REVIEW ARTICLE

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The Role of Nutrition in Rheumatic Disease – A Global Perspective *As Easy As A, B, Ghee?*

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Introduction

Rheumatic diseases encompass a wide range of disorders that are characterised by inflammation and destruction of tissue, with the musculoskeletal system most frequently impacted. Several forms of categorizing rheumatic diseases exist, with one form basing rheumatic diseases on their nature – autoimmune, autoinflammatory and degenerative and metabolic disorders. The aetiopathology of rheumatic diseases are often multifactorial, with genetic, environmental, autoimmune and mechanical factors frequently involved (Calle and Gómez-Puerta, 2018).

Among environmental and lifestyle influences, diet is increasingly appreciated as being implicated in inflammatory processes in the body and therefore an important link to rheumatic diseases. With several studies demonstrating the benefit of the Mediterranean diet (MD), rich in extra virgin olive oil and vegetables, national bodies such as NICE (UK) (National Institute for Health and Care Excellence, 2018) and the French Society of Rheumatology (Daien *et al*, 2021) have recommended the MD in patients with chronic rheumatic disease, most notably in rheumatoid arthritis.

Whilst the MD has received the most attention, dietary patterns vary considerably across populations. The traditional Indian diet, largely plant based with distinctive cooking fats and spices and the rise of the Western diet globally, warrant consideration due to their potential influence on rheumatic disease.

Diet is a modifiable factor that influences the aetiopathology of various rheumatic disease. Rheumatologists and other health professionals can play a key role in encouraging patients to consider an anti-inflammatory diet to potentially lower their incidence risk and disease prognosis. However, there is currently a general lack of well-conducted clinical trials to inform relevant recommendations on more specific diet-related areas, such as the use of supplements. This review discusses the pro-inflammatory and anti-inflammatory aspects of diet globally, including the Mediterranean, Western and Indian diets and their potential impacts on rheumatic disease.

Mediterranean and Western Diet

The Mediterranean diet (MD) compared to other diets emphasizes plant-based foods such as unrefined cereals, extra virgin olive oil (EVOO) as the main fat source, a higher use of vegetables and a lower consumption of red meat and sweets (Nikiphorou and Philippou, 2023). As such, the MD is a known anti-inflammatory diet (Nikiphorou and Philippou, 2023) and in a 3-year longitudinal study, has been associated with decreased serum concentrations of pro-inflammatory cytokines implicated in rheumatic diseases, including IL-1β, IL-6 and Tumour Necrosis Factor (TNF)-α (Urpi-Sarda *et al*, 2021).

Due to the higher consumption of oily fish and EVOO in the MD, higher MD adherence is positively correlated with tissue levels of anti-inflammatory omega-3 fatty acids (FA) (Mantzioris *et al*, 2022) and negatively correlated with omega-6 FA (Monserrat-Mesquida *et al*, 2023). Omega-3 and omega-6 FA form part of the 'polyunsaturated fatty acids' (PUFA) family. FA such as alpha-linolenic (ALA, an omega-3 FA) and linoleic acid (LA, an omega-6 FA) are labelled essential as they need to be obtained from exogenous sources as the body cannot synthesize them. Whilst the long-chain FA eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can be formed via the conversion of the shorter chain omega-3s, this process in the body is inefficient and thus dietary intake of EPA and DHA is recommended, with EPA and DHA levels significantly elevated in those taking omega-3 supplementation compared to controls (Wang *et al*, 2024).

A meta-analysis involving 1464 patients - 1014 of which had rheumatoid arthritis (RA) - found PUFA supplementation led to a significant decrease in all clinical parameters studied – including Disease Activity Score (DAS)28, Health

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Assessment questionnaire and Erythrocyte Sedimentation rate – with a large effect in the Visual Analogue Scale activity (Daien *et al*, 2021). Whilst no dose-dependent effect on joint symptoms was found, a 2-gram (g) PUFA dose was suggested, in part due to a 2 g dosage used in 25 of the 31 studies. Whilst omega-3 supplementation has been associated with benefits in systemic lupus erythematosus (Duarte-García *et al*, 2020), evidence across other rheumatic (Stamp *et al*, 2022) or autoimmune diseases is inconclusive (Hong *et al*, 2024). Given the existing literature, PUFA supplementation's strongest evidence and recommendations are for its use in RA (Daien *et al*, 2021; Sigaux *et al*, 2022). Mendelian randomisation evidence, despite its limitations, provides support for the protective role of omega-3 FA in rheumatic disease, with genetically higher circulating levels of EPA associated with a reduced risk of psoriatic arthritis (Xu *et al*, 2024). Whilst no other beneficial causal effects were identified for other PUFA on gout, juvenile idiopathic arthritis, Sjögren syndrome or ankylosing spondylitis, the findings suggest the need of further clinical trials to assess omega-3 FA supplementation in rheumatic disease.

