Health Resource Utilization among Patients with Warm Autoimmune Hemolytic Anemia in Sweden: A Retrospective Registry-Based Study

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Key Takeaways

- **This real-world study is the first to describe the healthcare burden incl. HRU and direct medical cost associated with wAIHA in Sweden.**
- **Management of both primary and secondary wAIHA is associated with a high long-term HRU, high cumulative healthcare cost, and ongoing mortality risk.**
- **High HRU - including an ongoing need for emergency and inpatient care – was observed in the first year after diagnosis and remained elevated in subsequent follow-up years.**
- **Limitation: While the reported direct medical cost is high, the total cost burden for wAIHA is underestimated as costs for primary care and key medicines such as rituximab are not included.**
- **Unmet medical need remains for more effective treatment options to improve outcomes and quality of life for patients with wAIHA.**

Background

Warm autoimmune hemolytic anemia (wAIHA) is a rare and severe disorder characterized by autoantibody-mediated red blood cell hemolysis [1].

wAIHA management is challenging as it impacts a heterogeneous patient population, has limited effective treatment options and an increased risk of mortality [1].

Data on healthcare resource utilization (HRU) among patients with wAIHA is scarce [2,3] and direct medical cost has not been described previously.

Objectives

Evaluate the burden of disease for patients with primary and secondary wAIHA including HRU (all-cause specialized care), direct medical cost associated with specialized healthcare, and overall survival.

Methods

Data Sources

- Linked Swedish population-based healthcare registries: National Patient Register (NPR) and Cause of Death Register; linkage through unique personal identity numbers

Study Population

- Inclusion criteria
  - Diagnosed with wAIHA (ICD-10-SE: D59.1B in NPR) between 1st July 2005 and 30th June 2023
  - ≥18 years at diagnosis
- Exclusion of Evans Syndrome patients based on records of immune thrombocytopenia.
- Patients are followed from wAIHA diagnosis (index) – defined as first wAIHA record – until death, emigration, or end of follow-up (30th June 2023).
- Classification as primary or secondary based on the presence of records of associated underlying diseases within ±180 days of wAIHA diagnosis.

Study Measures

- All-cause specialized HRU
  - Includes inpatient admissions (IP) and outpatient visits (OP)
  - Assessed from 4 years prior to wAIHA diagnosis until 4 years after wAIHA diagnosis
  - Acute care defined as visits registered by the emergency room or intensive care unit
  - Reported as average per-patient-per-year (PPPY); defined as total visit count or total time in care divided by total patient-time in follow-up period.
- Direct medical cost for specialized care
  - Based on diagnosis-related group (DRG) codes, which capture hospital-based treatment and care cost but exclude costs for primary care, prescription medicines and specific high-cost hospital-administered medicines such as rituximab.
  - Reported as average cost PPPY; defined as total cost divided by total patient-time in follow-up period.
- OS was defined as the time from wAIHA diagnosis until death from any cause or censoring (end of follow-up or emigration), whichever occurred first.

Results

412 patients with wAIHA were identified in this study.

- Among these, 139 patients (34%) were defined as having secondary wAIHA based on underlying conditions.
- Among patients with secondary wAIHA, 74.1% had underlying hematological malignancies and 24.5% had autoimmune/connective tissue diseases.

Patients with wAIHA had considerable ongoing need for specialized healthcare, reflected in high healthcare resource utilization.

- All patients accessed specialized care in the first year post-diagnosis. 92% of patients with primary and 99% of patients with secondary wAIHA required specialized care in the period 2-4 years post-diagnosis.
- During the period 2-4 years post-diagnosis, acute care was required by 27% of patients with primary wAIHA and 44% of patients with secondary wAIHA. In the same period, inpatient admission was required by 45% of patients with primary wAIHA and 71% of patients with secondary wAIHA.
- On average, time spent in specialized care during the period 2-4 years post-diagnosis was increased by 110% in patients with primary wAIHA and 170% in patients with secondary wAIHA, compared to the period 2-4 years pre-diagnosis (p<0.0001 in both cases).

The ongoing need for specialized care translated to high direct medical cost.

- On average, cost in year 2-4 post-diagnosis was increased by 190% for patients with primary wAIHA and 230% for patients with secondary wAIHA, compared to year 2-4 pre-diagnosis.
- Patients with secondary wAIHA require management for both wAIHA and underlying conditions, which was associated with high burden and costs and ongoing mortality risk.
- Note: Even though patients with wAIHA are diagnosed and treated in a specialist care setting, treatment for initial symptoms, comorbidities, and underlying diseases is often provided in primary care. Costs for primary care are not considered in current cost estimates.

