolonged cold ischemia time of 23 H and 55 minutes.

3.2 Pathologic findings

Protocol biopsies were not done in our center prior to 2012. All biopsies were for cause and were reexamined. Results of the eleven reexamined biopsies out of the sixteen patients in the study are summarized in Tables 2 and 3. Table 2 shows pathological findings based on '97 Banff criteria. Five of eleven patients had biopsy proven rejection. Four of five had borderline changes suspicious for rejection and one patient had Banff 1 B rejection after subtherapeutic immunosuppression. Sequential for-cause biopsies obtained in two patients with acute kidney injury (AKI) episodes, showed increased interstitial fibrosis and tubular atrophy after the episodes of rejection.

The renal oxalate burden in relation to creatinine and time after transplant are summarized in Table 3. Three of eleven patients had significant oxalate deposits in the biopsy. Among

patients with oxalate deposition experiencing graft loss, the intratubular calcium to glomeruli ratio (Ca T/G) was increased at 1.5 to 16 compared to 0 to 0.4 among those with functional grafts. There was absent to minimal fibrosis that accompanied acute tubular injury on initial biopsy of a patients that developed oxalate nephropathy. With progression of renal dysfunction, subsequent biopsy showed moderate to severe interstitial fibrosis with increased oxalate deposition, as seen in Figure 1.

Table 1. Patient characteristics and renal outcomes

Case	Age/ Sex	Race	DM	ESRD Etiology	Type of Donor	Donor Age and Sex	HLA Match	DR MM	Type of Bariatric Surgery (BS)	BMI prior to BS	Weight lost (kg)	BMI at Renal Transplant Evaluation	Months of Follow Up	Follow up Creatinine (mg/dl)
1	47M	AA	(-)	HTN	SCD	51 F	2	0	Proximal Roux en Y	43	45	30.5	35	1.7
2	54M	C	(-)	HTN	SCD	35 M	1	2	Proximal Roux en Y	54	54	36.5	81	0.9
3	42F	C	(-)	FSGS	SCR	59 F	5	0	Proximal Roux en Y	42	55	22	8	1.2
4	48F	AA	(-)	HTN	SCD	56 F	2	1	Proximal Roux en Y	48	32	34.8	65	2.1
5	59F	C	(-)	HTN	SCD	26 M	1	1	JI bypass	66	102	32	77	1
6	59F	AA	(-)	HTN	SCD	49 F	1	2	Proximal Roux en Y	51.7	50	30.1	84	0.9
7	61 M	C	(+)	DM/HTN	SCD	63 M	0	2	Gastroplasty with DS	55.9	83	30.2	6	1.7
8	66 M	C	(-)	HTN	SCD	43 F	6	0	Proximal Roux en Y	80.1	160	31.8	6	ESRD
9	68 F	C	(+)	DM/HTN	SCD	53 M	2	1	Proximal Roux en Y	41	21	34.1	18	1.8
10	55 M	C	(-)	NSAIDs	LR	43 M	3	1	JI bypass	55.8	81	30.7	74	1.7
11	45 F	C	(+)	DM	DCD	44 M	5	0	Proximal Roux en Y	NA	NA	35	70	1.4
12	60 F	C	(-)	HTN	SCD	20 M	4	0	Proximal Roux en Y	51	50	35	9	2
13	38 M	AA	(-)	HTN	SCD	15 M	5	1	Proximal Roux en Y	46	46	31.3	60	2
14	69 F	C	(-)	HTN	ECD	51 F	0	0	Proximal Roux en Y	NA	NA	29	86	3.4
15	59F	C	(-)	Oxalo sis	LR	53 F	2	1	JI bypass	NA	NA	22	10	ESRD
16	67M	C	(-)	HTN	SCD	54 F	2	1	Proximal Roux en Y	49	76	30	10	ESRD

Note: AA - African American; C- Caucasian; SCD - Standard Criteria Donor; LR - Living Related Donor; ECD - Expanded Criteria Donor; DCD Donor after Cardiac Death ; DS - Duodenal Switch

3.3 Clinical outcomes

The renal outcome for the cohort is summarized in Table 1. Three of sixteen (18%) patients (cases 8, 15, and 16) had renal graft loss with a mean time to graft failure of 9 months (range 6 to 11 months). Among the patients who had a biopsy for cause (cases 1, 3, 4, 8, 9, 11, 12, 13, 14, 15, and 16), acute rejection rate was 45% (5/11) and all except one with 1B had borderline changes suspicious for rejection based on Banff '97 criteria. The mean follow up creatinine was 1.6 mg/dl (range 0.9 to 3.4 mg/dl) over a median follow up period of 51 months (range 6 to 84 months).

