Retrospective Real-World Data Analysis of Morbidity Burden and Healthcare Costs in Idiopathic Multicentric Castleman Disease Compared with Controls (BURDEN-iMCD)

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INTRODUCTION

- Idiopathic multicentric Castleman disease (iMCD) is a rare, cytokine-driven hematologic disorder characterized by diffuse lymphadenopathy and systemic inflammation.
- Prior studies have suggested increased rates of hematologic abnormalities and organ dysfunction in iMCD.
- The broader comorbidity burden and its economic impact remain poorly understood due to diagnostic challenges associated with accurate identification of iMCD.

OBJECTIVE

- The objective of this analysis was to characterize the prevalence and economic impact of morbidities in patients with iMCD compared with matched controls, to inform understanding of disease burden and unmet need in clinical and health system contexts.

METHODS

- This retrospective study utilized administrative claims data from the Merative™ MarketScan® Databases for the period from January 1, 2016, to June 30, 2024.
- Patients with iMCD were identified based on the initial claim for CD (ICD-10 code D47.Z2; index date) and minor diagnostic and treatment criteria for iMCD[1,2] (**Table 1**).
- Controls were identified among patients with no evidence of CD or lymphadenopathy during the study period (index dates were randomly assigned based on index date of patients with iMCD).
- Patients with iMCD and controls were enrolled for ≥6 months pre-index (baseline) and ≥30 days post-index (minimum follow-up).
- Patients with iMCD were propensity score matched (PSM) to controls (1:3 using nearest neighbor and 0.25 caliper width) based on demographics and baseline Charlson Comorbidity Index (CCI).
- Post-index prevalence per 1,000 person-years (PY) and costs per patient per month (PPPM) for specific morbidities were compared between patients with iMCD and controls.

Table 1. iMCD Minor Diagnostic & Treatment Criteria

Diagnostic criteria* (1/01/2016 to 6/30/2024, unless otherwise noted)
Clinical diagnostic criteria
Fatigue, fever, night sweats or weight loss within +/-120 days of index date
Hemangiomatosis
Fluid accumulation (ascites, anasarca, edema, pleural effusion)
Large liver and/or spleen
Lymphocytic interstitial pneumonitis
Lab-based diagnostic criteria
Anemia within +/- 120 days of index date
Elevated C-reactive protein or erythrocyte sedimentation rate
Hypoalbuminemia
Renal dysfunction or proteinuria
Polyclonal hypergammaglobulinemia
Thrombocytopenia or thrombocytosis within +/-120 days index date
Treatment criteria (index date through 6/30/2024)
≥1 claim for siltuximab, with no cytokine release syndrome diagnosis
≥1 claim for tocilizumab, with no cytokine release syndrome diagnosis
≥1 claim for rituximab

*Identified by non-rule out claims for the condition, which are claims that are not for lab tests or other procedures used to initially identify a diagnosis.

RESULTS

- A total of 140 patients with iMCD met all eligibility criteria **(Figure 1**) and were included in the analysis.
- Out of 76.2 million potential controls without CD or lymphadenopathy, more than 17 million met enrollment requirements and 420 were matched to patients with iMCD.
- Demographic characteristics and the CCI score were well balanced between patients with iMCD and matched controls (standardized mean difference [SMD] <0.10) (**Table 2**).
- During follow-up, patients with iMCD had a prevalence rate of 1,124.9 per 1,000 PY for any morbidity, compared to 162.9 per 1,000 PY among matched controls, resulting in a rate ratio of 6.9 (95% confidence interval [CI]=6.7, 7.2) **(Figure 2).**

Figure 1. Selection of Patients with iMCD

[a]CD and minor diagnostic criteria identified by non-ruleout claims; [b]Lymphoma, myeloma, rheumatoid arthritis, and Sjogren's syndrome assessed 12 months post-index. [c]Full follow-up ended at the end of continuous enrollment or 6/30/2024. *CD: Castleman disease; CRS: cytokine release syndrome; HIV/HHV-8, human immunodeficiency virus/human herpesvirus-8; iMCD, idiopathic multicentric Castleman disease*

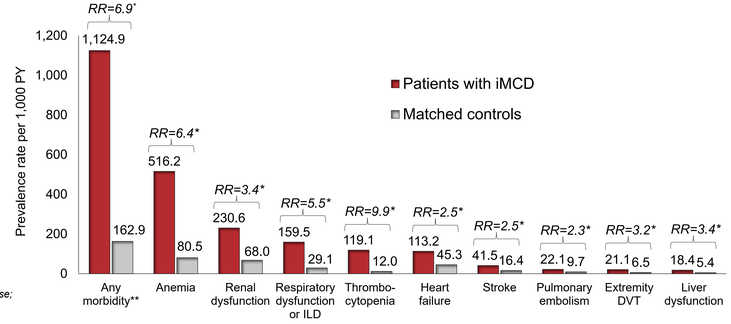
Table 2. Characteristics of Patients with iMCD and Controls