Although the MD is a known anti-inflammatory diet (Nikiphorou and Philippou, 2023), with the rise of urbanisation, nations are shifting to a more Westernised and processed diet, featuring higher salt, sugar and alcohol intake (Azzam, 2020; Baker *et al*, 2020). Alcohol consumption has complex effects on rheumatic disease, with low alcohol intake demonstrating a 17% reduction in RA risk (Jin *et al*, 2013) and a lower mean DAS28 score by 0.34 in drinkers compared to non-drinkers with RA (Turk *et al*, 2021). However, moderate alcohol intake (≥2.5 units for women, ≥3.75 units for men) may accelerate radiological progression of early-stage RA in women, whilst no significant effect was found in men (Sageloli *et al*, 2018). A genome-wide association study found no causal inverse link between alcohol and RA incidence (Bae and Lee, 2018), suggesting findings may reflect confounding rather than direct effects.

The association between alcoholism and gout is more defined, with significant dose-response relationship between alcohol consumption and risk of recurrent gout flares found (Neogi *et al*, 2014). Compared with no alcohol consumption in the preceding 24 hours, the risk of a recurrent gout flare was 1.36 for >1 - 2 drinks and 1.51 times higher for >2 - 4 alcoholic beverages.

The Indian Diet

Whilst the associations between the MD, common in Egypt, Greece and Italy (da Silva *et al*, 2009; Obeid *et al*, 2022), the WD and rheumatic disease are becoming clearer, these diets differ substantially to those traditionally consumed in other global regions. Despite this, some overarching themes across diets emerge. For example, the use of cooking oils and herbs is common across the Mediterranean, Western and Indian diets. EVOO, a staple in the MD, is high in anti-inflammatory omega-9 FA, whereas sunflower oil, frequently used in WD is high in omega-6 FA (Orsavova *et al*, 2015). Similarly, herbs such as parsley, thyme and rosemary are more common in the MD, whilst Indian diets frequently incorporate spices such as ginger and turmeric, which are increasingly known for their anti-inflammatory and anti-oxidant properties (Salis *et al*, 2021).

India, with a population of over 1.4 billion and significant regional variance in culture and geography, represents an extremely diverse dietary landscape. With prevalence rates of knee OA significantly higher in India, and SLE rates significantly lower (incidence rate of 3.2 people in India compared to 14.6 - 124 people per 1,00,000) than the worldwide average, investigation is warranted to potential dietary contributors (Misra *et al*, 2024). Whilst providing a detailed account on each diet in India is beyond the scope of this review due to the extreme diversity, there are certain themes and trends of the Indian diet which should be noted.

Traditionally, the Indian diet is plant-based, consisting of grains and pulses, such as beans and lentils. *Masalas,* a mixture of spices, is also extensively used. Other staples include pickled food, fermented food, and milk-based products such as *dahi* (curd) and *chaas* (curd-based drink) (Salis *et al*, 2021). Contributing to a higher saturated fats (SFA) intake in certain Indian households are coconut oil and ghee, with 91% and 60% SFA contents respectively (Salis *et al*, 2021). Although a genetic predisposition to higher SFA levels has been linked to having higher risk of developing RA, most studies only show a positive association rather than a causal relationship between SFA and rheumatic disease (Yao *et al*, 2024). A WHO meta-analysis of 880,835 participants showed that higher tissue concentrations of SFA is associated with an increased risk of type 2 diabetes, however whether SFA intake directly influences the development of rheumatic disease remains inconclusive (Christ *et al*, 2019; Reynolds *et al*, 2022).

However, seemingly more important than the absolute percentage of SFA is the source (Hewlings, 2020). The SFA in coconut oil is predominantly medium-chain, whilst ghee and many processed foods are higher in long-chain SFA, which may be metabolised differently and hence have different effects on the pathways implicated in rheumatic disease (Hewlings, 2020).