The clinical course of the patients who had early graft loss was reviewed. Case 8 had delayed graft function requiring dialysis for volume overload and hyperkalemia post operatively. The transplant course was complicated with multiple admissions for volume depletion, acute kidney injury, urosepsis and cellulitis culminating in graft loss 6 months post-transplant. No oxalate deposition was noted on the first biopsy (creatinine of 2.5 mg/dl), but was present on subsequent biopsies when creatinine increased to 4.6 and then 6.8 mg/dl. Case 15 was the only case who had documented oxalate nephropathy as a cause of her native kidney disease presumably related to remote jejunoileal bypass. She had a living related kidney transplant from her 53-year-old sister. She received cinacalcet for tertiary hyperparathyroidism and citrate supplementation for calcium oxalate stone prevention. The nadir creatinine was 0.7 mg/dl 2 days post transplant and increased to 1.7 mg/dl at 3 months. A graft biopsy showed no rejection but isometric vacuolization suggestive of calcineurin inhibitor (CNI) nephrotoxicity. Oxalate deposits were noted on her biopsy accompanied by acute tubular injury and interstitial fibrosis. Given CNI toxicity, mycophenolate mofetil (MMF) was switched to everolimus and tacrolimus was minimized. She then developed Banff 1B rejection in the setting of subtherapeutic tacrolimus and everolimus levels 7 months after transplant. The creatinine progressively increased and she was initiated on dialysis ten

months after transplant. She received a second renal transplant from a 52-year-old male deceased donor 14 months after her first graft failed. Her second transplant was done in 2013 and is not included in this cohort. Her maintenance immunosuppressions include tacrolimus, mycophenolate mofetil and prednisone. She was started on an oxalate free diet and calcium supplementation in the immediate post transplant period which she has maintained to date. A 6 month protocol biopsy did not show any calcium oxalate deposit and her creatinine at 10 months was normal. Case 16 had multiple admissions, for pseudomonas UTI, urosepsis, and episodes of acute kidney injury secondary to volume depletion due to chronic diarrhea. Colonoscopy did not reveal any pathology and infectious work up was negative for viral, parasitic and bacterial causes of enterocolitis. His nadir creatinine was 1 mg/dl but after multiple admissions for AKI had stabilized at 1.8 mg/dl - 2 mg/dl. He continued to have diarrhea and MMF was intermittently discontinued. He was lost to follow up for 5 months at our center and had multiple admissions in another center for diarrhea, cytomegalovirus (CMV) viremia, pneumonia, deep vein thrombosis (DVT) and episodes of acute kidney injury. His creatinine when he returned to our institution ranged 3.5 to 4 mg/dl. A renal biopsy was done which showed moderate to severe interstitial fibrosis and extensive calcium oxalate intratubular deposits. He had progressive graft dysfunction and was initiated on dialysis 10 months after transplant.

Table 2. Renal biopsy findings by '97 Banff criteria

Case (N=11)	Number of Glomeruli	Number of Sclerotic Glomeruli	Glomerulitis (g)	Interstitial Inflammation (i)	Tubulitis (t)	Arterial Hyalinosis (ah)	Intimal Arteritis (v)	Glomerulopathy (cg)	Interstitial Fibrosis (IF)	Tubular Atrophy (TA)	Fibrous Intimal Thickening (cv)
1	6	0	absent	absent	absent	absent	absent	absent	absent	absent	mild
3	12	0	absent	absent	absent	mild	absent	absent	minimal	minimal	mild
4	5	1	absent	absent	absent	mild	absent	absent	mild	absent	moderate
8											
1st	7	1	absent	absent	absent	mild	absent	absent	absent	absent	absent
2nd	22	0	absent	minimal	mild	absent	absent	absent	mild	minimal	absent
3rd	35	2	absent	absent	absent	absent	absent	absent	mild	absent	absent
9	7	0	absent	absent	absent	absent	absent	absent	moderate	mild	absent
11	22	1	absent	absent	absent	absent	absent	absent	minimal	minimal	absent
12	12	0	absent	absent	absent	absent	absent	absent	absent	absent	absent
13	9	0	absent	minimal	severe	absent	n/a	absent	minimal	minimal	n/a
14	23	7	absent	mild	mild	absent	absent	absent	moderate to severe	moderate to severe	absent
15											
Perfusion	90	6	absent	absent	absent	absent	absent	absent	minimal	mild	absent
1st	8	0	absent	absent	absent	absent	absent	absent	absent	absent	absent
2nd	7	0	absent	absent	absent	absent	absent	absent	mild	mild	absent
3rd	8	1	absent	moderate	severe	absent	absent	absent	mild	mild	absent
4th	31	1	absent	moderate	severe	absent	absent	absent	moderate	moderate	mild
5th	7	0	absent	mild	severe	absent	absent	absent	moderate to severe	moderate to severe	absent
16	3	1	absent	mild	mild	absent	absent	absent	moderate to severe	moderate to severe	absent

