Pregnancy Outcomes in C3 Glomerulopathy

Lauren O. Fergus [1], Monica D. Hall [1, 2], Lynn Vining [1, 2], Yuzhou Zhang [1], Richard J. Smith [1, 2], Carla M. Nester [1, 2]
[1]Molecular Otolaryngology and Renal Research Laboratories, [2]The University of Iowa Hospitals and Clinics

University of Iowa Stead Family Children's Hospital

The University of Iowa

Background

C3 Glomerulopathy (C3G) is a glomerular disease characterized by underlying dysregulation of the alternative complement pathway. A majority of patients approach ESKD within ten years of diagnosis. Recurrence in renal transplants is high. Little is known of the role of pregnancy in the natural history of C3G or whether a coincident diagnosis affects comorbidities or maternal-fetal outcomes.

Methods

Female subjects in the University of Iowa's C3G Natural History Study who met consensus biopsy criteria (n=76) and had at least one pregnancy (n=17) were included in the cohort. Clinical and lab data, including genetic and acquired drivers of disease studies were assessed. Standard peri-pregnancy outcomes were considered. Pregnancy data from women with IgA Nephropathy and unspecified GN was utilized as a control.

Results

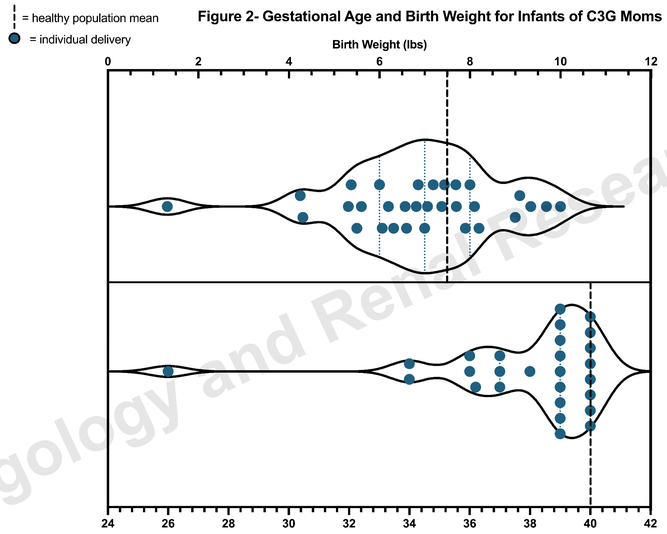

Figure 2- Gestational Age and Birth Weight for Infants of C3G Moms

Average gestational age was 37w 5d, with a range from 26w 2d-40w 3d. Average birth weight was 6.9 lbs, ranging from 1.3-10 lbs.

Figure 1- Peri-Pregnancy Outcomes in C3G Mothers

				n		
# of Pregnancies				44		
# of Live Births				34		
Average Age at Conception				26		
Average # of Children/Mother				2		
	n	Sample %	Healthy %	p value	Glomerular Disease %	p value
# of Preeclamptic Pregnancies	11	32.40%	4%	**<.0001**	approx. 9% (IgA nephropathy), 16-58% (unspecified GN)	**<.0001 (IgA),** .29 (unsp. GN, avg of 37%)
# of Premature Infants	7	20.60%	9.80%	**0.0171**	14.2% (IgA)	0.1425 (IgA)
# of Low Birth Weight Infants	5	14.70%	8%	0.075	13.1% (IgA)	0.3911 (IgA)
# of Eclamptic Pregnancies	0	0%	0.30%	0.625	N/A	N/A
# of C-Sections	6	17.60%	17%	0.46	49.1% (IgA)	**0.0001 (IgA)**
# of Miscarriages	8	18.20%	15%	0.2761	0-30% (IgA), 5-27% (unsp. GN),	.35 (IgA, avg of 15%), .28 (unsp. GN, avg of 16%)
Biopsy Performed	Before pregnancy n = 4		Between pregnancies n = 2		After pregnancy n = 11	
C3G Symptoms	Before pregnancy n = 4		Between pregnancies n = 2	During pregnancy n = 6	After pregnancy n = 5	

A one-proportion z-test was utilized to calculate p values from the cohort data and literature values for healthy populations and for other glomerular diseases, with a significance level set at .05. Low birth weight cutoff was 5.5 lbs, while premature birth cutoff was 37 weeks.

44 pregnancies and 34 deliveries were identified. Non-live birth pregnancy outcomes included eight miscarriages, one ectopic pregnancy and one elective abortion. The presumed driver of disease was known for eight patients; gene variants of unknown significance (n=3), nephritic factors (n=4), and a monoclonal protein (n=1). Six patients presented first C3G symptoms during pregnancy. Preeclampsia developed in 11. Six infants were premature. Five were born with low birth-weight. One infant suffered a stroke. One infant presented with AKI. [Maternal nephritic factor was identified in neonatal sera.]

Conclusions

We provide a summary of maternal-fetal outcomes in C3G mothers.

- Our data supports an increased risk of preeclampsia and prematurity in C3G mothers, compared to healthy mothers.
- While there was a trend toward lower birth weight, the difference was not statistically significant.
- A relatively higher risk of preeclampsia and lower risk of cesarean section as compared to women with IgA Nephropathy was identified.
- A similar risk of miscarriage, prematurity, and low-birth-weight was identified as compared to other GNs.
- Our data indicates that while most pregnancies in C3G are uneventful, the risk of preeclampsia, prematurity and the potential for a low-birth-weight infant supports the need for a collaborative approach between nephrology and high-risk OB.

Limitations and Future Directions

The limitations of our study include small sample size and limited availability of drivers of disease data. Future research will include defining trends in lab values over time and an exploration of the role of complement biomarkers in C3G related pregnancies.

References

1. *Am. J. Nephrol.*, 44(3), 187–193, (2016)
2. *Clin. J. Am. Soc. Nephrol.,* 12(11), 1862-1872, (2017)
3. *Am J Kidney Dis.,* 34(6), 1129-1131, (1999)

Research is funded in part by the NIH (CMN and RJHS), an unrestricted grant from Novartis and generous family related philanthropy.