Identification of a Warm Autoimmune Hemolytic Anemia (wAIHA) Population Using Predictive Analytics of a Known Clinically Profiled Cohort

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INTRODUCTION

- Warm autoimmune hemolytic anemia (wAIHA) is a rare, life-threatening autoimmune disorder, with an estimated incidence in adults of 1 to 3 per 100,000/year, a prevalence of 17:100,000, and a mortality rate of ~11%[1-4]
  - It is characterized by the premature destruction of red blood cells (RBCs), which is triggered in the majority of cases by pathogenic immunoglobulin G autoantibodies that bind RBCs (with or without complement) and lead to their clearance in the spleen and liver[5,6]
- There have been a limited number of studies assessing the disease burden and clinical journey of patients with wAIHA[1,7,8]
- Until recently, a diagnosis code specific for wAIHA did not exist, which presented challenges in identifying patients for real-world evidence analyses

OBJECTIVES

- The purpose of this analysis was to generate insights into the burden of wAIHA and the wAIHA clinical journey
- Given the absence of a diagnostic code specific for wAIHA at the time this analysis was carried out, we aimed to develop a clinical algorithm that could be used to identify a cohort of patients with wAIHA in a proprietary US claims database
- Following identification of a cohort of patients with wAIHA, the aim was to:
  - Categorize severe versus nonsevere patients with wAIHA
  - Compare the frequency of comorbidities, anemia symptoms, treatments, diagnostic tests, and health care provider (HCP) visits in severe and nonsevere patients with wAIHA

METHODS

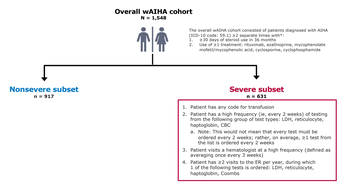
- This study used a deidentified, longitudinal, patient-level US claims database of >300 million US patients
- Study time frame: January 1, 2017, to January 31, 2020
- To identify patients with wAIHA, a diagnostic code for autoimmune hemolytic anemia (AIHA) had to be present at least twice along with chronic use of steroids for ≥30 days in the last 36 months (January 1, 2017, to December 31, 2019) and chronic use of ≥1 treatment associated with wAIHA
  - Treatments associated with wAIHA included rituximab, azathioprine, mycophenolate mofetil/mycophenolic acid, cyclosporine, and cyclophosphamide
- Severe patients were then identified from this cohort if they had ≥1 code within the last 36 months (January 1, 2017, to December 31, 2019) associated with the following:
  - Transfusion
  - High-frequency blood panel testing (on average every 2 weeks)
  - High-frequency visits with a hematologist (on average every 3 weeks)
  - ≥2 emergency room (ER) visits per year, at which time a lactate dehydrogenase, reticulocyte, haptoglobin, or Coombs test was ordered
- Diagnostic and procedural codes for anemia symptoms, comorbidities, treatments, and diagnostic tests were grouped and analyzed within the most recent 12 months (February 1, 2019, to January 31, 2020) for each patient in order to characterize the wAIHA patient journey and determine health care resource utilization
  - Interactions of patients with wAIHA with HCPs and sites of care based on codes are also reported
  - Not all patients who qualified for the full wAIHA cohort had claims with codes that could be analyzed in the past 12 months
  - The percentage of patients with a given code was calculated using the total number of patients with ≥1 claim out of the total number of patients, and claims with codes per total patients were calculated using the total number of claims divided by the total number of patients

RESULTS

wAIHA Patient Cohort

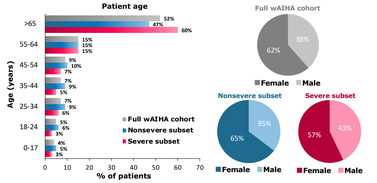
- Overall, 1,548 patients with wAIHA were identified, of whom 917 patients were categorized as nonsevere and 631 met the criteria for the severe subset (**Figure 1**)
- Median patient age was >65 years; a larger percentage of severe patients were in the ≥65 years age group, while larger percentages of nonsevere patients were in the younger age groups (**Figure 2**)
- Patients were predominately female, and similar distributions of gender were observed in the severe and nonsevere subsets (**Figure 2**)

Figure 1. Identification and Segmentation of Patients With wAIHA



wAIHA, warm autoimmune hemolytic anemia; AIHA, autoimmune hemolytic anemia; ICD-10, International Classification of Diseases, 10th Revision; LDH, lactate dehydrogenase; CBC, complete blood count; ER, emergency room.
Treatment with steroids and use of ≥1 treatment were not required to occur after AIHA diagnosis; however, patients with unrelated hemolytic anemia codes occurring after the most recent ICD-10 D59.1 code were removed to ensure the ICD-10 D59.1 code was the "current" hemolytic anemia diagnosis for that patient.

