Retrospective Analysis of the Outcomes of Mycophenolate Therapy in Retarding the Progression of Immunoglobulin A Nephropathy (REMISSION IgA)”

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An Extracorporeal Nephrology Group Initiative

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This retrospective single-center study from Christian Medical College, Vellore, aimed to assess whether mycophenolate mofetil (MMF), when added to steroids and ARBs, slows the progression of IgA nephropathy (IgAN) compared to standard therapies.

- Sample size: 515 patients with biopsy-proven IgAN and eGFR >15 ml/min/1.73m².
- Groups:
  - ARB alone (n=100)
  - ARB + Steroids (A+S) (n=130)
  - ARB + Steroids + MMF (A+S+M) (n=285)

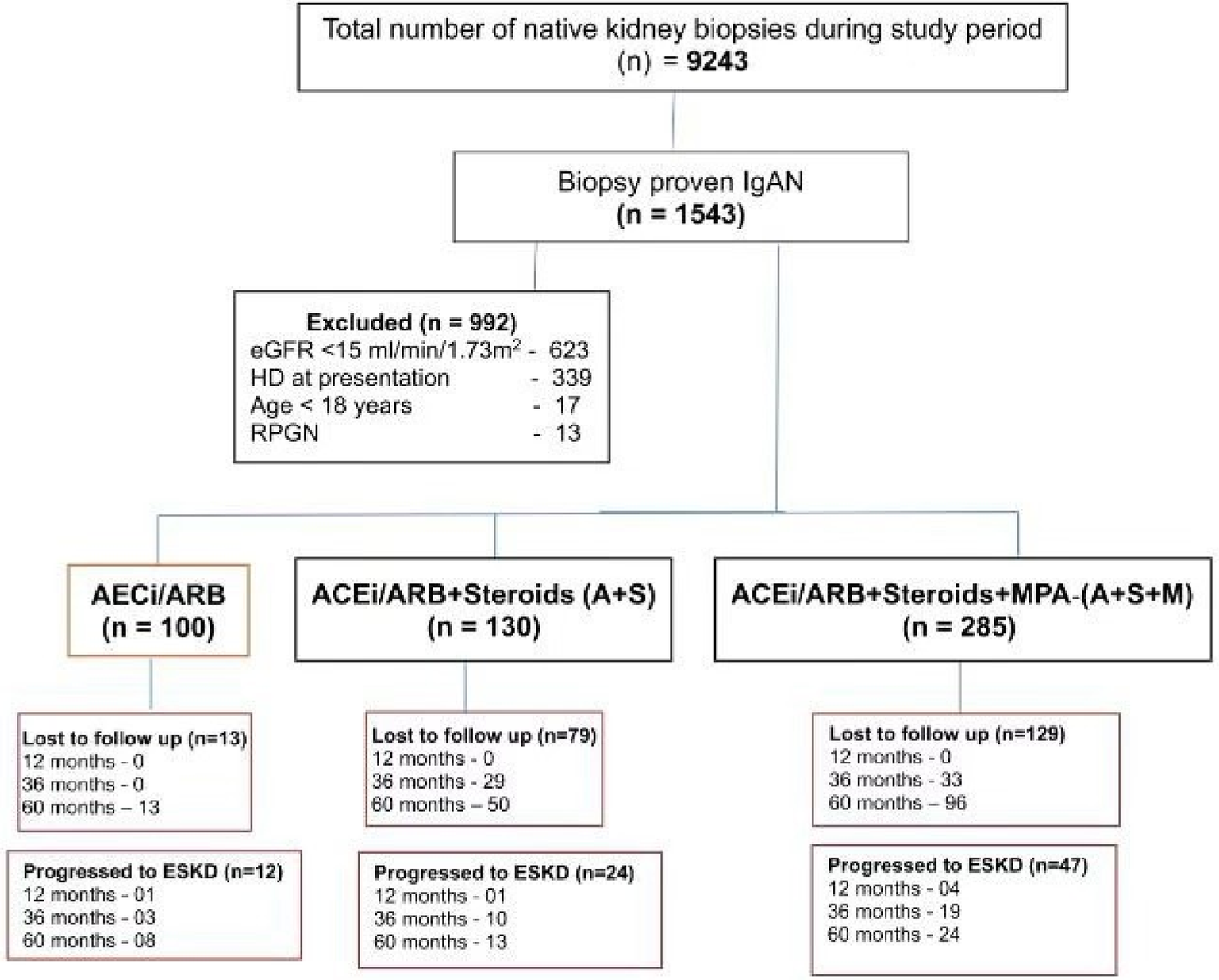

Figure 1: Study flow chart. ACEi: Angiotensin converting enzyme inhibitors, ARB: Angiotension receptor blockers, eGFR: Estimated glomerular filtration rate, ESKD: End stage kidney disease, HD: Hemodilaysis, IgAN: Immunoglobulin A neprhopathy, MMF: Mycophenolic acid, RPGN: Rapidly progressive glomerulonephriti.

- Follow-up duration: up to 60 months.
- Primary outcome: progression to End Stage Kidney Disease (ESKD)
- Result: No statistically significant difference in ESKD progression between the steroid (18.4%) and MMF groups (16.4%), though MMF group showed a trend toward better renal preservation.