4. DISCUSSION

Increasing reports of oxalate nephropathy and renal transplant graft loss likely due to enteric hyperoxaluria from gastric bypass are emerging.[15] This study shows that oxalate nephropathy and graft loss do not uniformly occur in renal transplant recipients who have had malabsorptive forms of bariatric surgery such as Roux en Y and jejunoileal bypass surgery for obesity. The development of oxalate nephropathy in three of our patients is multifactorial and likely precipitated by AKI from volume depletion, sepsis or rejection.

A pathophysiologic schema for oxalate nephropathy and graft dysfunction in renal transplant among gastric bypass patients is outlined in the Figure 2. The primary contributors are likely hyperoxaluria, hypocitraturia, hypercalciuria which can increase urine calcium and oxalate supersaturation leading to ON and altered pharmacokinetics of immunosuppression potentially leading to higher risk of rejection and deterioration of renal function.[15–26] Other contributing factors include high oxalate diet, excessive vitamin C intake, diabetic gastroenteropathy, inadequate calcium supplementation, and hyperparathyroidism.[15,27–33]

Increased enteric oxalate absorption that results from intraluminal free fatty acid and calcium binding due to fat malab-

sorption can lead to hyperoxaluria and increased urine calcium oxalate supersaturation.[16] Aside from dietary source, oxalate that has accumulated due to decreased renal excretion among patients with kidney disease lead to hyperoxaluria after renal transplant.[34] Hypocitraturia in addition to hyperoxaluria has been well documented in gastric bypass surgery.[21,35,36] In a study of 19 patients, the prevalence of hyperoxaluria (47% *vs*. 10.5%, $p = .02$) and hypocitraturia (63% *vs*. 5%, $p < .01$) was significantly higher among those who had Roux en Y gastric bypass.[21] One patient was on cinacalcet for secondary hyperparathyroidism which was continued after transplant. Use of cinacalcet for secondary and tertiary hyperparathyroidism after transplantation has been shown to increase urinary calcium excretion.[37,38] Although hypercalciuria is a risk factor for development of nephrolithiasis, a study in mice did not increase urinary supersaturation for calcium oxalate with cinacalcet use.[39] This is further supported in a study of renal transplant recipients where cinacalcet use did not show graft calcium deposition despite hypercalciuria.[40]

The development of oxalate nephropathy in our patients was preceded by acute kidney injury. The causes of AKI are varied and include volume depletion, infection or rejection. Subsequent biopsies of two patients after AKI showed progression to severe fibrosis with tubular atrophy within 10 months of renal transplant including one patient who received a living donor. The worsening renal dysfunction from AKI likely decrease renal oxalate clearance and may further increase renal oxalate deposition.

Table 3. Oxalate findings on biopsy correlated to renal function

Case# (N=11)	Months Post Transplant	Serum Creatinine at Biopsy	Number of Glomeruli on Biopsy Core	Intratubular Calcium Oxalate Deposits	Intratubular Calcium /Glomeruli	Rejection on Biopsy
1	1	1.5	6	0	0	NA
3	2	1.2	12	5	0.4	NA
4	13	2.2	5	0	0	NA
8 -1st	1	2.5	7	0	0	NA
2nd	4	4.6	22	35	1.5	Borderline
3rd	5	6.8	35	58	1.6	NA
9	12	2.2	7	2	0.2	NA
11	53	1.7	22	3	0.1	NA
12	2	1.9	12	0	0	NA
13	10	1.6	9	0	0	Borderline
14	82	3.4	23	0	0	Borderline
15 - 1st	1	1.7	8	13	1.6	NA
2nd	2	2.2	7	13	1.8	NA
3rd	7	1.8	8	1	0.1	1B
4th	7	3	31	43	1.3	1B
5th	8	5.4	7	23	3.2	Borderline
16	10	7.7	3	48	16	Borderline

