SA108

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Clinical and Humanistic Burden of Giant Cell Arteritis and the Associated Unmet Medical Needs: A Targeted Literature Review

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This study was sponsored by Novartis Pharma AG, Basel, Switzerland.
Poster presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) EU Conference, Barcelona, Spain, 17–20 November 2024.

KEY FINDINGS & CONCLUSIONS

- GCA persists as a difficult condition to diagnose, and treatment delay can result in significant complications such as irreversible vision loss.
- GCA profoundly affects a patient's quality of life, hindering daily activities. Both physical and mental well-being can be affected.
- Glucocorticoids (GCs) remain the standard treatment, however there is a critical need for effective glucocorticoid-sparing alternatives that provide sustained remission and reduce the adverse effects of long-term glucocorticoid use.

INTRODUCTION

- Giant cell arteritis (GCA) is a systemic inflammatory disorder of medium- and large-sized vessels, common in people ≥50 years.[1,2] Varying clinical manifestations of GCA can be associated with significant burden to patients.[1]
- While glucocorticoids (GC) remain the standard treatment, there is a need for effective alternatives to minimize side effects and maintain remission.[3,4]
- The global pooled prevalence and incidence of GCA among people aged >50 years are estimated at 51.74 (95% CI: 42.04, 61.43) and 10 (95% CI: 9.22, 10.78) cases per 100,000 individuals, respectively.[5] The risk of GCA increases with advancing age, and as the population ages, the overall burden can be expected to grow.[5,6]
- **OBJECTIVE:** To identify and summarize existing literature on the clinical and humanistic burden of GCA and/or PMR* and the associated unmet medical needs.

* Refer to poster SA11 for further details on studies relating to PMR

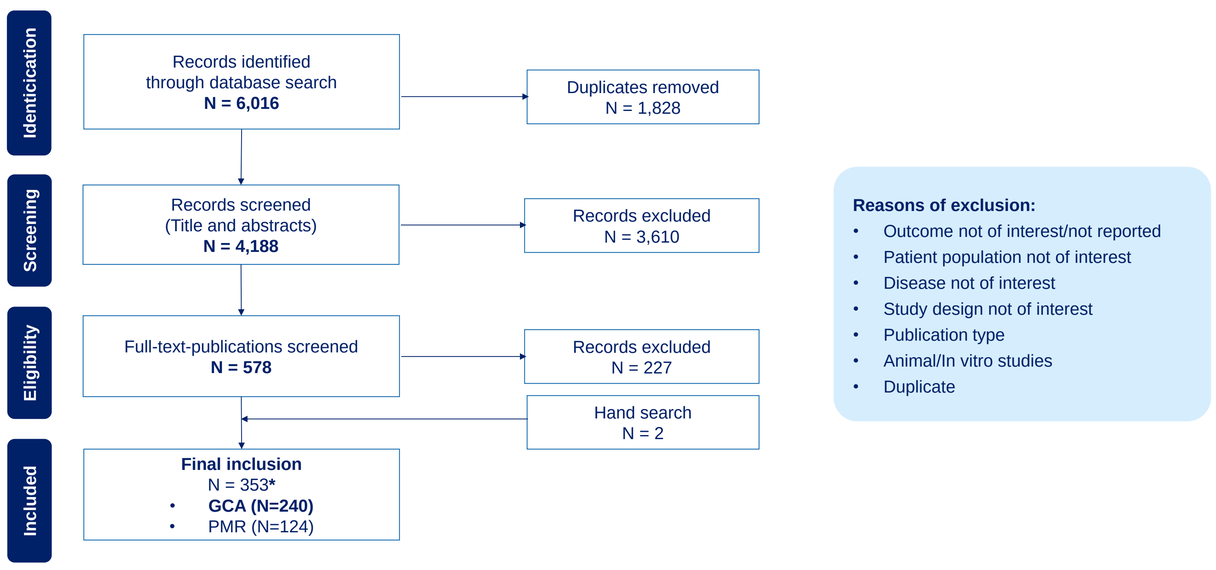
METHODS

- A targeted literature review was conducted in March 2024. Search strategies were applied in MEDLINE, EMBASE, CENTRAL and CDSR. Hand searches were performed on key congress websites and bibliographic sources.
- Pre-defined PICOS criteria were employed to screen identified records (**Table 1**) during the title/abstract (first pass) and full text (second pass) screening.
- English language studies were included, with the exception of editorials, case reports, case series, comments, notes, narrative reviews and animal studies.
- A first reviewer completed initial screening and data extractions. Quality checks of extracted data were undertaken by an independent reviewer, who also discussed any uncertainties.
- The selection of studies, data extraction and results summarization followed established and current best practices.

RESULTS

- A total of 6,016 records were identified, of which 353 were included and 240 specifically related to GCA **(Figure 1)**.