	Patients with iMCD N=140	Controls		SMD: Controls vs. iMCD	
		All N=17,049,093	Matched N=420	All	Matched
Age at index, mean (SD)	49.5 (18.6)	37.5 (20.5)	49.4 (18.4)	0.61	0.00
Sex, n (%)					
Male	73 (52.1)	8,307,982 (48.7)	219 (52.1)	0.07	0.00
Female	67 (47.9)	8,741,111 (51.3)	201 (47.9)	0.07	0.00
Payer, n (%)					
Commercial	118 (84.3)	15,841,646 (92.9)	352 (83.8)	0.27	0.01
Medicare	22 (15.7)	1,207,447 (7.1)	68 (16.2)	0.27	0.01
CCI[a], mean (SD)	1.9 (2.6)	0.3 (0.9)	2.0 (2.9)	0.86	0.02
Months of follow-up, mean (SD)	29.4 (25.2)	29.1 (24.9)	27.2 (22.9)	0.01	0.09

[a]Charlson Comorbidity Index (CCI) measured during the 6-month baseline period. *iMCD, idiopathic multicentric Castleman disease; SD, standard deviation; SMD, standardized mean difference*

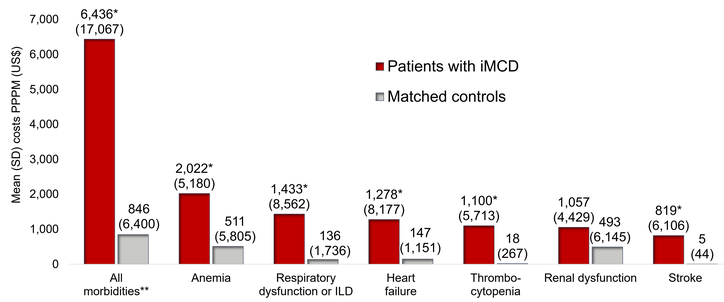
- Among patients with iMCD, the most prevalent morbidities included anemia (516.2 per 1,000 PY), renal dysfunction (230.6), respiratory dysfunction or interstitial lung disease (ILD) (159.5), thrombocytopenia (119.1), and heart failure (113.2) **(Figure 2).**
- Rate ratios [95% CI] comparing patients with iMCD to matched controls were highest for thrombocytopenia (9.9 [9.2, 10.6]), anemia (6.4 [6.1, 6.7]), and respiratory dysfunction or ILD (5.5 [5.0, 6.0]).
- Notably, thrombotic event diagnoses such as stroke, pulmonary embolism, and extremity deep vein thrombosis were significantly more prevalent among patients with iMCD (**Figure 2**).
- Total mean (SD) morbidity-related costs PPPM among patients with iMCD were 7.6 times as high as the matched controls (p<0.001) **(Figure 3).**
- Mean costs PPPM for most individual morbidities were significantly greater among patients with iMCD (p<0.01), including anemia, respiratory dysfunction or ILD, heart failure, thrombocytopenia, and stroke **(Figure 3).**

Figure 2. Prevalence Per 1,000 Person-Years and Prevalence Rate Ratios for Specific Morbidities Among Patients with iMCD vs. Matched Controls



*95% confidence intervals for all rate ratios (RR) indicate significant differences between patients with iMCD and controls (p<0.05). **Any morbidity also includes drug-induced diabetes, portal vein thrombosis, and transient ischemic attack. *DVT, deep vein thrombosis; ILD, interstitial lung disease; iMCD, idiopathic multicentric Castleman disease; PY, person-years*

Figure 3. Mean Costs Per Patient Per Month for Specific Morbidities Among Patients with iMCD vs. Matched Controls



*p<0.01 compared to matched controls. **All morbidities also includes drug-induced diabetes, extremity deep vein thrombosis, liver dysfunction, portal vein thrombosis, pulmonary embolism, and transient ischemic attack. *ILD, interstitial lung disease; iMCD, idiopathic multicentric Castleman disease; PPPM, per patient per month; SD, standard deviation; US$, United States dollars*

LIMITATIONS

- The MarketScan Databases used in this study only include patients with employer-sponsored commercial or Medicare insurance; results may not be generalizable to patients with other types of insurance (e.g., Medicaid) or those who are uninsured.
- Application of the iMCD diagnostic criteria was limited to data available from insurance claims; therefore, misclassification of iMCD patients is possible.
- Residual confounding from unmeasured variables such as race, socioeconomic status or treatment exposure cannot be excluded. In addition, increased medical surveillance amongst patients with iMCD may inflate morbidity detection rates relative to controls. The temporal relationship between diagnosis and morbidity cannot be definitively established because of variable follow-up duration.
- Propensity-score model variables were also limited to data available in the MarketScan Databases; differences in unmeasured patient characteristics may contribute to the observed differences between patients with iMCD and controls.
- Lack of a CD-specific diagnosis code prior to 10/1/2016 limited the period for identification of patients with iMCD and therefore the sample size of this study; future studies including more patients with iMCD may strengthen these findings.

CONCLUSIONS

- These findings are consistent with an increased morbidity (including organ failure and dysfunction across multiple organ systems and thromboembolic events) and cost burden amongst patients with iMCD compared with matched controls.
- Although causality cannot be established, the results reinforce the need for earlier recognition and optimized disease management.
- These data provide quantitative context for the clinical and economic burden of iMCD, which may inform future health technology assessments and value frameworks for targeted therapies to reduce both patient suffering and economic impact.

REFERENCES

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