Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*

Clinical and Histologic Prognostic Factors of IgA Vasculitis in Adults

Student Investigator's Name

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Date of Submission *(mm/dd/yyyy)*

3/17/2022

Graduation Year

2022

Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*

Scholarly Projects Curriculum

Co-Investigators *(Names, departments; institution if not OHSU)*

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Mentor's Name

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Concentration Lead's Name

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Project/Research Question

What are the clinical and histologic prognostic indicators of progression to kidney disease in adult patients with IgA vasculitis?

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*

Retrospective clinical analysis

Key words *(4-10 words describing key aspects of your project)*

IgA Vasculitis, MEST-C Score/Oxford Score

Meeting Presentations

If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).

Publications *(Abstract, article, other)*

If your project was published, please provide reference(s) below in JAMA style.

Submission to Archive

Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).

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Next Steps

What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

Next steps that would build on this project would be sharing our RedCap data collection tool with other groups to form an IgA Vasculitis repository. Next steps also included validating our preliminary analysis and completing remaining aspects of the analysis.

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*
This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

X _____
Student's full name

Mentor's Approval *(Signature/date)*

X _____
Mentor Name

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Report*: Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

Background: IgA Vasculitis (IgAV) is a systemic small vessel vasculitis that affects the skin, joints, gastrointestinal tract, and kidneys. IgAV is the one of the most common glomerulonephritides in children, yet it is rare in adults and is associated with a worse prognosis.

Significance: Though histologically similar to Immunoglobuin A Nephropathy (IgAN), IgAV is a systemic disease that has a unique clinical course. A few large retrospective trials in adults have shown that IgAV patients with a greater degree of proteinuria, kidney insufficiency at time of biopsy, and hypertension have worse overall prognosis and that 1/3 of these patients develop progressive kidney disease.

A scoring index known as the Oxford Classication (MEST-C classification) has been used to prognose patients with IgAN. Retrospective cohort studies in European and Asian populations have evaluated the prognostic capabilities of the Oxford classification for IgAV and have had varying results.

Study Objective: The goal of this study is to explore clinical and histologic prognostic factors (using the Oxford Classification) that predispose IgAV patients to progressive kidney disease. We also hope to compile and analyze treatment data. Identification of factors that are predictive of poor outcomes will improve patient treatment plans and education.

Study Aims:

A. To determine clinical predictors of progressive CKD in IgAV.

Hypothesis: Older age, initial renal insufficiency, degree of proteinuria, presence of macroscopic hematuria, and presence of hypertension are indicators of "kidney progressor status."

B. Determine histologic predictors of progressive CKD in IgAV; evaluate which measures of the MEST- C scoring system are prognostic of progression.

Hypothesis: MEST-C scoring is predictive of progressive CKD in IgAV

M – mesangial hypercellularity

E – endocapillary proliferation

S – segmental glomerulosclerosis

T – tubular atrophy and interstitial fibrosis C – crescents

C. To compile commonly used treatments for IgAV and to analyze treatment efficacy

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Hypothesis: Immunosuppressive therapy reduces the risk of progressive kidney disease.

Methods *(≥250 words)*

•**Design:** Retrospective cohort analysis of adult patients with IgA Vasculitis

•**Participants:** Local sample of ~30 OHSU patients from Cohort Discovery Tool

•**Primary Outcome**: Progressive kidney disease. A "kidney progressor" is defined as an IgA Vasculitis patient with nephrotic range proteinuria (> 1g/d), or > 30% creatinine elevation within 1 year of kidney biopsy, or ESRD

Inclusion Criteria:

- Age>18
- At least one of the following symptoms consistent with IgAV (cutaneous palpable purpura, arthritis, bowel angina) or a chart diagnosis of IgA vasculitis
- Kidney biopsy consistent with IgAV (mesangial IgA deposits)
- >8 glomeruli on kidney biopsy for evaluation

Exclusion Criteria:

- patients with IgA nephropathy on biopsy without systemic symptoms
- patients with SLE or cryoglobulinemia
- patients with clinical history of liver dysfunction
- patients with inflammatory bowel disease
- patients with acute staph infection at time of biopsy

Comparison Groups

•What are the defining clinical and histologic (MEST-C) features of an IgAV progressor vs. non-progressor?
•What are the defining clinical and histologic features between treated IgAV patients and non-treated patients?
•Do the patients included have other conditions at the time of kidney biopsy?
•What are the most common causes of death for IgAV patients?

Data Collection Methods and Statistical Analysis:

Data collection for each patient was done by chart review (specifics of data collected included in the following section). Once data collection was complete, preliminary analysis in SPSS with basic Pearson Correlation and Logistic Regressions were utilized between variables of interest, with a p value of <.05 showing significance.

Results *(≥500 words)*

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Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
Step 1[a]	Ages	.007	.074	.008	1	.930	1.007	.870	1.165
	SystolicBP	.090	.058	2.420	1	.120	1.095	.977	1.227
	Proteinuria	.031	.094	.112	1	.738	1.032	.858	1.241
	Base	.781	1.178	.440	1	.507	2.184	.217	22.001
	Constant	-13.073	7.769	2.832	1	.092	.000		

a. Variable(s) entered on step 1: Ages, SystolicBP, Proteinuria, Base.

