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EDITORIAL

COVID-19 and rheumatology: Reflecting on the first wave and preparing for the second wave

Cases of COVID-19 and associated hospitalizations are rising again, and we are at the start of a "second wave". As we prepare for the second wave, we must reflect on what we have learned from the first and how we are going to effectively manage rheumatology patients going forward.

Rheumatology patients were thought to be at a higher risk of contracting COVID-19 due to their disease and associated immunosuppressive treatments. In March, the British Society of Rheumatology developed a risk stratification tool to identify patients who were to shield during the height of the pandemic.[1] Shielding precautions included staying home or within 2 m of other individuals when in public. Patients deemed to be at high risk were those on high-dose corticosteroids, cyclophosphamide and 2 immunosuppressive agents.

Although shielding can reduce the risk of contracting COVID-19 we must also consider the psychosocial impact it has. Shielding renders patients to extreme isolation and rheumatology patients are already at higher risk of mental health disorders due to the challenges and chronicity of their disease. Superimposed social restrictions make them even more vulnerable to loneliness, depression and anxiety.[2] In addition, denying them access to gyms and swimming pools which is a key part of managing arthritis, can cause exacerbation of symptoms.

Another vital part of management are immunosuppressant drugs. When the pandemic began there was a theoretical risk that these drugs could increase the risk of developing severe COVID-19. Therefore, there was a hesitation in the rheumatology community to initiate disease-modifying antirheumatic drugs (DMARDs) in newly diagnosed rheumatic patients. However, since the start of the pandemic now pathophysiology of COVID-19 has come to light. It is thought the virus drives a "cytokine storm" leading to a hyper-inflammable state observed in conditions such as rheumatoid arthritis and lupus.[3] It is therefore postulated that some of the immunosuppressive therapies used to treat rheumatic conditions are protective against COVID-19.[4]

An observational study demonstrated that rheumatic patients did not have a higher risk of contracting COVID-19 and they did not suffer a more aggressive illness than the general population. Rather, outcome is more dependent on age and co-morbidities.[5] A case series revealed that baseline use of biologic therapy does not lead to worse outcomes compared to the general population.[6] More recently, the RECOVERY trial in the United Kingdom has demonstrated that the use of steroid dexamethasone, reduces 28-day mortality in COVID-19 patients with an oxygen requirement.[7] The interleukin (IL)-6 inhibitor tocilizumab has shown some benefit in observational studies in reducing mortality and invasive ventilation and is currently part of RECOVERY trial phase 2. Cumulative evidence so far suggests there may be a role for tocilizumab in controlling the cytokine storm induced by COVID-19 and it can have a protective factor in the rheumatoid cohort, but research is still ongoing, and the definite effect of tocilizumab is still yet to be determined. Furthermore, cohort studies in France have shown that anakinra, an IL-1 receptor antagonist, reduces the need for invasive ventilation in COVID-19 patients.[8] Barcitinib, a Janus-activated kinase inhibitor and canakinumab, a monoclonal antibody of IL-1B have been shown to improve oxygenation in severe COVID-19 infection.[9,10] There is a wealth of data suggesting that immunosuppressive therapy may be influential in downregulating the cytokine storm and in turn be protective against severe infection.

Early aggressive treatment of inflammatory conditions, especially rheumatoid arthritis, leads to a better long-term prognosis and having untreated overt inflammation can itself cause immunocompromise.[11] Current practice involves discussing the risks and benefits of starting DMARDs with patients and if they are agreeable then to favor drugs that have a shorter half-life such as hydroxychloroquine or sulfasalazine.[12] For biologics, guidelines suggest switching from intravenous to subcutaneous or oral where possible to reduce hospital attendance. Additionally, they advise patients who have suspected or confirmed COVID-19, to continue hydroxychloroquine and sulfasalazine but suspend all other DMARDs.[13] However, for COVID-free patients who are already established on DMARDs, stopping treatment abruptly will lead to a disease flare which will inevitably impact on their function. Therefore, many centers continued therapy for stable patients throughout the first wave. The risk of abruptly stopping DMARDs could cause hospitalization and requirement for high-dose systemic steroids ultimately leading to poorer disease outcomes.[14]

As COVID-19 cases are rising and lockdown measures are being reintroduced, it is necessary to consider the long-term plan for rheumatology patients based on what we have learned from the first wave.