Figure 2. Age and Gender Profiles Observed for wAIHA Cohort

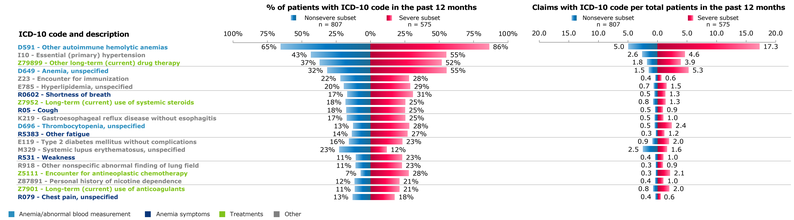


wAIHA, warm hemolytic autoimmune anemia.

Diagnostic Codes Among the wAIHA Patient Cohort

- Many of the diagnostic (*International Classification of Diseases, 10th Revision* [ICD-10]) codes among the full wAIHA cohort were related to anemia/abnormal blood measurements, anemia symptoms, and treatments (*data not shown*)
  - 21% of the full wAIHA cohort had a diagnostic code for long-term steroid use, and 43% had a diagnostic code for long-term therapeutic treatment of any kind
  - 16% of the full wAIHA cohort had a diagnostic code for encounter for antineoplastic chemotherapy
  - The diagnostic code for long-term use of anticoagulants was observed in 15% of the full wAIHA cohort, which may reflect the risk of venous thromboembolism in 15% to 30% of adult patients with wAIHA[9]
  - Other diagnostic codes were associated with comorbidities, including those related to hypertension, hyperlipidemia, type 2 diabetes, and systemic lupus erythematosus
- The percentage of patients and claims with disease-relevant diagnostic codes were disproportionately higher in the severe subset versus the nonsevere subset (**Figure 3**)
  - Diagnostic codes related to comorbidities such as hypertension, hyperlipidemia, and type 2 diabetes were more common in the severe cohort versus the nonsevere cohort, while the diagnostic code for systemic lupus erythematosus was less common in severe patients versus nonsevere patients
- Over the 12-month study period, higher claim volumes related to anemia/abnormal blood measurements, anemia symptoms, and treatments were observed in the severe subset versus the nonsevere subset (**Table 1**)
  - Diagnostic codes related to anemia symptoms and wAIHA treatment were 211% and 152% higher in the severe subset versus the nonsevere subset, respectively

Figure 3. Diagnostic Codes in Patients With wAIHA by Disease Severity



wAIHA, warm autoimmune hemolytic anemia; ICD-10, International Classification of Diseases, 10th Revision.

Procedural Codes Among the wAIHA Patient Cohort

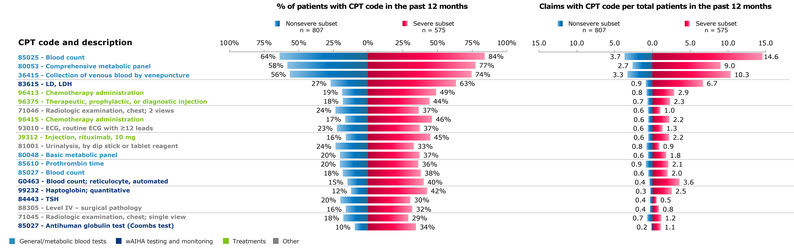
- Procedural (Current Procedural Terminology [CPT]) codes among the full wAIHA cohort included those related to general/metabolic blood tests, wAIHA testing and monitoring, and treatments (*data not shown*)
  - Two different procedural codes for chemotherapy administration (CPT code: 96413, 31%; CPT code: 96415, 29%) were observed in the full wAIHA cohort
  - 28% of the full wAIHA cohort was prescribed rituximab
- Similar to diagnostic codes, the percentage of patients and claims with disease-relevant procedural codes were more common in the severe subset versus the nonsevere subset (**Figure 4**)
  - A higher percentage of severe patients (45%) were prescribed rituximab versus nonsevere patients (16%)
- Over the 12-month study period, higher claim volumes related to general/metabolic blood tests, wAIHA testing and monitoring, and treatments were observed in the severe subset versus the nonsevere subset (**Table 1**)
  - Procedural codes related to wAIHA testing and monitoring and treatment were 569% and 265% higher in the severe subset versus the nonsevere subset, respectively

