

Introduction and Objectives

Glomerulonephritis (GN) is a common cause of chronic kidney disease (CKD) and end stage renal disease (ESRD) which is associated with significant mortality.¹ Treatment may include immunosuppressants (IS) such as glucocorticoids which decrease glomerular destruction, hence inducing remission and reducing ESRD. However, these agents have significant metabolic effects such as altering glucose and lipid homeostasis which can lead to atherosclerosis and cardiovascular diseases.² We thus aimed to evaluate metabolic complications in patients with glomerular diseases treated with IS.

Methods

- This was a retrospective cohort study of adults with biopsy-proven GN diagnosed between 1st January 2011 and 31st July 2015.
- Patients under the following categories were excluded: <21 years old, no IS therapy received, pre-existing diabetes mellitus (DM) or hyperlipidemia, treatment with anti-diabetic and anti-lipid medications prior to IS and history of previous kidney transplant
- Demographic, comorbidity, clinical and pharmacotherapy data were retrieved from electronic medical records.
- The most recent laboratory values for fasting glucose, triglyceride (TG), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) within 6 months preceding kidney biopsy and the peak values within 6 months after IS therapy, as well as need for anti-lipid medications after diagnosis and IS therapy were recorded.

Results

- Among the 198 patients studied, majority were female (68.8%) with the ethnicity composition of 151 Chinese (75.9%), 32 Malays (16.1%), 4 Indians (2.0%) and 11 classified as Others (6.0%).
- The most common GN diagnoses were Lupus Nephritis (43.7%), minimal change disease or focal segmental glomerulosclerosis (20.1%), Ig A nephropathy (14.1%), membranous nephropathy (6%), ANCA-associated vasculitis (3.0%) and Others (12.1%).
- Median follow up was 31.8 (14.1, 52.3) months.
- For pre-biopsy blood pressure, median systolic blood pressure was 125 (114, 136) mm Hg while median diastolic blood pressure was 71 (66, 80) mm Hg.
- Median pre-biopsy HbA1c is 5.3 (4.7, 6.0) %.
- Compared to before IS therapy, post-IS metabolic profile showed the following trend: plasma glucose (5.8 (5.0, 7.1) vs. 5.1 (4.7, 6.0) mmol/L, p<0.001) and HDL levels (1.48 (1.15, 1.89) vs 1.21 (0.94, 1.82) mmol/L, p=0.01) increased while TG (1.42 (1.01, 2.04) vs. 1.51 (1.11, 2.25) mmol/L, p=0.03) and LDL levels (3.47 (2.58, 4.43) vs. 3.48 (2.65, 4.96) mmol/L, p=0.05) decreased.
- Anti-lipid medications were prescribed in 88 patients (44.4%) after IS therapy. Patients who required anti-lipid medications were compared with those who did not require them (Table 1).
- Baseline demographics was similar for both groups. However, compared to patients who did not require anti-lipid medications, patients who required them had higher UPCR and pre-biopsy LDL.
- Patients who required anti-lipid medications received higher prednisolone doses but this was not statistically significant (p=0.06).
- None of the other immunosuppressants studied (calcineurin inhibitors, cyclophosphamide, mycophenolate mofetil and azathioprine) were associated with need for anti-lipid medications (p>0.05).

Table 1: Patients' demographics, baseline comorbidities, metabolic profile and pharmacological therapy

	All Patients N= 198	Requires anti-lipid medications N=88	Does not require anti- lipid medications N=110	p-value
Demographics				
Age of Diagnosis, years	42.5 (31.7, 52.8)	45.2 (32.3, 57.2)	40.6 (28.8, 50.4)	0.19
Male, n (%)	62 (31.2)	30 (34.1)	32 (29.1)	0.45
Chinese, n (%)	151 (75.9)	64 (72.7)	86 (78.2)	0.37
Pre-biopsy baseline comorbidities				
Hypertension, n (%)	51 (25.8)	18 (20.5)	33 (30.0)	0.13
Serum creatinine, µ mol/L	92 (63, 170)	97 (67, 188)	91 (60, 161)	0.19
UPCR, g/g	3.46 (1.40, 7.02)	4.46 (1.90, 8.89)	2.68 (1.27, 5.66)	0.002
Pre-biopsy metabolic profile				
Plasma glucose, mmol/L	5.1 (4.7, 6.0)	5.0 (4.6, 5.8)	5.2 (4.7, 6.1)	0.23
TG, mmol/L	1.51 (1.11, 2.25)	1.68 (1.27, 2.29)	1.49 (1.08, 1.96)	0.09
LDL, mmol/L	3.48 (2.65, 4.96)	4.29 (3.03, 6.52)	3.02 (2.25, 3.79)	<0.001
HDL, mmol/L	1.21 (0.94, 1.82)	1.43 (0.95, 1.88)	1.15 (0.94, 1.58)	0.34
Pre-biopsy medications				
Immunosuppressants, n (%)	68 (34.2)	25 (28.4)	43 (39.1)	0.11
Glucocorticoids, n (%)	71 (35.7)	29 (33.0)	42 (38.2)	0.44
Post-biopsy medications				
Glucocorticoids, n (%)	191 (96.5)	84 (95.5)	107 (97.3)	0.70
Prednisolone dose, mg/day*	45 (25, 55)	50 (30, 55)	40 (20, 50)	0.06
Cyclosporine, n (%)	20 (10.1)	12 (13.6)	8 (7.3)	0.14
Tacrolimus, n (%)	9 (4.5)	2 (2.3)	7 (6.4)	0.30
MMF, n (%)	111 (56.0)	49 (55.7)	62 (56.4)	1.00
Azathioprine, n (%)	54 (27.1)	19 (21.6)	35 (34.8)	0.11
Cyclophosphamide, n (%)	40 (20.2)	15 (17.0)	25 (22.7)	0.32
Hydroxychloroquine, n (%)	91 (46.0)	34 (38.6)	57 (52.3)	0.06

*Doses refer to peak dose within 1 month from biopsy

Abbreviations: UPCR = urine protein-to-creatinine ratio, TG = triglyceride, LDL = low-density lipoprotein, HDL = high-density lipoprotein, MMF = mycophenolate mofetil

Conclusion

Derangement in glucose and lipid metabolism is common among non-diabetic, normolipic patients with GN treated with IS.

References:

- Vinen, C.S. and Oliveira, D.B.G. (2003) Acute glomerulonephritis. *Postgraduate Medical Journal*, 79: 206-213
- Subramanian S and Trencle, D.L. (2008) Immunosuppressive Agents: Effects on Glucose and Lipid Metabolism. *Endocrinology & Metabolism Clinics of North America*, 36(4): 891-905