The Relationship between Proinflammatory Cytokines, Trait Mindfulness, and Psychological Well-Being in Rheumatoid Arthritis

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Abstract

Background: Rheumatoid arthritis(RA) is an autoimmune disease in which the body's immune system starts attacking its own cells especially, joints. Individuals with RA are 3 times more susceptible to depression and anxiety. Mindfulness-based interventions have been found efficacious in decreasing depressive symptoms and increasing psychological well-being(PWB) in this population, but the relationship between trait mindfulness and PWB with proinflammatory cytokines implicated in RA has not been explored to date.

Objective: This study aimed to understand the relationship between proinflammatory cytokines, trait mindfulness, and psychological well-being in rheumatoid arthritis patients.

Method: The study consisted of a total of 16 individuals from the 45-75 years age group who have been diagnosed with RA, taking treatment from Kasturba Medical College, Manipal. Proinflammatory cytokines in saliva, IL-6 and TNF-α levels were measured using an ELISA kit, and scales were administered to measure trait mindfulness, psychological well-being, and functioning. Descriptive analysis was done to study the relationship between the variables.

Results: A significant increase in IL-6 levels were observed in the present study, while TNF- α levels were within normal limits. 50% of the participants reported severe impairment and 75% reported depressive symptoms. These results provided evidence of a strong correlation between IL-6 levels and depression. There was a strong positive correlation between trait mindfulness and psychological well-being, (r(14)=.71, p*.01). Trait mindfulness however had a moderately negative correlation with depressive symptoms and disability. Moreover, the relationship between psychological well-being and depressive symptoms and disability was not significant. The relationship between depressive symptoms and disability was highly significant, (r(14)= .63, p*.01).

Discussion and Conclusion: People with RA experience difficulty carrying out everyday tasks and tend to suffer from depression. However, people who score high on Mindfulness and PWB experience less depression and face less interference in their daily activities. Thus, interventions that promote mindfulness practice and psychological well-being may prove to be effective in decreasing depressive symptoms in RA patients as well as proinflammatory cytokines.

Keywords: *Proinflammatory cytokines, Psychological well-being, Rheumatoid arthritis, Trait mindfulness.*

Introduction

Mindfulness originated in Eastern traditions and is linked with the practice of meditation**.** It is the ability to be in the present moment, with purpose and a non-judgemental attitude[19], which facilitates a sense of well-being and the ability to flexibly adapt to changing circumstances[21]. Mindfulness works by facilitating characteristics such as acceptance, decentring, and psychological and behaviouralflexibility[14]. Decentring helps in tackling cycles of ruminative processes which are characteristics of major depression. Deployment of conscious awareness also reduces ruminative thinking by occupying limited attention resources available to us[27]. Mindfulness decreases the impact of stressors[12], by increasing engagement of positive self directed strategies for coping rather than indulging in automatic, negative habitual patterns of responding to a stressor[7]. Mindfulness based Interventions are also found to be effective in increasing the immune function by better regulating the HPA axis[10], which was dysregulated by glucocorticoid receptor resistance caused by prolonged stressors[9].

Another variable that has been found efficient in improving body immune response by decreasing the effect of stressors is Psychological well-being(PWB) [1,6]. PWB components such as positive mood states and favourable social and personal functioning, strengthens the psychological balance[13],and enhances resistance towards disease, and make life more prosperous[1]. Present study aims at studying the relationship between those two variables and their relationship with the immunity biomarkers implicated in rheumatoid arthritis.

RA affects approximately 1% of the population in India[18],and an estimated 0.3 to 1% population worldwideaccording to WHO. It is an autoimmune disease in which the body's immune system starts attacking its own cells especially, joints. This results in inflammation that causes the joints (the synovium) to thicken, which results in swelling and pain in and around the joints[18]. Till now, the actual cause of RA is not clear, but many studies have indicated that proinflammatory cytokines lead to cartilage and bone destruction in RA[3,15]. Cytokines such as Tumor necrosis factor alpha(TNF-α) and Interleukin- 6(IL-6) are found to have a critical role in RA[30].

These patients are 3 times more susceptible for depression and anxiety[22] and RA has a significant impact on functioning[8], social interactions[16], and relations with family members[25], adding further to the disease burden. Mechanisms responsible for the prediction of RA by pre-existing depression are not clear, but altered immune functionality could be the shared mediating factor[20]. Understanding the relationship of trait mindfulness and PWB with immune biomarkers and functioning in rheumatoid arthritis patients will be helpful in devising adjunct treatments methods for the management of stress, depressive symptoms, and improving functioning in these patients. Thus, the present study aimed to study the relationship between proinflammatory cytokines, trait mindfulness, psychological well-being and functioning in RA patients.

