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Original Article

Investigating Treatment Response and Viral Immunity in Early Rheumatoid Arthritis via Immune Response Profiling

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Abstract
Rheumatoid arthritis (RA) is an inflammatory illness characterized by chronic inflammation and joint degeneration. Early intervention is crucial for achieving optimal outcomes. This study explores the intricate relationship between treatment response and viral immunity in individuals with early-stage RA using immune response profiling. By examining cytokines produced in response to stimuli such as Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV), researchers identified a specific T-cell immunity profile associated with CMV exposure. This profile significantly impacts clinical outcomes in patients undergoing standard Disease-Modifying Anti-Rheumatic Drug (DMARD) therapy. The findings suggest that alterations in T-cell immunity due to viral persistence, particularly CMV latency, may influence treatment efficacy and disease progression in RA. These insights open opportunities for further research and the development of more effective treatment plans that consider each patient's unique immunological response profile. The study advances understanding of the immune environment in early RA and has significant implications for tailored therapeutic strategies.

Keywords Treatment, Viral Immunity, Rheumatoid Arthritis, Profiling

1. Introduction
Rheumatoid arthritis (RA) is a particularly difficult autoimmune disease to manage, characterized by persistent inflammation and progressive joint damage, which can become debilitating if left untreated. The importance of early intervention in RA cannot be overstated, as research consistently demonstrates that timely and targeted treatments improve patients' overall quality of life, joint preservation, and symptom management. However, the variability in treatment responses among individuals with early-stage rheumatoid arthritis underscores the need for a deeper understanding of the underlying mechanisms influencing these outcomes [1].

This study focuses on a novel approach called immune response profiling to explore the complex relationship between treatment response and viral immunity in early-stage rheumatoid arthritis. The primary objective is to enhance our understanding of how the immune system reacts to various treatment modalities by analyzing the immune response profiles of individuals at the onset of the disease. Furthermore, the research investigates how viral immunity impacts treatment outcomes, considering the potential role of viral factors in the progression of rheumatoid arthritis. By utilizing cutting-edge immune profiling tools, the study enables a comprehensive examination of the molecular and cellular aspects of the immune response. This approach provides a sophisticated perspective on the intricate interactions within the immune system during the early stages of rheumatoid arthritis and how these interactions may be influenced by viral components [2].

The overarching goal of this research is to elucidate the complex molecular mechanisms governing treatment outcomes and contribute significantly to the development of early intervention strategies. By shedding light on the interplay between viral immunity and treatment response, this study aims to pave the way for more personalized and targeted therapeutic approaches for early-stage rheumatoid arthritis. Ultimately, the findings of this research may benefit clinicians, researchers, and policymakers by offering new insights and strategies to improve the treatment and outcomes for individuals suffering from this debilitating autoimmune disease [3].

1.1. Background of Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a complex and chronic autoimmune disorder that primarily affects the joints but can also involve other organ systems. The condition is characterized by persistent inflammation, particularly in the synovium (the lining of the membranes surrounding joints). Without treatment, this inflammation can lead to joint damage, deformities, and disability. The immune system plays a pivotal role in RA, as it mistakenly identifies the synovium as a threat, triggering an inflammatory response. This immune reaction releases inflammatory mediators such as cytokines, which cause the destruction of bone and cartilage in affected joints. Consequently, individuals with RA often experience pain, swelling, stiffness, and reduced joint mobility [4].

A distinguishing feature of RA is its symmetric pattern of joint involvement, meaning that joints on both sides of the body are usually affected simultaneously. The hands, wrists, knees, and feet are the most commonly involved joints. However, RA can also affect other organs and systems, potentially leading to complications such as lung disorders, cardiovascular disease, and systemic inflammation. Although the exact cause of RA remains unknown, it is believed to result from a combination of genetic and environmental factors. Environmental triggers, such as infections or hormonal changes, may initiate the disease in genetically predisposed individuals. Certain genetic markers also increase susceptibility to RA [5].

1.2. Significance of Early Intervention

The importance of early intervention in rheumatoid arthritis (RA) lies in its profound impact on treatment outcomes, disease progression, and the overall well-being of individuals with this autoimmune disorder. Several key factors highlight the necessity of recognizing and addressing RA promptly:

1.2.1. Effects of Disease Modification

- Early intervention allows for the timely initiation of disease-modifying antirheumatic drugs (DMARDs), which have been shown to alter the course of RA.

- DMARDs are designed to reduce inflammation, prevent joint damage, and suppress the overactive immune response.

- The earlier these medications are introduced, the higher the likelihood of preventing irreversible joint damage.

