A cross-sectional study of diet related disease flare in patients with rheumatic disease

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Abstract
Objective: There are very few studies conducted on the effect of diet on disease activity in rheumatic diseases. We surveyed patients to evaluate for diet related disease flare in different rheumatic disease conditions.

Methods: A cross sectional study of consecutive patients attending rheumatology out-patient department at a tertiary care hospital with various rheumatic diseases were surveyed for any diet related disease flare over a period of 1 year. Details of demographics, diagnosis and food triggers (pulses, cereals, fruits, vegetables, non-vegetarian food, oil, desserts/curd) were collected. Data were collected from electronic medical records which captured patients demographic, disease characteristics and diet history. All the raw data were transposed to an excel sheet and further exported into SPSS software (Version 16). Dichotomous outcomes were summarized using percentages and continuous data were presented as Mean and standard deviation (SD).

Results: Out of 2240 patients surveyed 1585 (70.75%) were females as compared to 655 (29.25%) males. About 10.08%; 95%CI (8.87%to 11.41%) rheumatology patients complained of flare of disease activity with diet. Among them vegetables, non-vegetarian food and fruits were the worst culprit in the order of frequency. Since vegetables were part of both vegetarian and non-vegetarian diet, they seem to be the most contributing factor. Within disease, Rheumatoid arthritis, Spondyloarthritis and Osteoarthritis is more prevalent in non-vegetarian patients than vegetarian.

Conclusion: Most rheumatic disease patients have no aggravation attributable to diet except for a few who need to abstain. The survey concluded that only one-tenth rheumatology patients complained of diet flare.

Keywords: Food trigger, vegetarian, non-vegetarian, rheumatic disease, survey.

Introduction
A wide spectrum of rheumatic disease (RD) is seen in the Indian subcontinent.¹ The COPCORD (community oriented program for control of rheumatic diseases) survey reported pooled age

sex adjusted (India census population 2001) prevalence of rheumatic diseases — rheumatoid arthritis (0.34%), osteoarthritis knees (3.34%), undifferentiated inflammatory arthritis (0.22%), spondyloarthritis (0.23%), ankylosing spondylitis
(0.03%), psoriatic arthritis (0.01%) soft tissue rheumatism (1.39%), gout (0.05%) and lupus (0.01%). Despite this staggering burden of RD in India, it is poorly recognized and many more population surveys would be required to measure a true burden and manifestation of RD.\textsuperscript{2} Dietary habits and individual's lifestyle choices has shown to greatly influence the progression and manifestation of RD.\textsuperscript{3} There has been intriguing observation that diet could affect the course of RD and that a variety of food items have been reported to have adverse effects.\textsuperscript{4-6} Researchers have postulated that in some, RDs may at least in part be due to "sensitivity" to certain foods or that food allergens may worsen some patients’ symptoms.\textsuperscript{4,5}

Recent routine clinical practices considered diet therapy with or without pharmacotherapy for management of cardiovascular diseases and hyperglycemia but less accepted by clinicians in the management of RA. Today, alternative and complementary medicine is a multi-billion dollar industry which make patients and clinicians confused.\textsuperscript{7} To be able to understand the dietary risk factors in the progression or symptom flare-up of RD, researchers typically need incident information based on follow-up of a population affected by diet or food patterns.\textsuperscript{8} Recent reviews conclude that salt seems to promote inflammation; consumption of curcumin, spicy food (capsaicin), chocolate and red wine (resveratrol) might attenuate immune hyperactivity; consumption of fatty acids and coffee seems to have ambivalent effects on RD.\textsuperscript{9}

Few studies showed an increase in severity of RD with a particular diet or nutrients that we take regularly in our daily life but they remain unproven.\textsuperscript{10} Many rheumatic disease patients believe diet has an influence on disease symptoms. Overall, the evidence for a role of diet in the aetiology of RD flare up is limited to a small number of observational studies of very different designs. Nevertheless, there is lack of data on RD patients who have experienced aggravation of symptoms after food intake, which foods are most commonly involved and what kind of symptoms they cause.\textsuperscript{11} As per our knowledge no studies have been conducted in India in this regard till date. Therefore, we conducted a cross sectional observation study to evaluate diet related disease flare in Indian patients with various RD conditions.