The drawbacks of shielding are extensive and there is no reproducible evidence that rheumatology patients are at increased risk of

developing COVID-19. Patient factors such as age, body mass index, ethnicity, gender, and co-morbidities are proven risk factors for poorer outcomes.[15] Thus, the previous recommendations of shielding to rheumatic patients who are an extremely heterogeneous cohort is not appropriate. We recommend conducting an individualized risk assessment like the one undertaken for hospital staff to identify who is at high risk and would benefit from additional protective measures. Those with multiple risk factors along with immunosuppressive therapy are likely to be at higher risk than stable patients on DMARDs alone. We agree with recent recommendations that vulnerable patients at high risk (over 65 years, medical co-morbidities as well as rheumatic disease) should not shield in this "second wave" but will mostly benefit from taking particular caution: reducing the number of social interactions, working from home where possible and limiting the use of public transport. Local rheumatology centers should strive to identify and appropriately advise these patients. We suggest for lower risk rheumatic patients to follow government guidance with the general population and continue with their medication.

The mode in which we deliver care has drastically changed since the pandemic. Although the majority of new referrals are seen face-to-face following strict social distancing guidelines and utilizing appropriate personal protective equipment, some new patients are reviewed virtually. History and investigations may be all that's needed to reach a diagnosis or create a management plan for certain conditions for example, those referred for osteoporosis, fibromyalgia, or ankylosing spondylitis (AS) where the main bulk of information is obtained from history. Examination is still important and should not become obsolete, but it adds value only when objective assessment of joints are needed, for example those referred for inflammatory arthritis. Therefore, a triage system to differentiate who will benefit from a face-to-face review will be helpful as the pandemic continues. Follow up of existing patients has largely become virtual over the last 4 months. Data on patient experience have been analyzed in our center and there has been an overwhelming amount of positive feedback. Patients feel safer staying at home but still appreciate the opportunity to speak to their rheumatologist. They feel that virtual appointments are less stressful with no commuting, parking or waiting and therefore a lot of patients are happy to continue virtual clinics for the foreseeable future and even after the pandemic. We acknowledge that there are drawbacks to virtual clinics such as the patient feeling lonely and lack of interaction, there are also fewer support group meetings which can all make the patient feel isolated. Virtual clinics also rely on patients to carry out their own disease activity assessment; some can be reliably done such as the Bath AS Disease Activity Index but measures such as the Disease Activity Score of 28 joints will be difficult for patients to do accurately, but they can give some idea on the extent of disease severity and whether a remote consultation is suitable. Although patients seem to have a good experience with virtual consultations, the effect on clinical outcome is not yet known, whether they experience any adverse effects or suboptimal care will require a longitudinal study. Virtual consultations can take away from the holistic approach to care that a face-to-face review provides but weighing up the risks and benefits and as the pandemic continues, we feel it puts more onus on patients to manage their condition and provide a safer review of patients.

In addition, we observed that many drug monitoring blood tests took place in the community with primary care following up results. We have not seen any detriment from this and believe that stable patients can safely increase blood to from 3-monthly to 6-monthly.[12]

Our recommendations for the second wave

1. Most patients can be continued to be reviewed in virtual clinics, along with a defined triage system to reduce delay in diagnosis and management.
2. Rheumatology patients should have individualized risk stratification based on age, ethnicity, and burden of other medical co-morbidities.
3. Patients should be initiated early onto DMARD therapy as part of a swift treat-to-target approach and stable patients' blood monitoring can be predominately done in primary care 6-monthly.

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