Method

Participant characteristic

Sample of the current study consisted of 16 participants(13 female) from the age group of 45-75, who have been diagnosed with RA and have been taking treatment from the department of medicine, Kasturba medical college, or from the Department of Ayurveda, Manipal academy of higher education. All the participants were residents of Karnataka, who can either speak Kannada or English.

Sampling procedure

The sample of the study was obtained by using a

convenience sampling method. Individuals diagnosed with RA were approached and were required to fulfill the following inclusion criteria: Individuals between the ages of 45-75 years, individuals of either gender,who can read and speak either Kannada, Hindi or English. Individuals were excluded from participation if they fulfilled criteria of a comorbid psychiatric disorder(excluding depression and anxiety) as screened on modified MINI-International Neuropsychiatric interview[2]; individuals with severe disabilities as assessed on the Global Disability scale[17]; Individuals who underwent mindfulness, yoga, and another traditional form of intervention two months before being selected for the study; individuals with intellectual disability as ruled out clinically; active self-reported alcohol and other drug dependency; scheduled for major surgery; Individuals with other major medical illness. Screened individuals who were willing to take part in the study were given a consent form and were recruited.

Procedure

Individuals were approached and were oriented about the study and were informed that participation is voluntary and participants can leave the study whenever they want. Afterward, interested participants were screened according to the inclusion and exclusion criteria and 7 individuals were excluded as 2 did not meet the age criteria, 3 had other comorbid conditions such as Hypertension, Chronic heart disease and 2 could not read either in Kannada or English. Then written consent from the screened-in individuals was taken and a form to collect demographic details(Age, gender, residence, education, marital status, occupation, and duration of illness) was filled by the participants. Scales to measure trait mindfulness, psychological well-being and functioning were administered in the department of Clinical Psychology. Then Unstimulated saliva samples were obtained from all the participants. Participants were instructed to brush their teeth, not to eat at least 2 hours before sample collection. They were asked to make chewing motions for 30 seconds to stimulate salivary flow. Subjects were then instructed to first swallow, tilt their head forward, and spit 5ml of unstimulated saliva into a small chamber. Saliva samples from participants were taken at the department of biochemistry, to measure proinflammatory biomarkers(TNF-α, IL-6), which then were assessed in the Biochemistry lab, Department of Biochemistry. Study was carried out from 10th september, 2019 to 30th April, 2020

Study tool: The Five Facet MindfulnessQuestionnaire (FFMQ)[5] gives scores on total mindfulness and its five facets: observation, description, aware actions, non-judgemental inner experience, and non-reactivity. Psychological well-being scale-shorter version[26] was used to measure PWB. Global disability index[17] is a self administered measure and was used to measure overall disability and day to day functioning. Self-reporting questionnaire-24(SRQ-24) was developed by WHO to screen for mental illness and was used to measure depression and anxiety. All the tools were translated into Kannada by experts.

Statistical Analysis

A statistical package for social sciences(SPSS version 25) was used to analyze the data and descriptive analysis was used. Pearson correlation test was used to study the correlation between trait mindfulness, PWB, and disability. The Spearman rank test was used to study the correlation of trait mindfulness and PWB with functioning.

Results

Socio-demographic characteristics:

The socio-demographic characteristics of the participants are mentioned in table 1.

Table 1: Demographic details of participants

Characteristic

Mean age(years)	
Male	60 Years 7 months
Female	60 Years 2 months
Gender ratio(F/M)	4.3: 1
Education level	5th Std and above
Mean duration of Illness	9 years 11 months

Proinflammatory levels

Participants' IL-6 and TNF-□ serum levels are presented in Table 2.

Table 2: *Proinflammatory marker levels*

Participants	**TNF-□(pg/ml)**	**IL-6(pg/ml)**
1	27	123
2	146	266
3	5	98
4	1	629
5	1	142
6	23	98
7	1	194
11	94	228
16	1	283
Mdn	5	194
Interquartile range	59.5	164

Relationship between mindfulness, psychological well-being, functioning and disability

Individual scores on FFMQ, PWB scale, SRQ-24, and global disability scale are presented in table 3. Overall PWB and mindfulness were found to be strongly positively correlated,r(14)=.71, p<.01. Depressive symptoms and disability were found to be strongly positively correlated, r(14)= .63, p<.01.

Mindfulness and disability were found to have a moderate negative correlation, r(14)=-.58, p<.05. mindfulness and depressive symptoms were found to have a moderate negative correlation, r(14)= -.40, p=.12, but the findings were insignificant. PWB and disability were found to be moderately negatively

correlated, r(14)=-.49, p=.053, but the scores were insignificant. PWB and depressive symptoms were found to be moderately negatively correlated, r(14)=-.47, p=.067, but the scores were insignificant.

