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Original Article

Comparative analysis of immune markers in multiple sclerosis and rheumatoid arthritis patients with oral disease

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Abstract

Introduction: A substantial body of research has underscored the intricate nature of diagnosing oral disorders in conjunction with chronic inflammatory diseases.

Aim: Multiple sclerosis (MS) and rheumatoid arthritis (RA) are chronic autoimmune diseases, which are usually difficult to distinguish in the early stage of the diseases. The objective of this study was to explore the differences of immune mechanism and diagnostic markers through bioinformatics analysis of the pro-inflammatory cytokine's markers (IL-1β, IL-6, and TNF-α) to evaluate the role of immunological markers in patients with MS and RA with oral diseases.

Materials and methods: This study enrolled 54 patients with oral disorders and chronic inflammatory diseases admitted to our hospital between January 2020 and December 2022, among 587 patients who had MS or RA and 50 healthy controls without oral disorders, with age, sex, and familial and genetic factors matching. Oral disorders were diagnosed and staged according to the method of dental examination. Blood (IL-1β, IL-6, and TNF-α) levels were measured using ELISA to detect chronic inflammatory diseases.

Results: Important changes were found in RA and MS patients in terms of their age at onset of disease: RA patients exhibited a higher average age of onset (47.29 years) compared to MS patients (30.56 years), with both conditions showing a female predominance. Genetic factors did not differ significantly between the two conditions. Patients with both chronic inflammatory diseases and oral disorders had elevated levels of the studied markers (IL-1β, IL-6, and TNF-α) compared to those without oral disorders, indicating a substantial impact of oral diseases on immunological responses.

Conclusions: RA typically affects older individuals, while MS onset occurs at a younger age with a higher female prevalence. Xerostomia was more common in RA, while oral candidiasis was more common in MS. Both active MS and patients with oral disorders exhibit high concentrations of IL-1β, IL-6, and TNF-α markers. These outcomes may have inferences for understanding the immune reaction and inflammation in these conditions.

Keywords

chronic inflammatory diseases, immunological markers, multiple sclerosis, oral disorders, rheumatoid arthritis

Introduction

Multiple sclerosis (MS) and rheumatoid arthritis (RA) are chronic inflammatory disorders resulting from dysfunction of the immune system.[1] MS primarily impacts the CNS, while rheumatoid arthritis targets the joints.[2] Both conditions have connections to oral health issues, including periodontitis, caries, and xerostomia.[3] MS is a condition distinguished by the demyelination of nerve fibers inside the central nervous system, specifically the brain and spinal cord, resulting in manifestations such as muscular weakness and sensory numbness, vision problems, and cognitive impairment.[4] While the precise cause remains to be elucidated, it is believed that environmental factors in genetically susceptible individuals act as triggers. An important immunological marker of MS is the presence of autoantibodies against myelin proteins, detectable in the cerebrospinal fluid and blood, which contribute to myelin sheath damage.[5] RA involves inflammation and joint destruction, causing pain, swelling, stiffness, and deformities. Like MS, its exact cause remains elusive, influenced by both genetic and environmental factors.[6]

Oral disorders are connected with increased concentrations of pro-inflammatory cytokines, namely IL-1β, IL-6, and TNF-α, including periodontal disease, oral ulcers, and TMJ problems, reflecting their roles in local and systemic inflammation.[7] Oral diseases are prevalent in both MS and RA patients, often having bidirectional relationships with the systemic diseases.[8] For instance, periodontitis, a gum disease caused by bacterial infection, can elevate pro-inflammatory cytokine levels in the blood such as TNF-alpha, IL-6, and IL-1β, potentially worsening inflammation and tissue damage in MS and RA.[9] Conversely, MS and RA can impact oral health by causing dry mouth (xerostomia), reduced salivary flow, taste alterations, difficulty in chewing and swallowing, and heightened susceptibility to infections.[10] Immunological markers in MS and RA hold implications for oral health, and vice versa.[11] While there are already 2.8 million MS patients globally and 18 million people with RA, this interplay underscores the importance of monitoring and treating both systemic and oral diseases in these patients, as they can influence each other's progression and severity.[12,13]