All three patients with ON had interruption of mycophenolate mofetil because of diarrhea or had subtherapeutic levels of tacrolimus and everolimus prior to rejection and graft failure. Studies on pharmacokinetics of modern immunosuppression for transplant among GB patients are limited. In one pilot study, the area under the concentration (AUC): dose ratio for tacrolimus and sirolimus, and mycophenolic acid (MPA) AUC were lower among GB patients compared to historical controls.[23] This is consistent with what has been previously reported in cyclosporine (CsA). The weight adjusted CsA dose increased after RYGB and absolute requirement increased 33% in three renal transplant patients.[41] The pharmacokinetics of tacrolimus has been investigated in animal studies and showed over 60% of the oral tacrolimus dose is absorbed in the duodenum and jejunum, and may explain the altered PK after GB.[42] This indicates that a higher dose of immunosuppression is required for GB patients to achieve same exposure among those who did not have the procedure.

Based on our experience, we suggest a preventive strategy in this population that has been effective for our index case. Case 15 had a second transplant (not included in cohort) in 2013 from a deceased donor after early graft loss due to ON, creatinine was 1 mg/dl at 16 month follow up and without oxalate deposits on 1 year protocol biopsy.

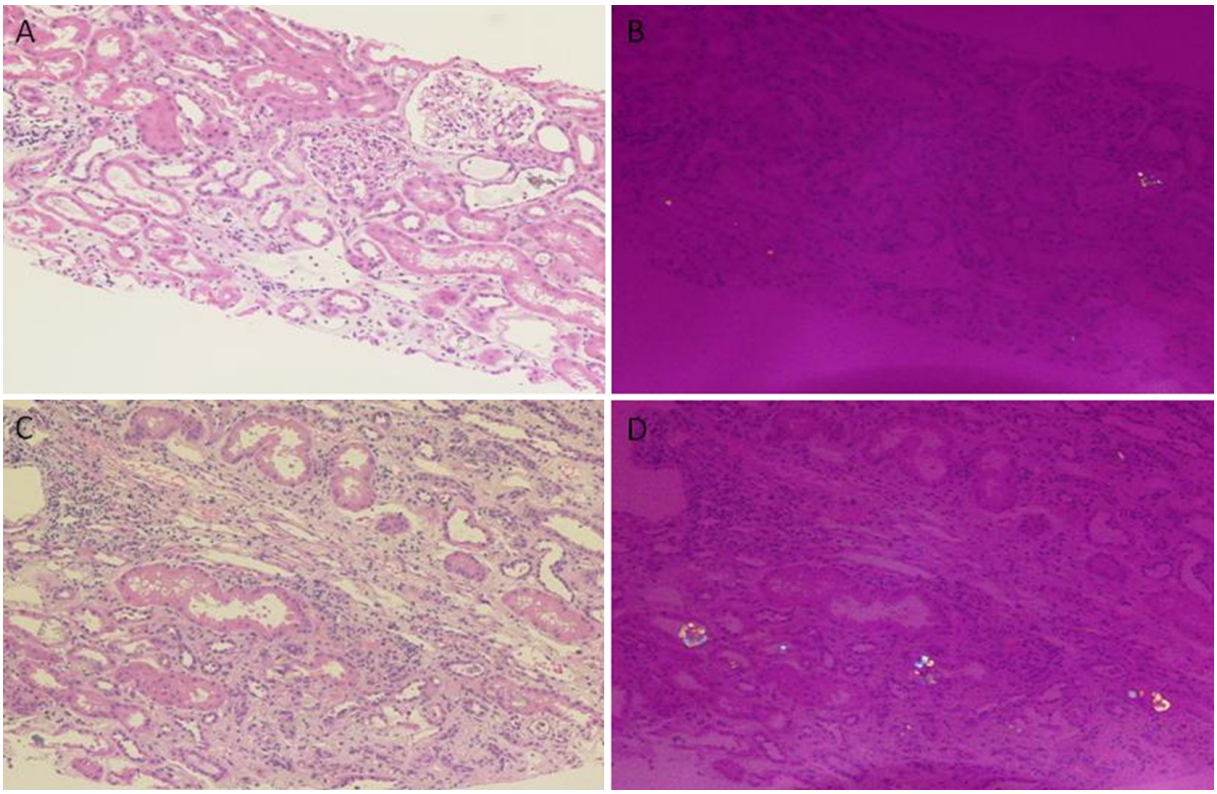

Figure 1. Serial pathologic findings in a patient with oxalate nephropathy

A. Hematoxylin and Eosin (H&E) of first biopsy for AKI with Cr of 1.7 shows absent inflammatory infiltrate and no interstitial fibrosis nor tubular atrophy. B. Polarized of A. Few scattered calcium oxalate crystals noted in the tubules. C. H&E of 5th biopsy with Cr of 5.4 after 5 months, with mild mononuclear infiltrate noted in areas of fibrosis with focal tubulitis; moderate to severe interstitial fibrosis and tubular atrophy. D. Polarized image of C. Numerous scattered calcium oxalate crystals in tubules. Magnification 100×.