**Methods**

A cross sectional study of 2240 consecutive patients attending rheumatology out-patient department at a tertiary care hospital with various rheumatic diseases were surveyed for any diet related disease flare over a period of 1 year from May 2016 to April 2017. Details of demographics, diagnosis and food triggers (pulses, cereals, fruits, vegetables, non-vegetarian food, oil, desserts/curd) were collected. Data were collected from electronic medical records which captured patient’s demographic, disease characteristics and diet history. All the raw data were transposed to an excel sheet and further exported into SPSS software (Version 16). Dichotomous outcomes were summarized using percentages and continuous data were presented as Mean and standard deviation (SD). The statistical hypothesis testing of association between diet and disease conditions were analyzed using chi square test and two proportion tests to determine P value. We have presented the incidence of symptoms flare along with 95% confidence intervals.

**Ethical approval**

The study was approved by the ethics committee of Institutional Ethics Committee, YAMER. Oral informed consent was obtained from all patients.

**Results**

Out of 2240 patients surveyed 1585 (70.75%) were females as compared to 655 (29.25%) males. About 60.0% of patients belonged to middle age (21-50 years) group, only 44.6% of patients had a healthy BMI and majority (85.4%) of the patients
were from urban area and patients on non-vegetarian diet were more than those on vegetarian diet (72.59% vs 27.41%). Baseline characteristics of all patients (n=2240) are mentioned in Table 1.

**Incidence of symptom flare:** Out of the total 2240 rheumatology patients, 226 (10.08%) 95% CI (8.87% to 11.41%) complained of flare up of disease activity with diet (see Fig. 1).

**Types of rheumatic diseases:** Out of 226 patients who complained of diet related flare; the most frequent rheumatological diagnosis was Rheumatoid Arthritis (RA, n=82) followed by Spondyloarthritis (SpA, n=57) and Osteoarthritis (OA, n=31).

**Various foods causing symptom flare:** The diet pattern of subjects with symptom flare up is as shown in Fig. 3A. Vegetables, fruits, curd/dessert, spices, pulses, cereals, oil are common ingredients consumed by all the participants, hence there is an overlap of patients and the percentages. Figure 3B demonstrated that chicken followed by mutton were the major reason for diet flare frequency in patients with non-vegetarian diet. Figure 3C showed that among the vegetables; potato, tamarind, lemon, brinjal, tomato, and green leafy vegetables were the major reason for diet flare frequency. Figure 3D demonstrated that banana followed by orange were the major reason for diet flare frequency in patients eating fruits.

**Incidence of food causing flares in different RD:** Within diseases, the incidence of symptom flare was high in RA (61 vs. 21), SpA (42 vs. 15), OA (26 vs. 5) and SLE (15 vs. 3) for patients consuming non-vegetarian food as compared to vegetarian as shown in Fig. 4.

### Table 1: Baseline characteristics

| Characteristics | No of patients, n (%) |
|-----------------|-----------------------|
| Total population| 2240 (100%)           |
| Gender          |                       |
| Male            | 655 (29.25%)          |
| Female          | 1585 (70.75%)         |
| Age group (Years) |                 |
| <10             | 9 (0.4%)              |
| 10-20           | 93 (4.2%)             |
| 21-50           | 1357 (60.5%)          |
| >50             | 781 (34.9%)           |
| Occupation      |                       |
| Agriculture     | 51 (2.27%)            |
| Business        | 163 (7.28%)           |
| Housewife       | 1417 (63.25%)         |
| Professional    | 61 (2.72%)            |
| Retired         | 57 (2.54%)            |
| Service Desk/Field Job | 95 (4.24%)          |
| Software        | 51 (2.28%)            |
| Student         | 147 (6.56%)           |
| Teacher         | 36 (1.61%)            |
| Others          | 162 (7.23%)           |
| Area            |                       |
| Rural           | 327 (14.60%)          |
| Urban           | 1913 (85.40%)         |
| BMI             |                       |
| Under Weight    | 179 (7.9%)            |
| Healthy weight  | 1001 (44.6%)          |
| Slightly overweight | 712 (31.1%)       |
| Heavily overweight | 348 (15.5%)         |
| Type of food    |                       |
| Non-vegetarian  | 1626 (72.59%)         |
| Vegetarian      | 614 (27.41%)          |
| Severity of disease |               |
| Asymptomatic    | 13 (0.58%)            |
| Mild-moderate   | 1610 (71.88%)         |
| Severe          | 617 (27.54%)          |