Patients with RA and MS show that in response to foreign or self-antigens, the tissue immune cells such as macrophages and dendritic cells release cytokines such as IL-1 and TNF-α. These cytokines induce the injury-site endothelial cells to release selectins and integrins, which stimulate chemotaxis and diapedesis of the circulating leukocytes. In addition to the recruitment of leukocytes, the tissue macrophages, and dendritic cells also play a role in the clearing of the antigen by phagocytosis, the release of cytokines and serving as antigen-presenting-cells to lymphocytes.[14] Once the circulating leukocytes enter the local injury site, they are activated by various cytokines and chemokines secreted by the macrophages and dendritic cells. On activation, the leukocytes further release cytokines and mediators of inflammation. Neutrophils are the initial cells and most predominant in the acute phase of inflammation. Neutrophils contain granules rich with lysozyme, matrix metalloproteinases, myeloperoxidase which are released on the foreign or self-antigen leading to its destruction. Neutrophils also destroy the antigen by phagocytosis, the release of reactive oxygen species and cytokines such as IL-1, IL-6, and TNF-α.[15] Lymphocytes including T-lymphocytes and B-lymphocytes are the next line of defense, and they play a crucial role in mediating inflammation by several complex mechanisms including secreting of cytokines, costimulation of lymphocytes, and production of antibodies and immune complexes. Circulating platelets can also play a role in inflammation by platelet aggregation, thrombus formation, and degranulation releasing chemokines and inflammatory mediators.[16]

Aim

The purpose of this study was to explore the differences in the immune mechanism and diagnostic markers through bioinformatics analysis of the pro-inflammatory cytokine's markers (IL-1β, IL-6, and TNF-α) to evaluate the role of immunological markers in patients with MS and RA with oral diseases.

Materials and methods

In this study, 587 patients with autoimmune diseases were admitted to the hospital in Baghdad, Iraq, between January 2020 and December 2022 with oral disorders (OD), which we retrospectively evaluated randomly, including a total of 54 patients with RA (28 females and 8 males) aged 18 to 50 years and 18 patients with MS (7 males and 11 females) aged 16 to 48 years, in the active stage of the disease (all cases were diagnosed according to McDonald criteria).

Exclusion criteria:

- current drug usage,
- alcohol use,
- pregnancy, or nursing,
- excluding tobacco use
- weight less than 55 kg,
- current use of anticoagulants such as heparin or daily aspirin,
- anemia (a hemoglobin value of less than 13.5 gm/dl in men and less than 12.0 gm/dl in women),
- other inflammatory diseases or health issues (like active coronary heart disease, diabetes, or other autoimmune diseases),
- active infection (indicated by fever, ESR test, and CRP test).

Control group: Selected 50 people with MS and RA without OD (20 males and 30 females), aged from 18 to 51 years old.

Collection method

Collection and measuring of TNF alpha, IL-6, and IL-1β from blood was carried out by following the process in which initially we collected 5 ml of fasting morning blood from patients before starting treatment. Subsequently, these samples were centrifuged at 3000 rpm for 15 minutes. This centrifugation step helps separate the serum containing the desired cytokines from components in the blood. Once done we carefully collect the serum from designated tubes for analysis. To maintain their quality, the samples are stored in a refrigerator at 4°C to get rid of their damage or corruption until analysis is performed.

ELISA assay

TNF alpha assay

The samples, kit reagents, and microplate that were set aside for the investigation were given time to reach the ambient temperature. The enzyme linked immunosorbent assay (ELISA) method with the assistance of a kit from Bioassay Technology Laboratory (Catalog No: EA0142Hu, China) was used to measure the concentration of human TNF alpha in the sample. This kit utilizes the biotinylated double sandwich approach for measurement. This kit utilizes a microplate that has been pre-coated with pure rat monoclonal TNF alpha antibody. Fifty microliters of TNF alpha standards (48, 24, 12, 6, and 3 nanograms per milliliter) and 40 microliters of samples were introduced into the wells. The samples were supplemented with 10 µL of biotinylated anti-TNF alpha antibody. Next, 50 µL of strepdavin-HRP was introduced to both the samples and standards, and the mixture was placed in a Sanyo Sterilizer incubator from Japan, keeping the temperature at 37°C for a period of 1 hour. After the incubation period ended, ELISA (Biotek ELx50, USA) underwent a cleaning process using a dedicated washing apparatus. Subsequently, 50 microliters of solutions containing chromogen B and chromogen A were introduced and kept at a temperature of 37°C for 15 minutes under light-restricted conditions. The reaction was halted by subjecting it to darkness to facilitate color production and subsequently introducing an acidic solution. The color intensity was measured at a wavelength of 450 nm using an ELISA reader (Biotek ELx800, USA). TNF alpha levels were determined using typical graphical methods.