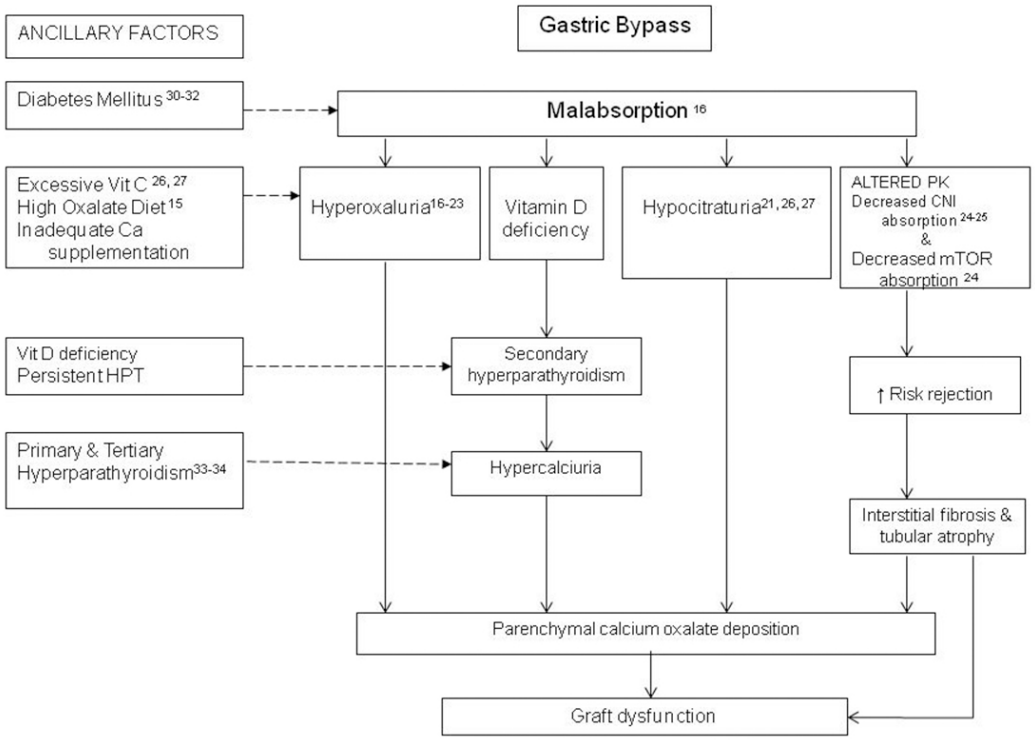

Figure 2. Pathophysiologic schema of oxalate nephropathy and graft dysfunction post GB

ISSN 2331-2726 E-ISSN 2331-2734

Every patient that has had prior gastric bypass surgery must receive an oxalate free or low oxalate diet. A low oxalate diet to avoid hyperoxaluria should be emphasized pre and post transplantation. Among dietary components star fruit and rhubarb have very high oxalate content and are well recognized, but emphasis should be on the avoidance of the more commonly available food such as Swiss chards, spinach, okra, lentils, soy products, beer, cocoa and peanuts which can lead to a very high oxalate dietary content.[15,27,43,44] Dietary counseling should also emphasize low sodium, high potassium, avoidance of animal protein as well as avoidance of carbohydrate restricted diet which can cause hypocitraturia.[45] Urinary metabolic abnormalities that can lead to development of calcium oxalate nephrolithiasis including hyperoxaluria, hypocitraturia and hypercalciuria should be evaluated by a 24 hour stone profile once creatinine is stable after transplant. We also prescribe citrate and calcium supplementation in this group of patients. Altered pharmacokinetics of immunosuppression in this population may explain the high rate of rejection in our cohort. More frequent drug monitoring other than routinely set by transplant centers may be warranted. Aside from close monitoring of tacrolimus, CsA, sirolimus and everolimus after transplant, MPA AUC may be considered in select patients especially if with episodes of rejection or dose interruption.