Table 2: Comparison of ARB+Steroid and ARB+Sterois+MPA groups

Variable	ARB + Steroid group	ARB + Steroid + MPA	p value
Age	37.04±10.43	37.41±9.94	0.73
eGFR (ml/min/1.73m^2) at			
Baseline	48.73 (35.77, 75.84)	45.60 (32.00, 62.85)	0.01
12 months	57.74 (40.05, 86.58)	48.71 (37.07, 70.30)	0.02
36 months	50.00 (35.40, 83.84)	48.90 (33.95, 68)	0.13
60 months	49.21 (23.10, 82.10)	43.60 (26.05, 68.73)	0.42
Up/Uc (g/g) at			
Baseline	1.59 (0.79, 2.54)	1.88 (0.97, 3.29)	0.14
12 months	0.38 (0.15, 0.94)	0.56 (0.23, 1.10)	0.02
36 months	0.48 (0.15, 1.10)	0.55 (0.23, 1.00)	0.38
60 months	0.67 (0.21,1.17)	0.62 (0.26, 1.28)	0.56
No. of patients progressed to ESKD at 60 months	24	47	RR-0.96

Mann-Whitney test, Age expressed in mean + standard deviation, eGFR and Up/Uc– expressed in Median & Inter Quartile ranges (0.25, 0.75), Relative risk 0.96 and the chi-square statistic is 0.24, the p-value is 0.62. ARB: Angiotensin receptor blocker, MPA: mycopheolate acid, RR: Relative risk, Up/Uc: Urine protein creatinine ratio, eGFR: estimated glomerular filtration rate, ESKD: End stage kidney disease.

Salient Features

- Disease burden: IgAN accounted for 16.7% of kidney biopsies.
- Baseline: Most patients were middle-aged (mean ~36 years), male predominant (~2:1), and hypertensive (~89%).
- eGFR trend: Stable or mildly declining eGFR over time in all groups; MMF group showed slight advantage at 36 months but not at 60 months.
- Proteinuria (Up/Uc): Reduced across groups, with better control initially in the steroid group.

- Side effects:
  - Steroid group: diabetes (13.8%), AVN (2.3%)
  - MMF group: leucopenia (11.5%), infections (rare)
- Kaplan-Meier analysis: No significant survival advantage with MMF ($p = 0.65$).
- Cost & adherence: A few patients stopped MMF due to financial constraints.

Critical Appraisal

Strengths

- Large cohort for a single-center study in South Asia.
- Real-world setting reflects clinical practice.
- Longitudinal data over 5 years.
- Addresses a relevant clinical gap: steroid-sparing options in IgAN management.

Limitations

- Retrospective design limits control over confounders.
- Non-randomized treatment allocation may introduce selection bias.
- Unequal group sizes reduce statistical power.
- Lack of MEST-C histological scores for all patients.
- Side effect reporting likely underestimated (retrospective data).
- No SGLT2i use due to the historical period studied (2010–2017).

Table 3: Comparison of present study with previous studies on mycophenolate therapy in IgA Nephropathy

Parameter	Present study	Chen[19] (2002)	Frisch[20] (2005)	Hogg[21] (2015)	Hou[22] (2017)	MAIN Trial[23]
Place of study	India, 2024	China	America	Canada	China	China
Type of study	Retrospective study	RCT	RCT	RCT	RCT	RCT
Duration	2010-2017	2002	2005	2015	2017	2013-2015
No. of patients included	515	62	32	44	174	85
Comparing groups	MMF/Prednisolone	MMF/Prednisolone	MMF/RASi	MMF/Placebo	MMF/Prednisolone	MMF/Standard of care alone
Sample size in each group	130/285	31/31	17/15	22/22	86/88	85
Follow up	60 months	18 months	24 months	6 months	6 months	60 months
Outcomes assessed	eGFR/ proteinuria/ ESKD	Clinical remission (Proteinuria)	Clinical remission /eGFR/ESKD	Complete remission (Up/Uc-0.2g/g)	Complete remission, ESKD	Doubling of creatinine, ESKD
Outcomes	Progressed to ESKD in MMF group - 16.4%	Remission rate MMF- 44.4%	In both groups, all patients reached ESRD.	MMF did not reduce proteinuria significantly	At 12 months, complete remission rates were 48% and 53% in the MMF and prednisone groups, respectively (p-0.06)	Progressed to ESKD in MMF group - 8.2%
	Progressed to ESKD in steroid group - 18.4%	Remission rate in steroid group - 19.1%				Progressed to ESKD in other group 27.1%

RCT: Randomized controlled trial, MMF: Mycophenolate mofetil, ESKD: End stage kidney disease, RASi: Renin angiotensin aldosterone system inhibitors, Up/Uc: Urine protein creatinine ratio, eGFR: Estimated glomerular filtration rate.

Interpretation & Clinical Relevance

- MMF as adjunct therapy to steroids and ARBs showed comparable efficacy to steroids alone in slowing disease progression.
- Not statistically significant, but a clinically favorable trend in ESKD prevention supports further exploration.
- Highlights the need for RCTs in Indian populations and tailored protocols (e.g., MMF AUC targeting in glomerular diseases).

Recommendations

- MMF may be considered in IgAN patients, particularly those intolerant to high-dose steroids.
- Future RCTs with balanced arms, clear inclusion criteria, and standardized immunosuppression are needed.

Thank you