IL-6 assay

The samples, kit reagents, and microplate that were set aside for the investigation were let to reach the ambient temperature. The level of human IL-6 in the samples was measured using an enzyme-linked immunosorbent assay (ELISA) method with a kit provided by Bioassay Technology Laboratory (Catalogue No: E6022Hu, China). This kit utilizes the biotinylated double sandwich approach for measurement. This kit utilizes a microplate that has been pre-coated with pure rat monoclonal IL-6 antibody. 50 µL of IL-6 standards (2400, 1200, 600, 300, and 150 nanograms per liter) and 40 µL of samples were added to the wells. Samples were supplemented with 10 µL of biotinylated anti-IL-6 antibody. Next, 50 µL of strepdavin-HRP was introduced to both the samples and standards. The mixture was then placed in a Sanyo Sterilizer incubator from Japan and kept at a constant temperature of 37°C for 1 hour. Once the incubation period concluded, ELISA (Biotek ELx50, USA) underwent a cleaning process using a dedicated washing apparatus. Subsequently, 50 µL of chromogen A and chromogen B solutions were introduced and placed in an incubator set at a temperature of 37°C for 15 minutes in a light-restricted environment. The reaction was halted by subjecting it to darkness to facilitate color production and subsequently introducing an acidic solution. The color intensity was quantified using a spectrophotometer at a specific wavelength of 450 nm using an ELISA reader (Biotek ELx800, USA). IL-6 levels were determined using standard graphical methods.

IL-1β assay

The samples, kit reagents, and microplate that were set aside for the investigation were allowed to reach the ambient temperature. The quantity of human IL-1β (Bioassay Technology Laboratory, Catalog No: E6022Hu, China) the quantification of the samples was performed using an enzyme linked immunosorbent assay (ELISA) kit. This kit utilizes the biotinylated double sandwich approach for measurement. This kit utilizes a microplate that has been pre-coated with pure rat monoclonal IL-1β antibody. Fifty microliters of IL-1β standards (2.5, 1.25, 0.625, 0.312, and 0.156 nanograms per liter) and 40 microliters of samples were added to the wells. Ten microliters of biotinylated anti-IL-1β antibody was introduced into the samples. Next, 50 µL of strepdavin-HRP was introduced to both the samples and standards, and the mixture was placed in a Sanyo Sterilizer incubator from Japan, maintaining a temperature of 37°C for 1 hour. Following the completion of the incubation period, the ELISA (Biotek ELx50, USA) was rinsed using the washing device. Subsequently, 50 µL of chromogen A and chromogen B solutions were introduced and incubated at 37°C for 15 minutes under light-restricted conditions. The reaction was halted by subjecting it to darkness to facilitate color production and subsequently introducing an acid solution. The color intensity was measured at a wavelength of 450 nm using an ELISA reader (Biotek ELx800, USA). IL-1β levels were determined using conventional graphics.

Statistical analysis

The Statistical Package for the Social Sciences was used for statistical analyses (SPSS, v25). The data were presented as mean ± SD. For categorical measurements, frequencies and percentages were utilized. Subject groups were tested for significant differences in baseline demographics, clinical characteristics, and cytokine production using Student's *t*-test and chi-square test, with results considered significant at $p<0.05$.

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Results

During this study, 54 (9.2%) patients were diagnosed with chronic inflammatory diseases and were admitted to our hospital with oral diseases. Of these, 36 patients (66.7%) had RA, and 18 patients (33.3%) had MS. **Table 1** provides a comprehensive demographic overview of the participants. The data is crucial for understanding key distinctions between these conditions.

Firstly, the age of onset varies significantly between RA and MS. While 47.22% of RA cases emerge between the ages of 20-40, 72.22% of MS cases begin within this age range. Moreover, MS shows a higher prevalence of early onset (<20 years old) at 22.22% compared to RA's 8.33%. The average age (mean±SD) for RA patients is notably higher (47.29±7.216) compared to those with MS (30.56±8.438), and this difference is statistically significant (p=0.0001) **(Table 1) (Fig. 1)**.

Sex distribution showed no significant difference between the two diseases (p=0.1973). However, more females were affected in both groups, with 77.78% in RA and 61.11% in MS **(Table 1)**.