We recognize the limitations of our study. It is retrospective data, lacking control group and is based on single center experience. Because of concern for enteric oxalosis from malabsoption due to bariatric procedures, we limited our series only to those who had RYGB and jejunoileal bypass. Serum and urine oxalate levels were not measured since patients who developed significant oxalate nephropathy already had advanced kidney disease and about to be initiated on dialysis. Protocol biopsies were not done in our center prior to 2012, and therefore prevalence of oxalate nephropathy and renal pathology among post GB patients with normal renal function after transplant could not be described.

In summary, bariatric surgery is an effective method of weight loss for morbidly obese patients who may otherwise not be considered for renal transplant due to their weight. In our center, post gastric bypass patients did not uniformly develop oxalate nephropathy after renal transplant. Collaboration between transplant centers and bariatric surgery is suggested to manage morbidly obese ESRD patients who fail conservative measures for weight loss. Alternative, less invasive procedures including sleeve gastrectomy and gastric banding although less effective for weight loss, should be discussed if the transplant team is concerned about oxalate nephropathy after RYGB. More systematic studies are needed to elucidate the role of bariatric surgery in treating obese ESRD and waitlist patients.

REFERENCES

[1] Segev DL, Simpkins CE, Thompson RE, *et al*. Obesity impacts access to kidney transplantation. J Am Soc Nephrol. 2008; 19(2): 349-55.

[2] Srinivas TR, Meier-Kriesche HU. Obesity and kidney transplantation. Semin Nephrol. 2013; 33(1): 34-43. http://dx.doi.org/10.1016/j.semnephrol.2012.12.007

[3] Bennett WM, McEvoy KM, Henell KR, *et al*. Kidney transplantation in the morbidly obese: Complicated but still better than dialysis. Clin Transplant. 2011; 25(3): 401-5. http://dx.doi.org/10.1111/j.1399-0012.2010.01328.x

[4] Cannon RM, Jones CM, Hughes MG, *et al*. The impact of recipient obesity on outcomes after renal transplantation. Ann Surg. 2013; 257(5): 978-84. http://dx.doi.org/10.1097/SLA.0b013e318275a6cb

[5] Gill JS, Lan J, Dong J, *et al*. The survival benefit of kidney transplantation in obese patients. Am J Transplant. 2013; 13(8): 2083-90. http://dx.doi.org/10.1111/ajt.12331

[6] Schauer PR, Kashyap SR, Wolski K, *et al*. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med. 2012; 366(17): 1567-76. http://dx.doi.org/10.1056/NEJMoa1200225

[7] Colquitt JL, Picot J, Loveman E, *et al*. Surgery for obesity. Cochrane Database Syst Rev. 2009; (2): CD003641. http://dx.doi.org/10.1002/14651858.CD003641.pub3

[8] Deitel M, Shahi B, Anand PK, *et al*. Long-term outcome in a series of jejunoileal bypass patients. Obes Surg. 1993; 3(3): 247-52. http://dx.doi.org/10.1381/096089293765559250

[9] Drenick EJ, Stanley TM, Border WA, *et al*. Renal damage with intestinal bypass. Ann Intern Med. 1978; 89(5 Pt 1): 594-9. PMid: 717926. http://dx.doi.org/10.7326/0003-4819-89-5-594

[10] Gelbart DR, Brewer LL, Fajardo LF, *et al*. Oxalosis and chronic renal failure after intestinal bypass. Arch Intern Med. 1977; 137(2): 239-43. PMid: 836109. http://dx.doi.org/10.1001/archinte.1977.03630140085017

[11] Hassan I, Juncos LA, Milliner DS, *et al*. Chronic renal failure secondary to oxalate nephropathy: A preventable complication after jejunoileal bypass. Mayo Clin Proc. 2001; 76(7): 758-60. http://dx.doi.org/10.4065/76.7.758

[12] Hicks K, Evans GB, Rogerson ME, *et al*. Jejuno-ileal bypass, enteric hyperoxaluria, and oxalate nephrosis: A role for polarised light in the renal biopsy. J Clin Pathol. 1998; 51(9): 700-2. PMid: 9930077. http://dx.doi.org/10.1136/jcp.51.9.700

