Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) \(^1\) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines \(^2\).

Search Strategy

A combination of medical subject heading (MeSH) terms and keywords were used to conduct a systematic search of the following databases: MEDLINE (1946 – February 2016); EMBASE (1980 – February 2016); Cochrane Database of Systematic Reviews (2005 – February 2016) and the Cochrane Central Register of Controlled Trials (1898-February 2016). There were no restrictions on language or other limits on the search strategy.

Eligibility Criteria

We included observational studies published after 1980 that examined the frequency of live births in women with biopsy proven primary glomerular disease (Figure 1 - Appendix). In studies published prior to 1980, it was difficult to ascertain the pathological diagnosis. Furthermore, advances in neonatal intensive care occurring after 1980 significantly improved outcomes irrespective of maternal renal disease (e.g. surfactant use). We were primarily interested in the following 4 conditions: IgA nephropathy, minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS) and membranous nephropathy (MN). Studies were required to include a minimum of 10 women with one of the aforementioned conditions and report the number of live births within the given disease category. Where studies provided data on women in
more than one disease category of interest, results for each disease were included separately. Where two studies reported results based on an overlapping cohort, we selected the most recent study and/or the study with the largest sample size. Where studies did not specify the disease type or the pathological classification was unclear, we included these results as “glomerulonephritis, disease type not specified”. Titles, abstracts and full-text studies were reviewed in single, several months apart by one reviewer (AO). To ensure accuracy, a duplicate review of studies was conducted (KB).

**Quality Assessment**

We evaluated the methodological quality of included studies using the criteria developed by Loney et al. Studies were assessed based on 3 broad areas: 1) how the population was sampled 2) how the outcome was measured and 3) how the results were interpreted. The maximum number of points that could be achieved was 8 points, and studies were deemed to be at low risk of bias if they achieved at least 6 points (Table 1 - Appendix).

**Statistical and Qualitative Analysis**

The percentage of live births was calculated for each relevant disease category within each study. We refrained from conducting a meta-analysis because there was substantial heterogeneity (I²>70%) and few studies reported baseline data on participants to allow us to explore the sources of heterogeneity. Therefore, we conducted a qualitative, descriptive analysis only.

**Data Abstraction**

Data were independently abstracted by one reviewer (AO) and reviewed by a second reviewer (KB). Differences were reconciled by discussion or consultation with a third reviewer (MH). The following data
was abstracted: (1) General study characteristics, namely year of publication and study design; (2) Patient characteristics including number of women studied, number of pregnancies and number of infants, mean age, number of pregnancies with hypertension at baseline (pre-pregnancy), number of pregnancies with elevated creatinine at baseline; and (3) Outcome data including number of live births, spontaneous abortions, still births or neonatal deaths, birth weight and gestational age, number of pregnancies with an increase in post-pregnancy blood pressure and creatinine compared to baseline. Study specific definitions for the variables of interest are presented in Table 2 -Appendix where available.

REFERENCES


FIGURES

Figure 1: Identification of Included Studies

1890 studies identified - MEDLINE and EMBASE

Exclusion in Title and Abstract Screen (n=1794): Review article, did not examine primary GN and case studies

96 - Full Text Review

Excluded (n=76)
8 – Case series or case report
3 – Duplicate study
15 – Outcome of interest not reported
21 – Review article
2 – Small sample size
21 – Published prior to 1980
6 – Overlapping cohort