Median overall survival:

- 11.4 years (95% CI: 10.0 – not reached) for patients with primary wAIHA
- 4.1 years (95% CI: 3.2-5.1) for patients with secondary wAIHA

Primary wAIHA n=273

Secondary wAIHA n=139

TABLE 1. Patient characteristics at wAIHA diagnosis (n=412)

Characteristics	Primary wAIHA	Secondary wAIHA
Patient, n (%)	273 (66%)	139 (34%)
Age in years at diagnosis, mean (SD)	65.3 (19.0)	72.1 (13.2)
Sex, % of male patients	52.4	52.5
Follow-up time in years, median (IQR)	3.7 (1.6-7.0)	2.5 (0.9-4.9)

TABLE 2. Underlying conditions in patients with secondary wAIHA (n=139)

Underlying condition*	Secondary wAIHA
Hematological malignancies, n (%)	103 (74.1%)
Autoimmune diseases / Connective tissue diseases, n (%)	34 (24.5%)
Primary immunodeficiency, n (%)	23 (16.5%)
Chronic viral infections, n (%)	9 (6.5%)
Transplantations, n (%)	0 (0%)

*Conditions are not mutually exclusive, i.e., one patient can have multiple underlying conditions.

TABLE 3. HRU (IP and OP specialized care) among patients with wAIHA (n=412)

	Primary wAIHA			Secondary wAIHA		
Time period pre-/post-diagnosis	Year 2-4 pre	Year 1 post	Year 2-4 post	Year 2-4 pre	Year 1 post	Year 2-4 post
All specialized care (Inpatient and outpatient)						
Patients with ≥1 visit, n (%)	220 (81%)	273 (100%)	206 (92%)	130 (93%)	139 (100%)	99 (99%)
Number of visits PPPY	2.8	11.2	6.0	4.5	17.0	8.6
Days spent in care PPPY	5	21	10	7	38	18
Acute specialized care (Inpatient and outpatient)						
Patients with ≥1 visit, n (%)	64 (23%)	69 (25%)	59 (27%)	40 (29%)	49 (35%)	44 (44%)
Inpatient specialized care						
Patients with ≥1 admission, n (%)	110 (40%)	178 (65%)	101 (45%)	72 (52%)	113 (81%)	71 (71%)
Days spent admitted to hospital PPPY	3	12	4	4	26	11

IP: Inpatient admissions, **OP**: Outpatient visits, **Post**: Post-diagnosis, **PPPY**: per-patient-per-year, **Pre**: pre-diagnosis

FIGURE 1. Time spent in specialized care (IP+OP) per-patient-per-year

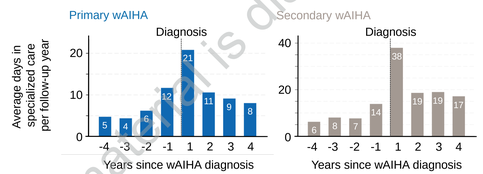


TABLE 4. Comparing time spent in specialized care (IP+OP) during the year 2-4 post-diagnosis period vs. the year 2-4 pre-diagnosis period

	Rate Ratio* (95% CI)	p-value
Primary wAIHA	2.1 (1.5-2.8)	<0.0001
Secondary wAIHA	2.7 (1.9-3.8)	<0.0001

*Rate Ratio can be interpreted as the ratio between the time in care PPPY during year 2-4 post-diagnosis and the time in care PPPY during year 2-4 pre-diagnosis. The Rate Ratio was calculated using a generalized estimating equation model with an autoregressive correlation structure.

TABLE 5. Direct medical cost associated with specialized care among patients diagnosed with wAIHA 2012-2022* (n=337)

	Time period	Cost for IP+OP care, PPPY
Primary wAIHA	Year 2-4 pre-diagnosis	€2,798 / $3,026
	Year 1 post-diagnosis	€13,993 / $15,131
	Year 2-4 post-diagnosis	€7,186 / $7,770
Secondary wAIHA	Year 2-4 pre-diagnosis	€4,079 / $4,411
	Year 1 post-diagnosis	€26,193 / $28,322
	Year 2-4 post-diagnosis	€11,956 / $12,928

*As DRG cost weights were available from 2012, cost analysis was restricted to patients diagnosed 2012 onwards.

FIGURE 2. Direct medical cost (IP+OP) per-patient-per-year

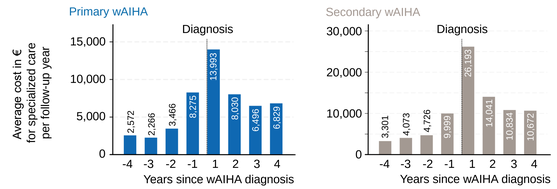
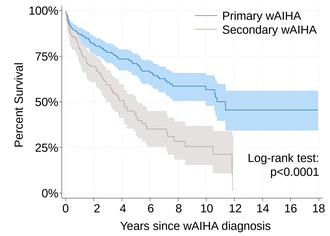


TABLE 6. Comparing direct medical cost during the year 2-4 post-diagnosis periods vs. the year 2-4 pre-diagnosis period

	Rate Ratio* (95% CI)	p-value
Primary wAIHA	2.9 (2.1-3.9)	<0.0001
Secondary wAIHA	3.3 (2.3-4.5)	<0.0001

*Rate Ratio can be interpreted as the ratio between cost PPPY during year 2-4 post-diagnosis and cost PPPY during year 2-4 pre-diagnosis. The Rate Ratio was calculated using a generalized estimating equation model with an autoregressive correlation structure.

FIGURE 3. Overall survival of patients with wAIHA (n=412)



Patients with primary wAIHA at risk

273	191	127	82	49	29	16	8	3	0

Patients with secondary wAIHA at risk

139	80	45	21	10	6	0	0	0	0

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