Featured in the modern WD and in traditional Indian cuisine are trans fatty acids (TFA) - unsaturated fatty acids which contain at least one double bond in the *trans* configuration (Dhaka *et al*, 2011). Due to this, TFA are metabolised differently and have demonstrated different effects than their *cis* counterpart, such as increased activation of extracellular ATP-induced apoptosis (Hirata *et al*, 2017). Found naturally in small quantities in animal products, TFA are found in higher doses in industrially produced vegetable oils that have been partially hydrogenated (Dhaka *et al*, 2011). These industrially produced TFAs can be found in some margarines, Vanasphati ghee, fried foods, and commercially baked goods such as biscuits and pies (World Health Organisation, 2024). Despite the World Health Organisation (2024) recommendations of TFA not exceeding 1% of total energy intake and the Food Safety and Standards Authority of India (2020) stating TFA should not exceed 2% in foods, regulation in some nations remains difficult. For example, the TFA elaidic acid was found to range from 1.04% to 12.09% of the FA content amongst forty-five vanaspati brands found in India (Dorni *et al*, 2018).

Observational data from Nurses' Health Studies found concentrations of TNF Receptors, involved in pro-inflammatory responses, in the highest quintile of TFA consumption to be 10% higher compared to the lowest quintile of TFA consumption (Mozaffarian *et al*, 2004). Similarly, the National Health and Nutrition Examination Survey (1999 - 2010) involving 5,446 participants found that higher circulating TFA levels were associated with increased markers of inflammation, including C-reactive protein (CRP) and fibrinogen (Mazidi *et al*, 2017). Whilst causality cannot be established, even after adjusting for other potentially inflammatory impacting factors such as age, smoking and BMI (Mozaffarian *et al*, 2004), these findings demonstrate the potential role of TFA in modulating systemic inflammation.

A potential key contributor to the inflammatory processes in the everyday Indian diet is white rice, which has a high glycaemic index (GI) of approximately 70 and is also usually consumed in large portions, thus increasing the overall dietary glycaemic load (GI multiplied with the carbohydrate content) (Salis *et al*, 2021). Higher white rice consumption is associated with higher fasting blood glucose levels and as such can promote the formation of AGEs within joint tissues (Zuñiga *et al*, 2014). Increased AGEs accelerate cartilage degradation and increase the formation of reactive oxygen species, exacerbating the inflammatory pathways found in OA and RA (Wei *et al*, 2023). For individuals aiming to avoid pro-inflammatory foods, brown, long-grain rice is a good alternative to the short-grain, polished white rice. Featuring a lower GI of approximately 50, containing more nutrients such as magnesium (Salis *et al*, 2021), brown rice can help with inflammation and BMI - a study conducted in overweight and obese women found that the group consuming 150 g of brown rice every day for 6 weeks had lower CRP levels and more weight loss compared to the group consuming 150 g white rice daily (Kazemzadeh *et al*, 2014).

On the other hand, beans and pulses – such as kidney beans, red gram, and black gram – which are frequently used in traditional Indian cuisine (Salis *et al*, 2021), have a low GI. In many rheumatic diseases, the gut microbiome – the microorganisms lining the gut – is less diverse, a feature associated with systemic inflammation and altered immune tolerance (Semerano *et al*, 2017). However, beans and pulses feature high amounts of polyphenols and fermentable fibre, making them potent prebiotics (Salis *et al*, 2021), with diets rich in beans and pulses having shown to increase the gut microbiome diversity, increase the species linked to anti-inflammatory effects and increase the production of small chain FA such as butyrate (Fernando *et al*, 2010; Kadyan *et al*, 2022). Several studies have shown how increased butyrate concentrations leads to the inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells pathway, leading to decreased levels of pro-inflammatory cytokines, such as TNF-alpha (Ali *et al*, 2022). Whilst research assessing the direct impact of beans and pulses in rheumatic disease is limited, their impact on the gut-immune axis and systemic inflammation suggests a potential beneficial role that warrants further investigation.

Salt, Sugar and Spices

Salt, sugar, and spices also feature in significant amounts in the Indian diet. Starting with salt, the estimated mean daily intake in India is 8.0 g (8.9 g/day for men and 7.1 g/day for women) (Mathur *et al*, 2023), much higher than the World Health Organisation recommendation of 5 g/day for adults (World Health Organisation, 2025). Moreover, the perception of the harmful effects of high salt intake and practices to limit salt intake was low in the study population. Excessive salt intake has been shown to promote pro-inflammatory pathways, notably the increased differentiation of Th17 cells, with a linear association between salt concentration and Th17 expression found in in-vitro studies (Balan *et al*, 2020; Sharif *et al*, 2018). Th17 cells, a type of pro-inflammatory T-Helper cell which secretes cytokine IL-17, implicated in cartilage and bone degradation as well as joint destruction (Miossec, 2021), have been demonstrated to be deposited in the tissues of a range of rheumatic disease, such as the skin of psoriasis patients and in multiple joints of RA patients (Balan *et al*, 2020). Epidemiological studies support this mechanism, with a Spanish study of 18,555 individuals finding that people in the highest quartile of salt intake (>4.55 g) showed a significant association with RA, with the association between salt intake and RA also dose-dependent across salt intakes (Salgado *et al*, 2015).