Regarding familial and genetic factors, 52.78% of RA patients have them, compared to 66.67% of MS patients. The p-value here is 0.3305, indicating no significant differences **(Table 1)**.

Table 2 provides a detailed overview of the distribution of oral diseases among individuals with two chronic inflammatory conditions, rheumatoid arthritis and multiple sclerosis. These findings shed light on the prevalence of various oral health issues within each group and offer insights into potential associations between these diseases and oral con-

Table 1. Demographics according to CID with OD (n=54).

		Chronic inflammatory diseases				*P* value
		RA		MS		
		n=36	**%**	**n=18**	**%**	
Age of onset	<20 years old	3	8.33%	4	22.22%	**0.01**
	20-40 years old	17	47.22%	13	72.22%	
	>40 years old	16	44.44%	1	5.56%	
Age (mean±SD)		47.29±7.216		30.56±8.438		**0.0001**
Sex	Male	8	22.22%	7	38.89%	0.1973
	Female	28	77.78%	11	61.11%	
Familial and genetic Factors	Yes	19	52.78%	12	66.67%	0.3305
	No	17	47.22%	6	33.33%	

* Significant difference between different percentages using Pearson chi-square test (χ^2) at 0.05 level; CID: chronic inflammatory diseases; OD: oral diseases

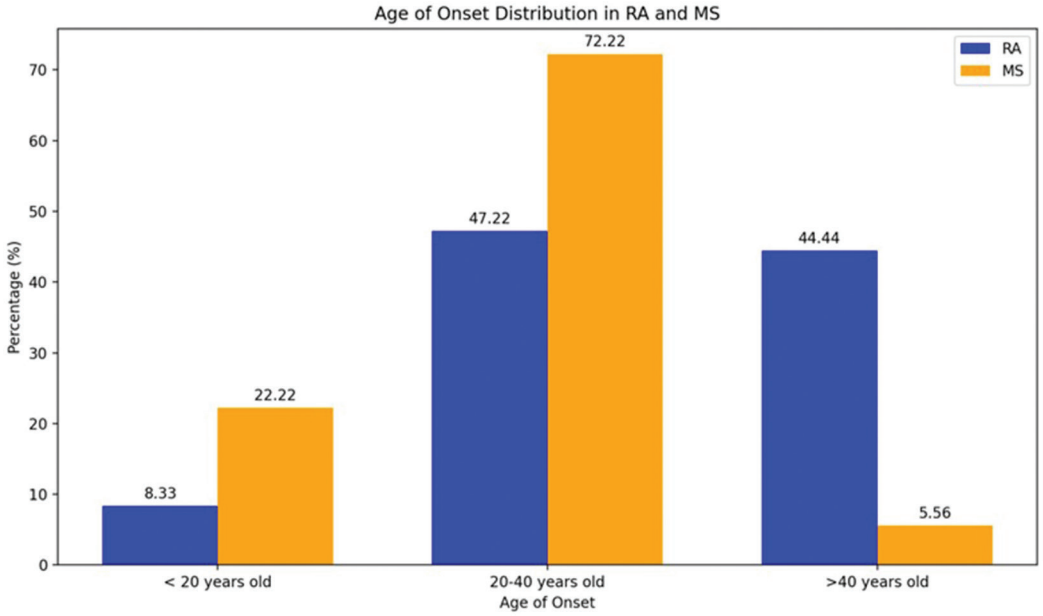

Figure 1. Distribution of RA and MS by age of onset.

ditions. Periodontitis, a severe form of gum disease, is observed in both RA and MS groups, with 13.9% and 33.3% prevalence, respectively. This indicates that individuals with both conditions may be at an increased risk of developing gum problems. Remarkably, 5.6% of the RA group reports instances of xerostomia or dry mouth, but there are none in the MS group. This may indicate a stronger correlation between dry mouth and RA or its management. With 30.6% of participants reporting temporomandibular joint (TMJ) issues, the RA group is remarkable for having these issues, whereas the MS group has no cases documented. It appears that there may be a connection between TMJ problems and RA. Of the two groups, 11.1% and 13.9%, respectively, report having mouth sores. These chronic inflammatory disorders have a comparable frequency. In both categories, gingivitis – a less severe type of gum disease – has been found, with RA accounting for 11.1% and MS for 5.6%. It is noticeable in both, but more so in the RA group. Swallowing difficulties are noted in both categories; in RA, the incidence is 5.6%, while in MS, it is 11.1%. This implies that swallowing difficulties may be a problem for people with certain illnesses. Fungal infections such as oral candidiasis are more prevalent in the MS group (33.3%) than in the RA group (11.1%). The immunosuppressive effects of multiple sclerosis or its therapies might be the cause of this disparity. Both groups report having oral herpes, with the RA group having a significantly greater frequency (8.3%) than the MS group (5.6%) **(Table 2)**.