Table 3: Mean scores on different scales

Variables	Participant																Mean	SD
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16		
FFMQ-total	139	89	91	158	84	72	146	134	135	150	103	72	90	145	126	167	118.8	32.19
Scale 1	33	22	22	34	21	14	40	33	31	30	25	18	19	30	27	32	26.94	7.08
Scale 2	33	19	23	30	20	23	33	28	28	38	15	17	18	36	29	39	26.87	7.68
Scale 3	30	16	16	39	16	14	28	28	30	28	23	14	22	34	27	39	25.25	8.37
Scale 4	24	16	16	39	13	8	21	20	20	28	24	12	18	20	18	31	19.87	6.30
Scale 5	19	16	14	36	14	13	24	25	25	26	16	11	12	25	25	26	6.30	5.96
PWB-total	161	130	135	193	118	164	219	116	127	209	156	117	101	210	187	216	159.94	40.84
Disability	37	59	45	47	50	56	27	40	51	34	32	70	61	49	63	40	47.56	12.18
Functioning	13	11	14	6	15	13	3	14	14	6	6	16	14	10	17	15	11.69	4.24

Discussion

The current study was conducted to study the relationship between biomarkers implicated in rheumatoid arthritis, trait mindfulness, psychological well-being, and functioning in rheumatoid arthritis patients. A total of 16 individuals diagnosed with rheumatoid arthritis were part of the study out of which 13 were females, as more females are affected by RA than males[3]. The mean duration of illness was 9 years 11 months, which depicts the chronic nature of RA. On the Global disability scale, 50% of the participants reported severe disability, which indicates that RA significantly affects individuals' physical functioning and daily activities. On SRQ-24, 75% of the individuals reported depressive symptoms, adding further to the disease burden.

IL-6 level values were higher than the control(31pg/ml) indicating compromised immune functioning, supporting the previous research that IL-6 is implicated in the pathogenesis of RA[3,15,23,29]. Elevated IL-6 levels could also be due to significant stress experienced by these patients due to chronic pain, decreased functioning, depressive symptoms[11,28], and aging [32]. TNF-□ values were found to be elevated in 5 out of 9 individuals, but the difference was not significantly different from the control value(15 pg/ml). Our results are not consistent with the previous literature where TNF-α levels were found to be elevated in individuals with RA[31]. One possible explanation is that these individuals have been taking treatment for a long time and with medicines, the disease activity was under control.

One of the objectives was to explore the relationship between trait mindfulness and PWB, and findings indicate that trait mindfulness and PWB had a strong positive correlation. This means that individuals with high trait mindfulness experience good positive PWB and vice versa, as established in the previous studies[21, 24]. Mindfulness was also found to have a moderate negative correlation with both disability and

depressive symptoms, which indicates that individuals with higher scores on trait mindfulness reported lesser symptoms of depression, and faced less difficulty in carrying out activities of daily living. Another objective was to study the relationship of PWB with disability and functioning. PWB was found to have a moderate negative correlation with both disability and depressive symptoms, which indicates that individuals with higher scores on PWB reported fewer symptoms of depression and anxiety, and faced less interference in carrying out activities of daily living.

Depressive symptoms were found to have a strong positive relationship with disability, which indicates that RA patients with higher scores on depression experienced more difficulty in carrying out activities of daily living.

Conclusion

This study concludes that individuals with RA are more susceptible to depression and face significant difficulty in carrying out activities of daily living. The current study failed to conclude whether the elevated IL-6 levels were due to the direct effect of rheumatoid arthritis or due to higher levels of stress and depressive symptoms experienced by these patients. Individuals with higher scores on Mindfulness and PWB report fewer depressive symptoms and face less interference due to RA in carrying out everyday work.

Findings indicate that interventions aimed at improving mindfulness skills and psychological well-being might prove to be effective in decreasing the depressive symptoms and proinflammatory cytokines in the RA population, which can be tested in future studies.

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Ethical Clearance: Taken from the Department of Clinical Psychology, Department of Psychiatry, and Institutional Ethics committee, Manipal Academy of Higher Education. The research was registered with the Clinical trials registry India(trial number: CTRI/2019/12/022461).

Author Contribution

Conceptualization, PI, A2 and A3; Recruitment, PI, A4; Scale administration, PI; Biomarker collection and measurement, A3; Methodology, PI, A2; Writing and editing the original draft, PI, A2, A3; Funding acquisition, PI.

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Conflicts of Interest: Nil

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