Fig. 1: Diet complaints in total population (n=2240)
Fig. 2: Number of patients with different rheumatic diseases complaining diet flares (n=226)

Fig. 3A: Diet pattern in patients (%) with symptom flare (n=226)

Fig. 3B: Patients with symptom flare on non-vegetarian food (n=179)

MCTD: Mixed connective tissue disease; APLA: Antiphospholipid antibody syndrome
Fig. 3C: Patients with symptom flare on vegetables (n=226)

Fig. 3D: Patients with symptom flare on fruits (n=56)

Fig. 4: Incidence of food causing flares in different RD (n=226)

MCTD: Mixed connective tissue disease; APLA: Antiphospholipid antibody syndrome
Discussion
According to earlier studies, between 33 to 75% of RA patients believed food plays an important role in their symptom severity whereas 20 to 50% have tried dietary manipulation to relieve their suffering.\(^7,12\)

According to a questionnaire-based survey, \(1/3\)rd of the patients with RA, ankylosing spondylitis and psoriatic arthropathy reported aggravation of disease symptoms after intake of certain foods, while 43% of the patients with juvenile RA and 42% of the patients with primary fibromyalgia stated the same.\(^11\)

This 1year survey was conducted as a cross sectional study in patients attending rheumatology out-patient department at a tertiary care hospital with various rheumatic diseases. The outcome evaluated was diet related disease flare. According to our study, 10.08% of the patients with RD reported disease aggravation after intake of certain foods. Vegetables (100%), non-vegetarian food (79.2%), fruits (24.7%) dessert/curd (14.15%) and spices (7.9%) were the culprit in order of diet flare frequency. Since vegetables were part of both vegetarian and non-vegetarian diet, they seem to be the most contributing factor. However, excluding vegetables and categorizing patients into non-vegetarian and vegetarian group, demonstrated that non-vegetarian food was the most contributing factor to the RD flare up. Current results are in accordance with the study carried out by Tanner SB et al., wherein among 704 RA patients who reported associations between foods and clinical status, 10.7% indicated unfavorable effect of foods. Foods reported to be associated with unfavorable effects included preservatives (6.8%), pork (6.6%), beef (6.0%), citrus, fruits (5.0%), sugar (4.8%), additives (4.4%), milk and dairy products (3.2%), fish (2.2%), vegetables (2.0%), cereals and grains (1.3%), chocolate (1.2%), alcohol (1.2%), coffee and caffeine (1.0%).\(^13\)

According to the present study, about 79.2% patients on non-vegetarian diet and only 20.7% patients on vegetarian diet complained of symptom flare. Among non-vegetarian diet, chicken (n=83), mutton (n=26), fish (n=20), egg (n=18) and mixed (n=32) were the main culprits in the order of frequency. Further, among four major rheumatic diseases noticed in our study; 61 of RA patients on non-vegetarian diet showed symptom flare as compared to 21 patients on vegetarian diet, 42 of SpA patients on non-vegetarian diet showed symptom flare as compared to 15 patients on vegetarian diet, 26 of OA patients on non-vegetarian diet showed symptom flare as compared to 5 patients on vegetarian diet. This could demonstrate a link between meat and aggravation of RD symptoms as also demonstrated by Pattison and colleagues. They report in their prospective investigation regarding the relationship between a widely consumed food item, meat, and the risk of inflammatory polyarthritis. Patients in the inflammatory arthritis group consumed high levels of red meat and meat products as compared to the healthy control group. The energy-adjusted analyses showed a statistically significant positive association between red meat intake and the risk of inflammatory polyarthritis (\(P=0.04\)). The study also demonstrated that higher consumption of red meat and meat products combined, and total protein was associated with increased risk for inflammatory polyarthritis.\(^10\)