The immunological indicators in MS and RA patients, specifically, TNF-alpha, IL-6, and IL-1β, are thoroughly examined in **Tables 3-5**, with an emphasis on the impact of oral illnesses on these markers. **Table 3** shows that in comparison to patients with active MS alone (TNF-alpha: 29.29 pg/mL, IL-6: 22.65 pg/mL, IL-1β: 12.33 pg/mL), patients with active MS who also have oral diseases (active MS with OD) have significantly higher levels of TNF-alpha (39.76 pg/mL), IL-6 (29.66 pg/mL), and IL-1β (15.15 pg/mL). *P*-values less than 0.00001 indicate how significant these changes are, highlighting the strong influence of oral disorders on immune responses in individuals with active multiple sclerosis. **Table 4** extends this analysis to RA patients, revealing analogous trends. RA patients with oral diseases (RA with OD) exhibit markedly higher levels of TNF-alpha (41.24 pg/mL), IL-6 (31.52 pg/mL), and IL-1β (15.70 pg/mL) compared to those without oral diseases (TNF-alpha: 31.23 pg/mL, IL-6: 23.37 pg/mL, IL-1β: 11.437 pg/mL), with all p-values again indicating profound statistical significance.

Table 5 consolidates these findings, showing that both active MS with OD and RA with OD share a common pattern of elevated immunological markers (TNF-alpha, IL-6, and IL-1β) compared to their respective counterparts without oral diseases. Importantly, there are no significant differ-

Table 2. The distribution of oral diseases

Oral diseases	Chronic inflammatory diseases			
	RA		MS	
	n=36	%	n=18	%
Periodontitis	5	13.9%	6	33.3%
Xerostomia	2	5.6%	0	0%
TMJ problems	11	30.6%	0	0%
Oral sores	5	13.9%	2	11.1%
Gingivitis	4	11.1%	1	5.6%
Difficulty swallowing	2	5.6%	2	11.1%
Oral candidiasis	4	11.1%	6	33.3%
Oral herpes	3	8.3%	1	5.6%

Table 3. Immunological markers among MS patients and control.

Immunological markers	Active MS with OD N=18	Active MS N=20	*P* value
TNF-alpha, pg/mL	39.76±4.31	29.29±4.04	0.00001
IL-6, pg/mL	29.66± 4.54	22.65±4.33	0.00001
IL-1β, pg/mL	15.15±1.01	12.33±1.35	0.00001

*Significant differences between different means using Student's *t*-test at 0.05 level

Table 4. Immunological markers among RA patients and control.

Immunological markers	RA with OD N=36	RA N=30	*P* value
TNF-alpha, pg/mL	41.24±6.87	31.23±2.59	0.00001
IL-6, pg/mL	31.52± 6.55	23.37±0.69	0.00001
IL-1β, pg/mL	15.70±0.83	11.437±2.44	0.00001

*Significant differences between different means using Student's *t*-test at 0.05 level

Table 5. Immunological markers among patients and control

Immunological markers	Active MS with OD N=18	RA with OD N=36	Active MS N=20	RA N=30	*P* value
TNF-alpha, pg/mL	39.79±4.58	41.60±6.65	29.43±4.33	31.143±3.8	0.00001
IL-6, pg/mL	29.34±4.54	30.83±9.87	22.65±4.33	23.23±1.54	0.00001
IL-1β, pg/mL	15.07±2.05	15.90±2.08	12.165±2.54	11.437±2.4	0.00001

*Significant differences between different means using Analysis of Variance (ANOVA) test at 0.05 level

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ences in these markers between MS and RA patients, irrespective of oral disease status, reinforcing the idea of a common immunological response mechanism in the presence of oral diseases. These results underscore the crucial role of oral health in autoimmune conditions like MS and RA, emphasizing the need for holistic patient care that includes oral health management to potentially mitigate the impact of these chronic conditions on patients' overall well-being.