Figure 1. PRISMA Flow*



*Note: The final included publications (n=353) encompass publications for both GCA and PMR indications, with 11 publications overlapping for both indications
Abbreviations: GCA, Giant Cell Arteritis; PMR, Polymyalgia Rheumatica; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLRs, Systematic Literature Reviews. *Page et al. BMJ 2021;372:n71 – Applied to a targeted literature review process

Table 1. PICOS Criteria*

Category	Inclusion Criteria		
Population	• Adult patients aged ≥50 years with Giant Cell Arteritis (GCA)		
Interventions/ Comparator	• Not applicable		
Outcomes	**Clinical Burden** – Clinical presentation – Complications – Disease severity – Comorbidities – Morbidity – Mortality – Therapy burden	**Humanistic Burden** – Symptomatic burden – Quality of life – Impact on daily activities – Physical, mental and emotional health/disabilities – Other patient reported outcomes	**Unmet Needs** – Identified from Patient's, Payer's and Physician's perspective
Study type	• All studies except case reports, case series, comments, editorials and notes		

*Methley et al. BMC Health Services Research (2014) 14:579

Therapy related burden

- Glucocorticoids are the standard of care despite the high rate of relapse (~50% of patients relapse) and risk associated with long term use.[3,25]
- ~94% of patients experience at least one GC-related adverse event, such as osteoporosis, fracture, diabetes, infections, and cardiovascular diseases.[25]
- Tocilizumab and methotrexate are adjunctive treatment options[26] but have their own associated burden and may not be suitable or effective for all patients.[27,28]

Clinical Burden

- GCA presents with a variety of symptoms. Most common clinical manifestations are presented in **Figure 2**.
- GCA diagnosis can be difficult due to varying presentations (mean diagnostic delay: 9 weeks) and not all patients show typical GCA clinical manifestations.[7] Subsequent treatment delay can result in significant complications such as irreversible vision loss (8%-29% of patients).[8,9,10]

Figure 2. Clinical manifestations in GCA Patients

Ischemic Symptoms[1,11]
- New-onset headache in ~2/3 of patients
- Tenderness of the scalp and temporal artery
- Jaw claudication in nearly 50% of patients

Constitutional Symptoms[1,12]
- Low-grade fever in approx. 40% of patients
- Malaise
- Night sweats
- Weight loss

Aortic involvement can lead to **aortic aneurysm formation** or **dissection[13,14]**

Visual disturbances in approx. **20%-36%** of **patients[1,15]**
- Blurred vision, diplopia, amaurosis fugax, eye pain[11,14]
- **Transient vision loss** can affect **2%-30%** of patients[11]
- **Permanent vision loss** can affect **8%-29%** of patients[8,9,10]
- 81% of GCA patients reported affected by AION, causing sudden vision loss[11]

Abbreviations: AION: Anterior Ischemic Optic Neuropathy

- GCA patients have been reported to have an increased risk of aortic aneurysms,[1] ocular manifestations, cardiovascular and cerebrovascular events (**Figure 3**). These conditions contribute to an increased mortality rate, with cardiovascular diseases being the primary cause of death among GCA patients.[11,16]

Figure 3. Comorbidities reported in GCA patients

Cerebrovascular Events 17,18,19,20,21
- **Affecting 2%-20%** of GCA patients
- **40% higher stroke risk** compared to general population → Predictive factors: Male gender, GCA ophthalmic symptoms, hypertension, smoking
- **Major mortality cause**, with 28% mortality within days/weeks post-stroke

Cardiovascular Disease 13,14,18,22,23
- **Doubled risk of cardiovascular disease** in GCA patients vs. general population
- **17 times higher risk** of developing thoracic aortic aneurysm
- Average of **1.1 years** from GCA to thoracic aortic dissection
- **Higher incidences** of coronary artery disease, hyperlipidemia with aortic issues

Ocular Manifestations 11,16,19,24
- **Occlusion of ophthalmologic arteries**, leading to CRAO and AION
- Increased risk of **visual deterioration** in early stages post-GCA diagnosis
- **1/3 of patients** may experience permanent **bilateral vision loss**
- **Delayed steroid treatment** can lead to permanent vision loss → **Early treatment** is **critical**

Abbreviations: AION: Arteritic Anterior Ischemic Optic Neuropathy; CRAO: Central Retinal Artery Occlusion

Humanistic Burden

- GCA places a substantial burden on patients affecting both physical and mental well-being, by hindering daily activities and overall functionality (**Table 2**).[12,29]
- Patients are also reported to have lower physical and mental quality of life than the general population.[9,30,31]
- GCA has a significant impact on patients' psychological well-being, leading to mental disability, depression, and anxiety (**Table 2**).[31,32,33]