20 Full Text Articles Included
### Table 1: Characteristics and Quality of Included Studies

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Cohort Name</th>
<th>Disease Type(s)</th>
<th>Risk of Bias Score (out of 8)</th>
<th>Overall Risk of Bias Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surian, 1984</td>
<td>Policlinico Hospital</td>
<td>IgA, FSGS</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Abe, 1985</td>
<td>Keio Hospital</td>
<td>MCD, GN, Disease Type Not Specified</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Hou, 1985</td>
<td>Multicentre survey, USA</td>
<td>GN, Disease Type Not Specified</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Barcelo, 1986</td>
<td>Universidad Autonoma, Spain</td>
<td>IgA, FSGS</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Jungers, 1986</td>
<td>Necker Hospital</td>
<td>IgA, MCD, MN</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Kincaid-Smith,</td>
<td>University of Melbourne</td>
<td>IgA, FSGS</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Packham, 1987</td>
<td>Royal Women's Hospital</td>
<td>MN</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Packham, 1988</td>
<td>Royal Women's Hospital</td>
<td>IgA</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Packham, 1988</td>
<td>Royal Women's Hospital</td>
<td>FSGS</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Packham, 1988</td>
<td>Royal Women's Hospital</td>
<td>GN, Disease Type Not Specified</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Nagai, 1989</td>
<td>Toho University</td>
<td>IgA</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Abe, 1991</td>
<td>Keio Hospital</td>
<td>IgA</td>
<td>2</td>
<td>High</td>
</tr>
<tr>
<td>Abe, 1996</td>
<td>Keio Hospital</td>
<td>GN, Disease Type Not Specified</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Malik, 2001</td>
<td>Royal Security Forces Hospital</td>
<td>GN, Disease Type Not Specified</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Limardo, 2010</td>
<td>Rene e Gravidanza Collaborative Group</td>
<td>IgA</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Shimizu, 2010</td>
<td>Tokyo Women's Medical University</td>
<td>IgA</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Waness, 2010</td>
<td>King Abdulaziz University Hospital</td>
<td>IgA</td>
<td>3</td>
<td>High</td>
</tr>
<tr>
<td>Liu, 2014</td>
<td>Peking University First Hospital</td>
<td>IgA</td>
<td>5</td>
<td>High</td>
</tr>
</tbody>
</table>

Glomerulonephritis (GN)
Table 2: Definitions Used in Individual Studies for Baseline Comorbidities and Complications During Pregnancy

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Pre-Pregnancy HTN</th>
<th>Increased Pre-Pregnancy Creatinine</th>
<th>Increased Post-Pregnancy BP</th>
<th>Increased Post-Pregnancy Creatinine</th>
<th>Preeclampsia</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgA Nephropathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surian, 1984</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Not Available</td>
<td>≥50% increase in serum creatinine compared to “initial values”</td>
<td>Not Available</td>
</tr>
<tr>
<td>Barcelo, 1986</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Not Available</td>
<td>≥50% increase in serum creatinine compared to “initial values”</td>
<td>No Definition</td>
</tr>
<tr>
<td>Jungers, 1986</td>
<td>BP ≥150/90 mmHg</td>
<td>Serum creatinine ≥1.3 mg/dL</td>
<td>Not Available</td>
<td>Not Available</td>
<td>No Definition. However, raw data was provided by authors. For the purposes of this review, we used a definition of ≥50% increase in serum creatinine at 6 months postpartum</td>
</tr>
<tr>
<td>Kindcaid-Smith, 1987</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Increase ≥15 mmHg DBP at 6 months postpartum</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td>Packham, 1988</td>
<td>DBP &gt;95 mmHg or need for anti-HTN agents</td>
<td>Serum creatinine &gt;1.24 mg/dL</td>
<td>DBP ≥90 mmHg or increase ≥15 mmHg DBP at 6 months postpartum</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td>Nagai, 1989</td>
<td>No Definition</td>
<td>No Definition</td>
<td>BP ≥140/90 mmHg</td>
<td>No Definition</td>
<td>Not Available</td>
</tr>
<tr>
<td>Abe, 1991</td>
<td>BP ≥140/90 mmHg or need for anti-HTN agents</td>
<td>Not Available</td>
<td>No Definition</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td>Limardo, 2010</td>
<td>No Definition</td>
<td>Serum Creatinine &lt;1.2 mg/dL</td>
<td>BP ≥140/90 mmHg or need for anti-HTN agents</td>
<td>No Definition. However data provided for those</td>
<td>New-onset HTN and proteinuria ≥20 weeks</td>
</tr>
</tbody>
</table>
### Limardo, 2010 \(^{18}\)
- **No Definition**
- Serum Creatinine $>1.2$ mg/dL
- Not Available
- Not Available
- No Available

### Shimizu, 2010 \(^{19}\)
- Not Available
- Not Available
- Not Available
- Not Available
- No Definition

### Waness, 2010 \(^{20}\)
- No Definition
- No Definition
- Not Available
- Not Available
- HTN, severe edema and heavy proteinuria

### Liu, 2014 \(^{21}\)
- No Definition
- Not Available
- No Definition
- Not Available
- Severe HTN ($\geq 160/110$ mmHg), severe proteinuria ($>5$ g/day) and additional symptoms (headache, abdominal pain etc.)

