The global Burden of ANCA-vasculitis – high but unquantified.

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The study of the global burden of disease is evaluation of disparities in health care provision, to improve outcomes and optimise care provision. A recent British Society for Rheumatology workshop highlighted the urgent need for a collaborative approach into research into rare rheumatic conditions, indeed, this is also a priority of UK NHS strategy for rare diseases. (1,2)

The ANCA vasculitides (AAV) are a group of complex autoimmune conditions characterised by inflammation and necrosis of blood vessels, leading to end organ dysfunction and failure. Overall the conditions are rare, this has impeded gathering of epidemiological data but also clinical trials and studies on the socio-economic consequences of AAV. The main types of AAV are granulomatosis with polyangiitis (GPA), and microscopic polyangiitis (MPA). Proteinase 3 ANCA (PR3) is associated with GPA and myeloperoxidase ANCA (MPO) is associated with MPA.

In most populations the overall annual incidence of AAV is 15-20/million (3) with considerable variations in the proportions of patients with PR3-ANCA and MPO-ANCA vasculitis or GPA and MPA. In Southern Europe, Japan and China MPO-vasculitis or MPA is the predominant form of vasculitis, with the reverse in Northern Europe. The age at presentation is greater in MPA (60-65 years) compared with GPA (45-55 years). The AAV are less common in some non-Caucasian populations, in the USA AAV appears to be less common in African-Americans. UK data suggests that there is no difference between the Caucasian population and non-Caucasian populations, but this study did not include African Americans. There is a paucity of data from the Indian subcontinent, Africa and Latin America, but AAV occurs in these populations. The clinical features of GPA and MPA are different, GPA tending to have more retro-orbital granulomatous disease and MPA more severe renal disease. The global DCVAS study has provided the opportunity to look at clinical features of AAV across different ethnicities. The main differences appear to be in the distribution of ANCA specificity rather than clinical features. The AAV have a high mortality. In the UK general practice CPRD data base the 1-year mortality of GPA is 13.6%, equal between sexes, despite the size of study it was not possible to analyse the

influence of ethnicity on outcome. In a trial setting the overall survival at 1-year is 88% and 78% at 5-years, compared to the background population mortality is increased 2.6 fold. (4) Age and renal function were the principal predictors of a poor outcome. A multi ethnic study from the USA observed that failure to achieve complete remission was associated with female sex, black ethnicity, severity of renal disease and MOP-ANCA. (5) This study has not been replicated in other multi-ethnic populations.

The socioeconomic status of AAV patients has not so far been studied in detail and whether AAV patients come disproportionately from poorer social economic groups is not known. There is no data on whether low socioeconomic status is associated with higher disease activity although this is likely; in GCA social deprivation is associated with an increase in cardiovascular disease and ischaemic events (6)

Patients with AAV have significantly impaired quality of life both physically and emotionally with lower Health related quality of life (HRQOL) than the normal population and their spouses. Fatigue is a much determinant of poor HRQOL and is relatively unresponsive to immunosuppressive therapy. (7) There is significant financial impact which may also reduce quality of life. Men with GPA have 2.6 fold increased risk of unemployment after diagnosis. (8)

In the UK only 16.8% of AAV have received education to degree level compared with 55% in the USA, although this could reflect different education systems. (9). In SLE low educational status is associated with a worse outcome and higher disease activity and again this is likely to also be true in AAV.

The AAV are rare conditions and this poses problems for patient education, patients have high educational needs especially in the period after diagnosis, (9) and many physicians in primary and secondary care have a poor understanding of the diseases. Due to the multi-system nature of AAV, patients can often be seen by different medical and surgical specialists. Patients report they can feel “lost in the system” and need help to navigate their way through often complex

healthcare set-ups. Social support networks such as relatives and friends also fail, because people have not heard of AAV or even the term vasculitis. The internet and patient support groups then become a key means of information provision. Low educational achievement makes patient education harder. Self management has been highlighted as an important aspect of care for patients with long term conditions within the NHS 5 year plan.

Calculation of both direct health and indirect costs is required to estimate the economic burden to society. The conditions are long term with the potential for organ damage and high morbidity, and are associated with considerable health costs. The highest costs will be associated with development of end stage renal disease and the need for dialysis or transplantation, these costs in the UK have been estimated to be £23,426 per patient per year. (10) Introduction of biological therapies such a rituximab increases the drug costs but some of these might be offset by better disease control. The personal costs to the patient and family have not been established. This lack of data can have serious consequences, in the UK poor quality health economic data delayed the introduction of rituximab into routine clinical practice.

There is urgent need to understand better the non-medical determinants of outcome. The rarity of the diseases makes their study challenging but does not pose insuperable obstacles. Development of large-scale population based studies permits study of the socio-economic determinants of disease occurrence and outcome. High quality detailed health economic studies are required to determine the direct and indirect costs to enable better resource allocation and to justify to health funders the introduction of novel biologic drugs. The vasculitis community is well networked and in a position to deliver, it needs to rise to the challenge to help our patients.

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