Table 2. Humanistic Burden in GCA patients

Humanistic Burden	Burden data
Moderate to severe physical disability[33]	46% of GCA patients
Moderate to severe mental disability[33]	33% of GCA patients
Depression[33]	82% of GCA patients
Anxiety* [32]	49% of GCA patients
Poor HRQoL	
SF-36 Score (Mean±SD); p-value vs general population[30]	PCS: 39.7±11.5; p<0.01 MCS: 47.2±12.8; p<0.01
EQ-5D utility, Mean (SD)[34]	0.7 (0.2)

Abbreviations: EQ-5D: EuroQoL-5 Dimensions; MCS: Mental Component Summary; PCS: Physical Component Summary; SD: Standard Deviation; SF-36: 36-Item Short Form Health Survey questionnaire
*Hospital Anxiety and Depression Scale (Anxiety Domain) ≥ 8, indicating possible/probable anxiety

Unmet Need

Lack of Sustained Remission and Relapse:
- When GCs are the sole treatment, sustained remission is reached by no more than 15%-20% of GCA patients.[35]
- Relapse rates of 34%–75% have been reported, when patients are treated with GCs.[26]

Need of alternative treatments:
- GC-related adverse events have been reported in 94% of GCA patients.[25]
- A proportion of tocilizumab-treated patients do not sustain remission post-discontinuation, and infections and hepatotoxicity have been reported in patients.[36]

Lack of healthcare awareness & faster time to diagnosis:
- Improvement in disease awareness and time to diagnosis.[37]
- Fast track clinics have shown to reduce permanent visual deficits by shortening diagnosis times: 9% vs 37% in conventional referral system.[38]
- Five themes identified which were most important to patients for future research: physical symptoms; function and daily living activities; participation in family roles, hobbies, and work; psychological impact; and effect on health-perception and sense of self.[12]

References

1. Ameer MA. Giant Cell Arteritis (Temporal Arteritis) StatPearls Publishing. 2024
2. Gonzalez-Gay MA. BMC Geriatr. 2019;19(1):200
3. Mainbourg S. Arthritis Care Res. 2020;72(6):838-49
4. Regola F. Ann Rheum Dis. 2022;81:692
5. Li KJ. Arthritis Res & Ther. 2021; 23(82)
6. Sharma A. Arthritis and Rheumatism. 2020; 50:1040-1048
7. Prior JA. BMC Medicine. 2017; 15:120
8. Farhey Y. Curr. Rheumatol. Rev. 2012;8(2):120-133
9. Ní Mhéalóid Á. Eur J Ophthalmol. 2021;31(2):727-733
10. Wang X. Rheumatol. Int. 2008;29:1-7
11. Chew SL. J Clin Neurosci. 2009;16(10):1263-8
12. Robson JC. Rheumatology 2021;60:4671-80
13. Crespo RR. Eur Geriatr Med; 2016, 7: 591-6
14. Eberhardt T. Cardiol Rev. 2007;15(2):55-61
15. Sanchez-Costa JT. Ann. of the Rheum. Dis. 2022;81:685-6
16. Carroll SC. Clin. & Exp. Ophthalmol. 2006; 34:159-73
17. Pariente A. J. Autoimmun. 2019;99:48-51
18. Arias M. Cureus 2021;13(2):e13391
19. De Boysson H. J. Clin. Med. 2022;11(4):1005
20. De Boysson H. J. Rheumatol. 2017;44(3):297-303
21. Dzhus M. Reumatologia. 2022;60(6):399-407
22. Jud P. RMD open. 2023;9(3): e003481
23. Therkildsen P. Rheumatology. 2022;61(7):2931-41
24. Elsideeg S. Ann. of the Rheum. Dis. 2014;73(Suppl 2):699
25. Castan P. J Clin. Med. 2022;11(4):1034
26. Hellmich B. Ann. Rheum. Dis. 2020;79:19-30
27. Harrington R. Biologics Targets & Therapy. 2021;15:17-29
28. Mackie S. Rheumatology 2020;59(3):e1-23
29. Kernder A. J Patient Rep Outcomes 2024; 8(1):4
30. Kermani T. Rheumatology 2019; 58 (Suppl 2)
31. Froehlich M. Frontiers in Med 2023;10
32. Martins-Martinho J. Rheumatol. Adv. Pract. 2024;8(1)
33. De Boysson H. Frontiers in Med 2021;8:777310
34. Unizony S. Ann Rheum. Dis. 2021;80(11):1467-74
35. Ehlers L. Ann Rheum. Dis. 2019;78:1160-6
36. Samec MJ. J Rheumatol. 2023;50(10):1310-7
37. Parashar A. Ann Rheum. Dis. 2024;83:508
38. Baig I. Eye & Brain 2019;11:1-12

Acknowledgements

The Authors acknowledge **Susie Golubowski** (Novartis Pharma AG), for supporting content development and **Mantosh Roy** for graphic support during the development of the poster.

The final responsibility for the content lies with the authors.

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