It was hypothesized that proinflammatory property of meat fats, high level of protein intake and imbalance in gut flora were the factors for association between meat intake and RA. In these studies, they only examined the association of red meat with RA but link with other non-vegetarian foods were not examined.\(^10,14\)

Similarly, study carried out by Lindberg 1973, Skoldstam et al., 1979, Skoldstam 1986 and Kjeldsen Kragh et al., 1991; evaluated the effects of following a vegetarian diet for at least 3 months in RA patients after a period of fasting. These studies demonstrated that eliminating meat might be beneficial in RA patients. However, it is not
easy to understand which aspect of diet was responsible for the observed effects on RA symptoms; either non consumption of meat or inclusion of fruits and vegetables that are rich in antioxidants.\textsuperscript{15-18} In certain cases, food intolerance is known to cause RA symptom flare, however elimination of such potential dietary antigens is known to provide limited relief of RA symptoms.\textsuperscript{19} In studies carried out among spondyloarthritis patients; 78% of patients believed that diet influenced the symptoms of their disease and one-third of the patients reported worsening symptoms after the intake of certain foods. According to Haugen et al., foods most frequently implicated were meat, coffee, sweets, sugar, chocolate, citrus fruits, and apples.\textsuperscript{11} Sundström et al. reported in a study of 111 patients that 7 patients experienced aggravated ankylosing spondylitis symptoms associated with a particular foodstuff, most commonly vegetables or fruits (n=2) or food rich in flour (n=2).\textsuperscript{20} In the Kyushu Sapporo SLE (KYSS) Study, dietary patterns and the risk of systemic lupus erythematosus in a Japanese population was evaluated. Three dietary patterns; vegetables, meat and dairy product patterns were identified. After adjustment for potential confounders, the dairy product pattern was significantly associated with an increased risk of SLE. However, in contrast to our study, meat dietary pattern characterized by high consumption of beef, pork and processed meat was not associated with SLE risk.\textsuperscript{21} According to our results, all patients consuming vegetables (100%) showed symptoms flare up. Potato (n=51), tamarind (n=30), lemon (n=28), brinjal (n=27), tomato (n=26), and green leafy vegetables (n=24) were the major reason for diet flare in the order frequency. These results are similar to the study by Tanner et al., among specific vegetables, unfavorable effects were reported for tomatoes by 1.9% of all patients studied, cabbage, broccoli, and cauliflower by 0.1%, eggplant by 0.1%, and potatoes by 0.1% of patients. However, in contrast to our study, green vegetable (1.9%) showed favorable effect. Vegetables reported as having favorable or unfavorable effects by different patients were cabbage and cauliflower.\textsuperscript{13} About 24.7% of patients who consumed fruits showed symptom flare up in our study and banana (n=14), orange (n=13), apple (n=8), grapes (n=4), pineapple (n=3) were the major reason for diet flare in the order frequency. In one of the studies, an equal distribution was seen for favorable or unfavorable effects of citrus fruits in different RA patients (5.1% vs. 5.0%).\textsuperscript{13} However contrary to our study, Khanna et al state that fresh fruits like grapes, oranges, apples, black grapes, pineapple, blueberries, pomegranates and dried plums rich in important phytochemicals can reduce oxidative stress and inflammation and further reduce progression and symptoms of rheumatoid arthritis.\textsuperscript{22} In few studies, the foods most frequently reported to cause aggravation of symptoms in patients with RA were dairy products.\textsuperscript{23-25} In our survey, 14% patients with RD reported aggravation of disease symptoms after consumption of dairy product (curd).

**Conclusion**

In conclusion, 10.08% of the all RD patients in our study reported disease aggravation after intake of certain foods. In this study, most of the patients complained flare up of disease activity with some of the item that they take regularly in their routine diet. Non-vegetarian food, in particular chicken was known to cause flare up in majority of the RD patients. Among vegetarian food; potato and citrus food was seen to cause flare up of symptoms. Most rheumatic disease patients have no aggravation of symptoms attributable to diet except for a few who need to abstain.

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