Discussion

Prior epidemiological research indicate that the prevalence of rheumatoid arthritis and periodontitis may be comparable, with approximately 5% of the population aged 50 years or older.[18] The study's principal finding was the notable disparity in the age at onset of disease between rheumatoid arthritis and multiple sclerosis in patients with optic disc edema. Rheumatoid arthritis often manifests at an average age of 47.29 years, whereas multiple sclerosis normally presents at a younger average age of 30.56 years. The findings of this study align with the findings of other research studies[19-22] in Iraq. This demographic contrast emphasized the differing disease-onset trends between these two illnesses. The study also revealed that both RA and MS primarily impacted females rather than males, consistent with other research demonstrating a greater frequency of autoimmune disorders in women. The findings of our study align with prior research undertaken by other researchers in Saudi Arabia, Egypt, and Norway.[20,21] Nonetheless, there was no notable disparity in sex distribution between the two groups. The study found no significant differences in the incidence of familial and genetic variables between patients with RA and those with MS[23,24]. This discovery indicated that both disorders may possess analogous genetic susceptibility characteristics, highlighting the necessity for additional genetic study to enhance the understanding of these diseases. This study's findings align with those of Goodin et al. and Mousavi et al.[25,26]

The findings of this study indicate that periodontitis was markedly more prevalent in the patient cohorts with rheumatoid arthritis and multiple sclerosis. This data indicates that gum disease is more prevalent among individuals with chronic inflammatory disorders. It underscores the significance of preventative dental health care for those with rheumatoid arthritis and multiple sclerosis. Furthermore, the study by Rodríguez-Lozano et al. demonstrated a significant correlation between rheumatoid arthritis and periodontitis.[27] Also, the 2023 study by Tsimpiris et al. demonstrated that individuals with multiple sclerosis exhibited a greater prevalence of periodontitis compared to the control group.[28] A research group investigating arthritis has identified oral problems potentially associated with rheumatoid arthritis or its treatment. This underscores the significance of delivering individualized therapy to patients with rheumatoid arthritis. Moreover, they identified TMJ issues within the rheumatoid arthritis cohort, indicating a potential correlation between TMJ disorders and rheumatoid arthritis that necessitates additional research. These findings align with a study conducted by Sadura-Sieklucka et al. in Poland and Al-Zahraa JJ et al.[29,30] Patients with rheumatoid arthritis and multiple sclerosis have ulceration rates that highlight shared oral health issues and the necessity for ongoing monitoring and therapy. Gingivitis was noted in both groups, underscoring the significance of screening and preventive strategies. Both groups had swallowing difficulties, highlighting the challenges encountered by patients with rheumatoid arthritis and multiple sclerosis. The MS group experienced an outbreak of candidiasis, a fungal infection, potentially attributable to MS-related immunosuppression, highlighting the necessity of meticulous oral health management for MS patients. These findings align with those conducted by da Cunha et al. in Brazil in 2020.[31] Finally, oral herpes cases were documented in both groups, with the RA group exhibiting a somewhat higher incidence. This underscores the importance of effectively managing viral infections in people with autoimmune diseases due to the potential detrimental impact on overall health. The findings of this study align with those of Burgos et al. in Mexico.[31]

The current investigation reveals that individuals with both MS or RA and OD exhibit significantly elevated levels of all three cytokines compared to those with only the aforementioned diseases, suggesting that OD intensifies the inflammatory response in both systemic ailments. Blood cytokines may serve as potential biomarkers for diagnosis and monitoring, indicating systemic and local inflammation caused by various diseases.[32] Levels of TNF-alpha are significantly elevated in active MS patients with concurrent oral diseases (active MS with OD) compared to those with active MS alone. In our analysis of RA patients, we observed that those with oral diseases exhibited significantly elevated TNF-alpha levels compared to RA patients without oral issues. Irrespective of the underlying autoimmune condition in both cases, those with oral disorders exhibited elevated levels of TNF-alpha compared to those without oral diseases. This outcome indicates a shared immune response mechanism that elevates TNF-alpha levels in individuals with both multiple sclerosis and rheumatoid arthritis, triggered by oral diseases. Our results suggests that TNF-alpha may play a similar role in the pathogenesis of both illnesses. TNF-alpha has previously been associated with synovial inflammation in rheumatoid arthritis and demyelination of nerve fibers in multiple sclerosis, indicating its potential as a target for therapeutic intervention.[33] The proinflammatory cytokine TNF-alpha can induce cell death, activate macrophages, stimulate the production of other cytokines, and enhance the expression of adhesion molecules on endothelial cells. TNF-alpha is associated with joint degradation and synovial inflammation in rheumatoid arthritis, as well as demyelination of nerve fibers in multiple sclerosis. This study indicates that TNF-alpha levels are significantly elevated in patients with rheumatoid arthritis. This corresponds with the French study by Noack et al.[34]