Table 1. Key Categories of Diagnostic and Procedural Codes by Disease Severity in the Past 12 Months

	Severe claims per total patient (n = 575)	Nonsevere claims per total patient (n = 807)	Severe vs nonsevere relative increase in claims per patient (%)
Diagnostic categories			
Anemia/abnormal blood measurement	24.91	6.97	257%
Anemia symptoms	4.98	1.60	211%
Treatments	9.41	3.73	152%
Other	13.30	8.38	59%
Procedural categories			
General/metabolic blood tests	39.81	11.76	239%
wAIHA testing and monitoring	14.40	2.15	569%
Treatments	9.58	2.62	265%
Other	5.28	3.10	70%

wAIHA, warm hemolytic autoimmune anemia.

Figure 4. Procedural Codes in Patients With wAIHA by Disease Severity

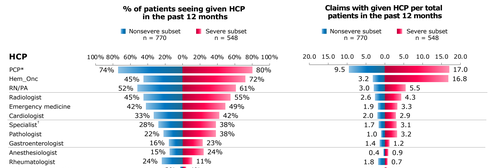


wAIHA, warm autoimmune hemolytic anemia; CPT, Current Procedural Terminology; LD or LDH, lactate dehydrogenase; ECG, electrocardiogram; TSH, thyroid-stimulating hormone; IV, intravenous.

wAIHA Patient–HCP Interactions and Sites of Care

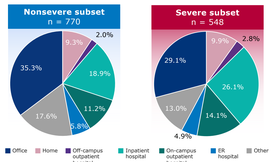
- Patients with wAIHA interacted the most with primary care physicians (76%), while a lower percentage of patients interacted with specialists, including cardiologists (37%), gastroenterologists (20%), and rheumatologists (19%)
  - The full wAIHA cohort was equally as likely to see registered nurses/physician assistants as hematologist-oncologists (56% of patients for both types of HCPs)
- Patients with severe wAIHA interacted more frequently with specialists that included hematologist-oncologists, radiologists, and cardiologists than the nonsevere subset (**Figure 5**)
  - Patients with severe wAIHA were less likely to interact with rheumatologists than were patients with nonsevere wAIHA, which is consistent with the lower incidence of systemic lupus erythematosus in severe versus nonsevere patients
- Patient sites of care in the full wAIHA cohort included in-office, inpatient hospital, and on-campus outpatient hospital
  - There were only modest differences in sites of care among severe and nonsevere subsets (**Figure 6**), including slightly more inpatient care and less in-office care in the severe subset versus the nonsevere subset

Figure 5. Interaction of Patients With wAIHA and HCPs by Disease Severity



wAIHA, warm autoimmune hemolytic anemia; HCP, health care provider; PCP, primary care physician; Hem_Onc, hematologist-oncologist; RN, registered nurse; PA, physician assistant.
*HCPs included family medicine, general practice, and internal medicine practitioners.
†HCPs who identified as generic "specialist" and did not specify specialty.*

Figure 6. Patient Sites of Care by Disease Severity in the Past 12 Months

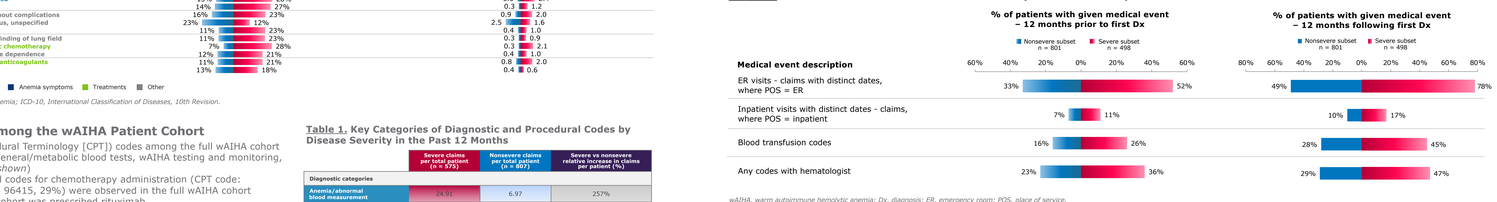


ER, emergency room; wAIHA, warm autoimmune hemolytic anemia.
Note: Site-of-care distribution is based on the total volume of claims among the full wAIHA cohort.