Excessive sugar consumption, similarly to salt, is also associated with inflammation. Although India's average per capita sugar consumption is lower than Western countries, it is around 20 kg/year, plateauing in recent years (Ministry of Statistics and Programme Implementation, 2024). Increased consumption of sugar as well as consumption of foods with a high GI, such as the prominent consumption of large amounts of white rice in the Indian diet, can also cause systemic inflammation via multiple mechanisms. Higher GI foods lead to a steeper increase in blood glucose concentration after consumption, promoting systemic inflammation, increasing insulin resistance (Kazemzadeh *et al*, 2014), oxidative stress, and formation and accumulation of advanced glycation end products (AGEs) in joint tissues (Wei *et al*, 2023). AGEs promote cartilage degradation, formation of reactive oxygen species and synovial inflammation, all of which are linked to rheumatic disease pathology (Wei *et al*, 2023). Supporting this, a study of 9,203 Korean participants (5,275 women) aged ≥50 years found a positive association between a higher dietary GI and symptomatic knee OA in women (So *et al*, 2018). Whilst the same association was not found in men, the reasons for this remain unclear, however factors such as hormonal balance and over-reporting of energy intake by men have been hypothesized.

In contrast to the above, herbs and spices which are prominent in the traditional Indian diet for centuries have demonstrated anti-inflammatory properties, drawing attention to their uses in rheumatic disease (Daien *et al*, 2021; Mathieu *et al*, 2022; Yang *et al*, 2019), with red chili powder, turmeric powder, coriander powder and cumin seeds/powder the most commonly used (Bhathal *et al*, 2020; Siruguri and Bhat, 2015). Notably, in a meta-analysis of 539 RA individuals, curcumin supplementation (found naturally in turmeric and used to make curry) has demonstrated improvements in erythrocyte sedimentation rate, CRP, DAS28, rheumatoid factor, tender joint count, and swollen joint count (Kou *et al*, 2023). Other spices also used in the Indian diet, such as ginger, cinnamon and garlic have demonstrated clinical benefit with reductions in inflammatory markers and tender and swollen joint scores (Daien *et al*, 2021) compared to placebo. However, even with the herbs and spices that have promising clinical features, recommending their use would be preliminary due to the studies showing such results being small and limited (Amirah *et al*, 2024). Additionally, the use of such herbs and spices mixed into cuisine at standard doses is unlikely to have the same clinical benefits as the high-dose spice concentrates often used in clinical trials (Daien *et al*, 2021; Yang *et al*, 2019).

Conclusion

Although current guidelines recommend the Mediterranean diet (MD) for its anti-inflammatory benefits, further randomised controlled trials are needed to evaluate the effects of individual ingredients as well as other culturally distinct dietary patterns. In clinical practice, rheumatologists and allied health professionals should recognise the significant influence diet can have on rheumatic disease management and reflect this in patient education. Adoption of an anti-inflammatory diet should always complement pharmacological treatment rather than replace it.

Nevertheless, given the cultural and geographical differences, the direct application of the MD, as originally defined, in distant regions such as India, can be challenging. The diversity of Indian cuisine – in terms of locally available produce, cooking methods, and traditional food habits – means that the MD may not be fully replicable in its classic form. Instead, efforts in health professional and patient education could focus on the health-promoting aspects of Indian diets such as the extensive use of spices, legumes, diverse vegetables, and whole grains, many of which possess anti-inflammatory and antioxidant properties, could direct efforts in health professional and patient education. These both align with the health-promoting principles of the Mediterranean diet and complement its anti-inflammatory aspects.

In essence, while acknowledging these contextual differences, it is feasible and beneficial to incorporate healthy MD principles in the Indian culinary framework such as emphasising healthy fats (like nuts and seeds), moderate use of dairy, and minimizing processed foods and added sugars. In addition, substituting salt with spices such as turmeric, ginger, garlic, cinnamon and other spices with known anti-inflammatory effects can also be highlighted as complementary to MD principles.

In conclusion, a culturally sensitive diet should be integral to patient management using personalised, sustainable dietary strategies in combination with other lifestyle aspects that incorporate local food and other traditions and promote anti-inflammatory nutrition in patients with rheumatic disease. This management approach aligns with the recent EULAR guidelines (Nikiphorou *et al*, 2021) and allows for a more holistic care using diet and other lifestyle factors to complement pharmacological management.

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