### Focal Segmental Glomerulosclerosis (FSGS)

#### Surian, 1984 \(^{4}\)
- Not Available
- Not Available
- Not Available
- $\geq 50\%$ increase in serum creatinine compared to “initial values”
- Not Available

#### Barcelo, 1986 \(^{7}\)
- Not Available
- Not Available
- Increase of $\geq 20$ mmHg DBP at 3-6 months postpartum
- $\geq 50\%$ increase in serum creatinine compared to “initial values”
- No Definition

#### Kindcaid-Smith, 1987 \(^{9}\)
- Not Available
- Not Available
- Increase $\geq 15$ mmHg DBP at 6 months postpartum
- Not Available
- Not Available

#### Packham, 1988 \(^{12}\)
- DBP $\geq 95$ mmHg or need for anti-HTN agents
- Not Available
- Not Available
- $\geq 50\%$ increase in serum creatinine at 6 months postpartum
- Not Available

### Minimal Change Disease

#### Abe, 1985 \(^{5}\)
- Not Available
- Not Available
- No Available
- No Definition
- Not Available

#### Jungers, 1986 \(^{8}\)
- BP $\geq 150/90$ mmHg
- Serum creatinine $\geq 1.3$ mg/dL
- No Definition. *However, postpartum BP $\geq 150/90$ mmHg was considered increased, and all participants had normal pre-pregnancy BP*
- No Definition. *However, postpartum creatinine $\geq 1.5$ mg/dL considered increased, and all participants had normal pre-pregnancy creatinine*
- Not Available
### Membranous Nephropathy

<table>
<thead>
<tr>
<th>Study</th>
<th>BP/Criteria</th>
<th>Creatinine/Criteria</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jungers, 1986</td>
<td>BP ≥150/90 mmHg</td>
<td>Serum creatinine ≥1.3 mg/dL</td>
<td>Not Available</td>
<td>No Definition. However, postpartum creatinine ≥1.5 mg/dL considered increased, and all participants had normal pre-pregnancy creatinine</td>
</tr>
<tr>
<td>Packham, 1987</td>
<td>DBP ≥90 mmHg</td>
<td>Not Available</td>
<td>Increase ≥15 mmHg at 6 months postpartum</td>
<td>≥50% increase in serum creatinine at 6 months postpartum</td>
</tr>
</tbody>
</table>

### GN, Disease Type Not Specified

<table>
<thead>
<tr>
<th>Study</th>
<th>Criteria</th>
<th>Creatinine/Criteria</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malik, 2001</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Development of reversible HTN</td>
</tr>
<tr>
<td>Abe, 1996</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Not Available</td>
<td>Diagnosed by attending physician using clinical criteria from the American College of Obstetricians and Gynecologists</td>
</tr>
<tr>
<td>Packham, 1988</td>
<td>DBP ≥95 mmHg or need for anti-HTN agents</td>
<td>Serum creatinine ≥1.24 mg/dL</td>
<td>DBP &gt;90 mmHg at 6 months postpartum</td>
<td>≥50% increase in serum creatinine at 6 months postpartum</td>
</tr>
<tr>
<td>Abe, 1985</td>
<td>Not Available</td>
<td>Not Available</td>
<td>BP ≥140/90 mmHg if not hypertensive at conception or the use of anti-HTN agents</td>
<td>No Definition</td>
</tr>
<tr>
<td>Hou, 1985</td>
<td>BP ≥140/90 mmHg</td>
<td>Serum creatinine ≥1.4 mg/dL</td>
<td>Serum creatinine increased ≥1.0 mg/dL at ≥3 months postpartum</td>
<td>Not Available</td>
</tr>
</tbody>
</table>

Blood pressure (BP), systolic blood pressure (SBP), diastolic blood pressure (DBP), hypertension (HTN). Definition was not available if no outcome data was provided (see Table 1, main manuscript) whereas no definition indicates that although outcome data was provided, the authors failed to define the variable.