[13] Nasr SH, D'Agati VD, Said SM, *et al*. Oxalate nephropathy complicating roux-en-Y gastric bypass: An underrecognized cause of irreversible renal failure. Clin J Am Soc Nephrol. 2008; 3(6): 1676-83. http://dx.doi.org/10.2215/CJN.02940608

[14] Nelson WK, Houghton SG, Milliner DS, *et al*. Enteric hyperoxaluria, nephrolithiasis, and oxalate nephropathy: Potentially serious and unappreciated complications of roux-en-Y gastric bypass. Surg Obes

Relat Dis. 2005; 1(5): 481-5. http://dx.doi.org/10.1016/j.soard.2005.07.002

[15] Troxell ML, Houghton DC, Hawkey M, *et al*. Enteric oxalate nephropathy in the renal allograft: An underrecognized complication of bariatric surgery. Am J Transplant. 2013; 13(2): 501-9. http://dx.doi.org/10.1111/ajt.12029

[16] Kumar R, Lieske JC, Collazo-Clavell ML, *et al*. Fat malabsorption and increased intestinal oxalate absorption are common after roux-en-Y gastric bypass surgery. Surgery. 2011; 149(5): 654-61. http://dx.doi.org/10.1016/j.surg.2010.11.015

[17] Nelson WK, Houghton SG, Milliner DS, *et al*. Enteric hyperoxaluria, nephrolithiasis, and oxalate nephropathy: Potentially serious and unappreciated complications of roux-en-Y gastric bypass. Surg Obes Relat Dis. 2005; 1(5): 481-5. http://dx.doi.org/10.1016/j.soard.2005.07.002

[18] Asplin JR, Coe FL. Hyperoxaluria in kidney stone formers treated with modern bariatric surgery. J Urol. 2007; 177(2): 565-9. http://dx.doi.org/10.1016/j.juro.2006.09.033

[19] Duffey BG, Alanee S, Pedro RN, *et al*. Hyperoxaluria is a long-term consequence of roux-en-Y gastric bypass: A 2-year prospective longitudinal study. J Am Coll Surg. 2010; 211(1): 8-15. http://dx.doi.org/10.1016/j.jamcollsurg.2010.03.007

[20] Hofmann AF, Laker MF, Dharmsathaphorn K, *et al*. Complex pathogenesis of hyperoxaluria after jejunoileal bypass surgery. oxalogenic substances in diet contribute to urinary oxalate. Gastroenterology. 1983; 84(2): 293-300. PMid: 6848409.

[21] Maalouf NM, Tondapu P, Guth ES, *et al*. Hypocitraturia and hyperoxaluria after roux-en-Y gastric bypass surgery. J Urol. 2010; 183(3): 1026-30. http://dx.doi.org/10.1016/j.juro.2009.11.022

[22] Kleinman JG. Bariatric surgery, hyperoxaluria, and nephrolithiasis: A plea for close postoperative management of risk factors. Kidney Int. 2007; 72(1): 8-10. http://dx.doi.org/10.1038/sj.ki.5002284

[23] Rogers CC, Alloway RR, Alexander JW, *et al*. Pharmacokinetics of mycophenolic acid, tacrolimus and sirolimus after gastric bypass surgery in end-stage renal disease and transplant patients: A pilot study. Clin Transplant. 2008; 22(3): 281-91. http://dx.doi.org/10.1111/j.1399-0012.2007.00783.x

[24] Chenhsu RY, Wu Y, Katz D, *et al*. Dose-adjusted cyclosporine c2 in a patient with jejunoileal bypass as compared to seven other liver transplant recipients. Ther Drug Monit. 2003; 25(6): 665-70. PMid: 14639052. http://dx.doi.org/10.1097/00007691-200312000-00004

[25] Park AM, Storm DW, Fulmer BR, *et al*. A prospective study of risk factors for nephrolithiasis after roux-en-Y gastric bypass surgery. J Urol. 2009; 182(5): 2334-9. http://dx.doi.org/10.1016/j.juro.2009.07.044

[26] Rudman D, Dedonis JL, Fountain MT, *et al*. Hypocitraturia in patients with gastrointestinal malabsorption. N Engl J Med. 1980; 303(12): 657-61. http://dx.doi.org/10.1056/NEJM198009183031201

[27] Chen CL, Fang HC, Chou KJ, *et al*. Acute oxalate nephropathy after ingestion of star fruit. Am J Kidney Dis. 2001; 37(2): 418-22. PMid: 11157385. http://dx.doi.org/10.1053/ajkd.2001.21333

[28] Nasr SH, Kashtanova Y, Levchuk V, *et al*. Secondary oxalosis due to excess vitamin C intake. Kidney Int. 2006; 70(10): 1672. http://dx.doi.org/10.1038/sj.ki.5001724

[29] Beebe DK, Walley E. Diabetic diarrhea. an underdiagnosed complication? Postgrad Med. 1992; 91(8): 179-86. PMid: 1603750.