Common Medical Events Before and After Diagnosis

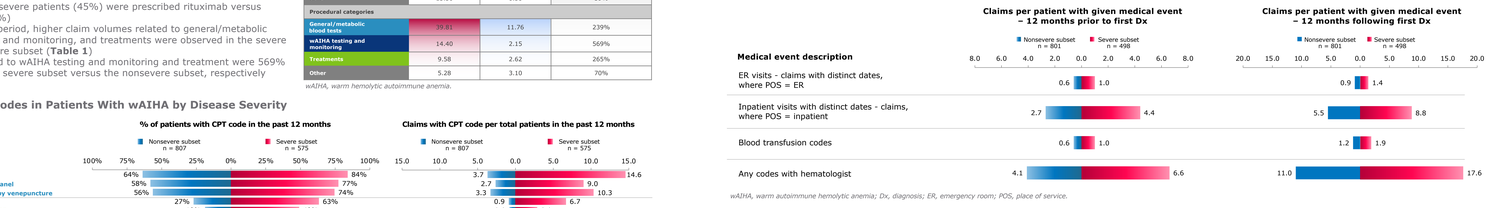
- We defined the following set of 4 common medical events related to wAIHA to understand the frequency of occurrence:
  - ER visit
  - Inpatient visit
  - Blood transfusion
  - Any visit or procedure related to a hematologist
- Splenectomy prevalence in the full wAIHA cohort was 0.6%; as prevalence was low, this was not included in the common medical events analysis
- In the defined set of medical events, the percentage of patients with a given medical event and claims with a given medical event were more common 12 months after the first diagnosis versus 12 months prior to the first diagnosis
- The percentage of patients (**Figure 7**) and claims (**Figure 8**) with a given medical event were more common in the severe subset versus the nonsevere subset

Figure 7. Medical Events in Patients With wAIHA by Disease Severity



wAIHA, warm autoimmune hemolytic anemia; Dx, diagnosis; ER, emergency room; POS, place of service.

Figure 8. Claims per Patient With wAIHA With a Medical Event by Disease Severity



wAIHA, warm autoimmune hemolytic anemia; Dx, diagnosis; ER, emergency room; POS, place of service.

CONCLUSIONS

- We developed and validated a method for defining patients with wAIHA using de-identified US claims data based on AIHA ICD-10 codes and relevant treatments
- This analysis was then used to better understand the disease burden and clinical journey of patients with wAIHA
- Diagnostic and procedural codes associated with anemia, symptoms, tests, treatments, and comorbidities mostly occurred at an increased frequency in severe patients during the same 12-month period
- Severe patients were more likely to be seen by specialists that included hematologist-oncologists, radiologists, and cardiologists in sites of care that were mostly the same as nonsevere patients
- In a defined set of medical events, events were more likely to occur in severe patients and 12 months after diagnosis, which may suggest that disease severity and diagnosis serve as a catalyst for patient treatment
- Limitations of this analysis include the following:
  - The use of diagnostic and procedural codes in this analysis was limited to data collected over the last 12 months, and some codes may have occurred at a lower-than-expected frequency; a future study with data collected over a longer period may be warranted
  - Since the 12-month period was fixed (February 1, 2019, to January 31, 2020) for the diagnostic and procedural code analysis instead of based on an index event, patients could have been at different points in their clinical journey after diagnosis, which could have impacted the results
  - The higher frequency of disease-relevant diagnostic and procedural codes in patients with severe wAIHA may be driven in part by the criteria used to define severe patients

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DISCLOSURES

KRM served as a consultant for Momenta and Novartis. TG is a previous employee of Momenta and Janssen. GKJ is an employee of IPM AI, which received funding from Momenta for the analyses reported. MLT is an employee of Janssen.

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