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Pregnancy and relapse among female Hodgkin Lymphoma patients

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Collaborators:
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Hodgkin lymphoma (HL)

- Malignant condition affecting B-lymphocytes
- Comprises around 10% of all lymphomas
- Characterised by presence of Hodgkin Reed-Sternberg cells
- Stage IA-IVB

Prognosis is very good - the 10-year relative survival is above 90% (Glimelius et al., 2015).
Together with improvements in survival, there is now an increasing number of survivors of HL who are interested in becoming pregnant.
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- Does pregnancy affect risk of HL?
- Do patients with HL diagnosed during pregnancy have worse prognosis?
- Does pregnancy trigger relapse among patients in remission from HL?
  - Has childbearing patterns after HL varied over time?
  - Do childbearing patterns differ between clinical characteristics?
Does pregnancy trigger relapse in HL patients?

Pregnancy and the Risk of Relapse in Patients Diagnosed With Hodgkin Lymphoma

Caroline E. Weibull, Sandra Eloranta, Karin E. Smedby, Magnus Björkholm, Sigurdur Y. Kristinsson, Anna L.V. Johansson, Paul W. Dickman, and Ingrid Glimelius

ABSTRACT

Purpose
Many patients and clinicians are worried that pregnancy after the diagnosis of Hodgkin lymphoma (HL) may increase the risk of relapse despite a lack of empirical evidence to support such concerns.
Motivations for studying pregnancy in relation to relapse

- Concern among patients in the clinics (which was confirmed in online forums for HL survivors).
- Potential mechanisms related to immunodeficiency experienced by both HL patients and pregnant women.
- Although some claimed “there is no relationship and this is known”, it had not been previously studied.

Sources:
- Swedish Lymphoma register (2001-2009)
- Medical records
  → Complete relapse information

Plus: data from the Medical Birth Register.
(All pregnancies resulting in a delivery)
Methods

- Survival analysis.
  - Outcome: Time to relapse
  - Exposure: Pregnancy + 5-year time window

- Follow-up started 6 months after diagnosis:
  - Women pregnant at diagnosis or < 6 months after were excluded.
  - Women with primary progressive disease were excluded.

449 women alive and in remission at start of follow-up
First step: look at your data!
Exposed number of cases

N=449

144 women with a pregnancy during follow-up
47 women with a relapse
1 woman
Why is that?
But is 1 what we would expect?

- How many relapses would we expect to see in women exposed to pregnancy if they would experience the same rate as women unexposed to pregnancy?
  - Estimate (adjusted) rate among unexposed
  - Apply that rate to the 144 exposed women

\[
\text{Expected number of relapses} = 3.76 \\
(\text{SIR}=0.27, \text{exact 95\% CI: 0.01 – 1.51})
\]
The absolute risk for relapse is highest within the first 2-3 years after diagnosis. Women should therefore be advised, if possible, to wait two years following cessation of treatment before becoming pregnant.

However, delaying pregnancy is not without complication as chemotherapy can cause early menopause resulting in involuntary childlessness.

There are many factors that should be considered when deciding about future reproduction, but the risk of pregnancy-associated relapse does not need to be considered.
Childbirth rates among women in remission from HL

449 women in remission from HL

Matched (1:5) comparators

- Time to first childbirth after diagnosis
- Follow-up [9 months, 7 years]
- Censor at relapse
- Estimate:
  - Hazard ratios (HR)
  - Cumulative probabilities of childbirth
Results; Patients versus comparators

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>[9mo, 3yrs]</th>
<th>[3yrs, 7yrs]</th>
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<tbody>
<tr>
<td>Comparators</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>HL patients</td>
<td>0.59 (0.42 – 0.82)</td>
<td>1.06 (0.81 – 1.39)</td>
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### Results; Childbirth rates by stage

<table>
<thead>
<tr>
<th></th>
<th>[9mo, 3yrs]</th>
<th>[3yrs, 7yrs]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comparators</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Limited stage patients</strong></td>
<td>0.68 (0.44 – 1.04)</td>
<td>1.09 (0.76 – 1.56)</td>
</tr>
<tr>
<td><strong>Advanced stage patients</strong></td>
<td>0.50 (0.30 – 0.82)</td>
<td>1.03 (0.71 – 1.50)</td>
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</tbody>
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#### Limited stage

![Childbirth rate over time for limited stage patients](chart LIMITED.png)

#### Advanced stage

![Childbirth rate over time for advanced stage patients](chart ADVANCED.png)
Results; Cumulative probability of childbirth

- Cumulative probability of childbirth over time since diagnosis for HL patients.
- Comparison with death and relapse rates.

Graphs showing probability of childbirth and death/relapse over time for HL patients and comparators.
Three years after diagnosis, childbirth rates in female HL survivors, regardless of initial stage and treatment, are comparable to those in the general population.

The cumulative probability of childbirth is, however, lower among female HL survivors the first seven years after diagnosis.

The high childbirth rates among young female relapse-free HL survivors are reassuring, and stresses that the most important issue is to avoid a relapse, also from a fertility perspective.
Thank you!
References