[30] Crook ED, Cook WJ, Bergman SM. Rapid renal deterioration secondary to oxalate in a patient with diabetic gastroenteropathy. Am J Kidney Dis. 1995; 26(1): 68-71. http://dx.doi.org/10.1016/0272-6386(95)90156-6

[31] Ogbonnaya KI, Arem R. Diabetic diarrhea. pathophysiology, diagnosis, and management. Arch Intern Med. 1990; 150(2): 262-7. http://dx.doi.org/10.1001/archinte.1990.00390140018005

[32] Kohri K, Kodama M, Umekawa T, *et al*. Calcium oxalate crystal formation in patients with hyperparathyroidism and hyperthyroidism and related metabolic disturbances. Bone Miner. 1990; 8(1): 59-67. http://dx.doi.org/10.1016/0169-6009(91)90141-L

[33] Koide T, Yoshioka T, Oka T, *et al*. Promotive effect of urine from patients with primary hyperparathyroidism on calcium oxalate crystal aggregation in an in vitro whole urine system. J Urol. 1988; 140(6): 1571-4. PMid: 3193546.

[34] Worcester EM, Fellner SK, Nakagawa Y, *et al*. Effect of renal transplantation on serum oxalate and urinary oxalate excretion. Nephron. 1994; 67(4): 414-8. PMid: 7969673. http://dx.doi.org/10.1159/000188014

[35] Armstrong WD. Correction: Hypocitraturia in patients with gastrointestinal malabsorption. N Engl J Med. 1981; 304(9): 547. http://dx.doi.org/10.1056/NEJM198102263040926

[36] Rudman D, Dedonis JL, Fountain MT, *et al*. Hypocitraturia in patients with gastrointestinal malabsorption. N Engl J Med. 1980; 303(12): 657-61. http://dx.doi.org/10.1056/NEJM198009183031201

[37] Borchhardt KA, Heinzl H, Mayerwoger E, *et al*. Cinacalcet increases calcium excretion in hypercalcemic hyperparathyroidism after kidney transplantation. Transplantation. 2008; 86(7): 919-24. http://dx.doi.org/10.1097/TP.0b013e318186b7fb

[38] Seager CM, Srinivas TR, Flechner SM. Development of nephrolithiasis in a renal transplant patient during treatment with cinacalcet. Ann Transplant. 2013; 18: 31-5. http://dx.doi.org/10.12659/AOT.883809

[39] Bushinsky DA, Laplante K, Asplin JR. Effect of cinacalcet on urine calcium excretion and supersaturation in genetic hypercalciuric stone-forming rats. Kidney Int. 2006; 69(9): 1586-92.

[40] Courbebaisse M, Diet C, Timsit MO, *et al*. Effects of cinacalcet in renal transplant patients with hyperparathyroidism. Am J Nephrol. 2012; 35(4): 341-8. http://dx.doi.org/10.1159/000337526

[41] Marterre WF, Hariharan S, First MR, *et al*. Gastric bypass in morbidly obese kidney transplant recipients. Clin Transplant. 1996; 10(5): 414-9. PMid: 8930454.

[42] Watanabe Y, Sato M, Abe Y, *et al*. Enteric absorption of FK 506: Estimation by a block liver perfusion technique in rats. Transplant Proc. 1998; 30(7): 3777-8. http://dx.doi.org/10.1016/S0041-1345(98)01233-0

[43] Holmes RP, Kennedy M. Estimation of the oxalate content of foods and daily oxalate intake. Kidney Int. 2000; 57(4): 1662-7. http://dx.doi.org/10.1046/j.1523-1755.2000.00010.x

[44] Massey LK, Palmer RG, Horner HT. Oxalate content of soybean seeds (glycine max: Leguminosae), soyfoods, and other edible legumes. J Agric Food Chem. 2001; 49(9): 4262-6. PMid: 11559120. http://dx.doi.org/10.1021/jf010484y

[45] Zuckerman JM, Assimos DG. Hypocitraturia: Pathophysiology and medical management. Rev Urol. 2009; 11(3): 134-44. PMid: 19918339.