Furthermore, IL-6 levels are elevated in persons with OD who have both active MS and RA. In patients with diverse autoimmune disorders, oral diseases are consistently linked to heightened levels of IL-6. Regardless of the diagnosis, it seems that oral diseases influence the increased IL-6 levels in individuals with RA and MS. This may exacerbate their symptoms and accelerate the advancement of their ailments. Both multiple sclerosis and rheumatoid arthritis appear to have a response mechanism activated by diseases, as evidenced by the elevated levels of interleukin-6. The study indicated that in comparison to controls, IL-6 levels were significantly elevated in persons with active MS and RA. These data reveal the parallels in IL-6-mediated inflammation across various autoimmune illnesses, highlighting the common aspects of the immunological responses. Notably, IL-6 levels exhibited no statistically significant differences between persons with active MS and those with RA. This suggests that the pathogenesis of both diseases may be similarly influenced by IL-6. Targeting IL-6 may hold therapeutic significance in the treatment of both rheumatoid arthritis and multiple sclerosis, since studies indicate that the inhibition of IL-6 signaling could reduce disease activity and impede progression in patients with both conditions.[33]

Finally, compared to controls, both RA and active MS patients had significantly elevated levels of IL-1β, highlighting the importance of this common cytokine in the symptoms associated with many illnesses. This indicates that IL-1β may equally contribute to the pathophysiology of both disorders, a finding subsequently corroborated by the statistical analysis in the current study. There was no statistically significant difference in IL-1β levels between patients with active MS and those with RA. Prior studies have demonstrated that the inhibition of IL-1β activity may exert anti-inflammatory and immunomodulatory effects in patients with rheumatoid arthritis and multiple sclerosis, hence reinforcing its viability as a therapeutic target.[30] Consequently, the inhibition of IL-1β activity through recombinant IL-1 receptor antagonists or neutralizing antibodies has been documented to exert anti-inflammatory and immunomodulatory effects in patients with rheumatoid arthritis and multiple sclerosis, as it diminishes disease activity, enhances joint function, and lowers the relapse rate.[31,34]

These significant discoveries have various crucial ramifications. Oral disorders markedly affect the immunological responses of people with MS and RA, as demonstrated by the persistent increase of pro-inflammatory cytokines in those with oral diseases. This highlights the crucial connection between dental health and the immune system's response, potentially intensifying the symptoms and progression of autoimmune illnesses.[35]

Secondly, the lack of substantial changes in immunological markers across MS and RA patients, irrespective of oral disease status, suggests that oral disorders trigger a common immunological response mechanism. This highlights the potential for dental health management to influence autoimmune disorders beyond merely MS and RA, underscoring the need for comprehensive patient care that incorporates oral health considerations.

These findings possess significant clinical implications, underscoring the essential significance of dental health in the management of autoimmune disorders such as multiple sclerosis and rheumatoid arthritis. Efficient management of oral disorders can increase oral health and lead to improved disease management and overall patient well-being.

Conclusion

This study examined the effects of chronic inflammatory disorders (rheumatoid arthritis and multiple sclerosis) on dental health. Rheumatoid arthritis predominantly impacts older adults, but multiple sclerosis often manifests at a younger age and exhibits a higher prevalence in females. Familial and genetic factors were analogous between the two situations. Patients with rheumatoid arthritis and multiple sclerosis exhibited an elevated prevalence of oral disorders, such as periodontitis, oral ulcers, gingivitis, and dysphagia. Xerostomia was more prevalent in rheumatoid arthritis, but temporomandibular joint disorders were widespread. Oral candidiasis was more prevalent in multiple sclerosis, perhaps attributable to immunosuppression. Patients with active multiple sclerosis and rheumatoid arthritis exhibiting ocular disease demonstrate elevated levels of TNF-alpha, IL-6, and IL-1β immunological markers relative to the control group. These findings may have ramifications for comprehending the immune response and inflammation in these disorders.

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