Correlations

		Age	Baseline	Six	Twelve
Age	Pearson Correlation	1	.075	-.386	-.174
	Sig. (2-tailed)		.748	.140	.570
	N	21	21	16	13
Baseline	Pearson Correlation	.075	1	-.012	.887**
	Sig. (2-tailed)	.748		.965	<.001
	N	21	21	16	13
Six	Pearson Correlation	-.386	-.012	1	.998**
	Sig. (2-tailed)	.140	.965		<.001
	N	16	16	16	11
Twelve	Pearson Correlation	-.174	.887**	.998**	1
	Sig. (2-tailed)	.570	<.001	<.001	
	N	13	13	11	13

**. Correlation is significant at the 0.01 level (2-tailed).

Data collection methods:

A cohort discovery tool for OHSU's was used to identify possible patients with IgA Vasculitis, which yielded roughly 200 patients. From this database, a final group of 24 patients with strongly suspected or confirmed IgA vasculitis (using our inclusion and exclusion criteria) were selected for preliminary analysis. For each of the included patients, initial clinical data at the time of presentation and biopsy with MEST-C score at the time of presentation were collected. Clinical data at 6 months, 12 months, and time of last follow up were collected if available. Clinical data included: systolic and diastolic blood pressure, creatinine, eGFR, urine protein: creatinine ratio, and presence of hematuria. Treatment at time of presentation, adverse events in response to treatment, and relapse during the follow up period were also recorded if

present. Other clinical outcomes recorded for each patient were progression to ESRD, initiation of dialysis, need for renal transplant, diagnosis of malignancy, and cause of death.

Once all of the above data was collected, patients were initially sorted into “progressors” or “non-progressors” using the following criteria: progresors were defined as patients with nephrotic range proteinuria (> 1g/d), or > 30% creatinine elevation within 1 year of kidney biopsy, or ESRD.

No significant correlations were found in this preliminary analysis between age, initial degree of proteinuria, or hypertension with progressor status, which conflicts with the findings of existing studies. Baseline creatinine was not associated with progressor status, but a significant correlation was found between initial creatinine and last follow up creatinine. Correlations between biopsy indicators (individual aspects of the MEST-C score) and progressor status were not yet assessed, as all included patients did not have MEST-C scores at the time of preliminary analysis. A correlation between the presence of hematuria and progressor status was also not assessed.

From initial qualitative assessment, the most common treatments utilized for this cohort of patients were corticosteroids, mycophenolate mofetil, and azathioprine. Correlations between treatment and progressor status were not assessed.

Discussion *(≥500 words)*

Current studies have established that initial degree of proteinuria, presence of hematuria, age, and baseline creatinine at presentation, along with the presence of segmental sclerosis on kidney biopsy, are early indicators of kidney progression in adults with IgA Vasculitis. Our early analysis did not validate these findings, but this was likely due to our extremely small sample size (other studies were at minimum five times the size) and errors in assigning patients to progressor versus non-progressor status. For example, a few patients who received renal transplant were not included in the progressor cohort, as their clinical data did not meet criteria for progressor at the 12 month follow up. The data in our preliminary analysis will need to be validated in addition to completing a final analysis including our other variables of interest. Furthermore, it is important for us to characterize the demographics of this cohort of patients to compare with existing studies’ cohorts.

Strengths of this study include studying a unique, predominantly caucasian population of IgA vasculitis adults compared with existing studies. Our research design in redcap can also be utilized by other groups studying IgA Vasculitis in adults in the future, and provides a structure for flexible retrospective analyses. Finally, we were able to do a more thorough chart review for each patient included in the study, as our patients data was readily available in Epic electronic charts.

Limitations of the study were many and include a small sample size and need for improved standardization of inclusion criteria and chart review processes. This was due to different levels of training and experience with the chart review process. Exclusion of patients with IgA nephropathy or other non-IgA Vasculitis autoimmune processes could also be improved upon.

Future directions for this study include continued analysis of our data, specifically correlations between each aspect of the MEST-C score and progressor status, correlations between treatment and progressor status, comorbidities most associated with IgA Vasculitis at the time of presentation, and leading causes of

death. Future studies could also assess development of the condition after medication exposure as well as the most common complications in adults with IgA Vasculitis, such as intussusception, and complication rates.

Overall, our study is a useful addition to the literature in the landscape of adults with IgA Vasculitis. We developed an important framework for approaching patients with this condition which can be utilized by other groups in the future, as IgA Vasculitis is a rare condition without solid understanding about what makes a patient progress to kidney disease versus spontaneously remit, and currently without an established standard of care.

Conclusions *(2-3 summary sentences)*

Based on our initial findings with 24 patients, no significant correlations can be assumed between age, degree of proteinuria, or hypertension at time of presentation and "progressor status" for adult patients with IgA Vasculitis. It is possible these correlations will change with additional included patients, but the small sample size is a main limiting factor in being able to validate the findings of existing studies. We have yet to compile and analyze possible correlations between hematuria, MEST-C scores from patient biopsies, and treatment with progressor status.

References *(JAMA style format)*

1.Audemard-Verger A et al; French Vasculitis Study Group. Characteristics and Management of IgA Vasculitis (Henoch-Schönlein) in Adults. Arthritis Rheumatol. 2017; 69(9):1862-1870.

2.Audemard-Verger A et al. IgA vasculitis (Henoch-Shönlein purpura) in adults: Diagnostic and therapeutic aspects. Autoimmun Rev. 2015; 14(7):579-85.

3.Pillebout E et al. Henoch-Schönlein Purpura in adults: outcome and prognostic factors. J Am Soc Nephrol. 2002;;13(5):1271-8.

4.Villatoro-Villar M et al. Clinical Characteristics of Biopsy-Proven IgA Vasculitis in Children and Adults: A Retrospective Cohort Study. Mayo Clin Proc. 2019; 94(9):1769-1780.