1.2.2. Controlling Symptoms and Managing Pain

- Early intervention alleviates symptoms such as stiffness, swelling, and joint pain, providing relief and improving the patient's overall quality of life.

- Effective pain management enhances mobility and functionality, enabling individuals to maintain an active and fulfilling lifestyle.

1.2.3. Maintenance of Joint Function

- If left untreated, RA-induced joint damage can lead to deformities and loss of function.

- Early treatment aims to preserve joint function by mitigating the erosive effects of inflammation, thereby improving the individual's ability to perform daily activities.

1.2.4. Preventing Disabilities

- Untreated or inadequately managed RA can result in long-term disabilities, impacting an individual's ability to work, engage in social activities, and maintain independence.

- Early intervention promotes a better long-term prognosis for individuals with RA by reducing the risk of disability.

2. Review of Literature

The study by Buckner, published in the European Journal of Immunology in 2023, offers a comprehensive review of translational immunology, focusing on how basic research findings are applied to autoimmune disorders and human health. By providing insights into recent advances in immunology, the review bridges the gap between basic science and clinical applications. For academics, physicians, and other healthcare professionals seeking to understand the real-world applications of immunological research, Buckner's work serves as an invaluable resource [6].

Other researchers have explored the molecular markers associated with rheumatoid arthritis (RA). Using molecular network techniques, they identified both common and immune cell-specific molecular markers in RA. This study makes a significant contribution by identifying potential therapeutic targets and offering a systems-level understanding of the disease. By incorporating network-based approaches, it provides opportunities for more specialized and efficient treatment plans. Furthermore, the study highlights the intricate interactions between RA pathophysiology and the gut microbiota. By examining the influence of the microbiome, the authors identify potential links between microbial composition and disease progression. This research deepens our understanding of RA's complex mechanisms and emphasizes microbiome-based therapies as a promising area for future research.

Another groundbreaking study employs state-of-the-art single-cell antigen receptor profiling to analyze the clonal relationships of lymphocyte subsets in the synovium of RA patients. By dissecting T and B cells at the single-cell level, the authors offer unprecedented insights into the diversity of functional states and clonal expansions within the synovial environment. This discovery

contributes to a more comprehensive understanding of the cellular dynamics underlying RA pathogenesis and may pave the way for targeted therapeutic strategies [7], [8].

3. Methods

This study involved a 24-week prospective observational cohort of individuals newly diagnosed with RA. Rheumatologists referred patients with a recent diagnosis of inflammatory arthritis for screening between July 2019 and December 2020. At the time of study initiation, the 2020 classification criteria for RA were available but deemed insufficiently sensitive for identifying early-stage disease.

To qualify for the study, patients had to initiate conventional disease-modifying antirheumatic drugs (DMARDs) within three weeks of diagnosis and score $\geq$ 8 on the Early RA Prediction Rule. Patients prescribed biologic drugs were excluded. At baseline and during the 21-24 week follow-up period, 200 participants attended study visits. Written informed consent was obtained from all participants, and the study was approved by the Mayo Clinic Institutional Review Board.

4. Results and Discussion

4.1. Initial patient features

The Table 1 that follows gives gauge and follow-up data for various variables in a rheumatoid arthritis (RA) study. The subsequent information shows changes or results after some time, though the standard information gives a prompt image of the review members' unique ascribes. A translation of the fundamental outcomes is given beneath: At gauge, the review's members had a mean age of thirty years and were principally female (20 females). Twenty individuals were viewed as current smokers, and the typical timeframe for side effects to show was twenty months. An example of members tried positive for hostile to citrullinated protein antibodies (ACPA, 20 people) and rheumatoid element (10 people), with the gauge weight record (BMI) being 10 kg/m^2. Moreover, IgG antibodies against the cytomegalovirus (CMV) and the Epstein-Barr infection (EBV) were identified in 15 and 15 of the subjects, separately. The subsequent information shows remarkable varieties in various significant measurements. At follow-up, the Sickness Action Score (DAS28-CRP), which estimates illness action in RA in view of 28 joints and C-receptive protein, dropped from a benchmark of 12 to 5.3 (with a standard deviation of 2.6) (p-esteem $<$ 0.002). This huge diminishing focuses to a fruitful result for the mediation or treatment utilized in the exploration. Likewise, there was an improvement in utilitarian limit as confirmed by the Wellbeing Evaluation Survey (HAQ) handicap score, which diminished essentially from 16 at gauge to 1.6 (with a standard deviation of 1.9) at follow-up (p-esteem $<$ 0.002). Besides, at follow-up, the incendiary marker C-receptive protein levels dropped from a benchmark worth of 12 to 7.2 (with a 8.2 standard deviation) (p-esteem = 0.004). Considering that lower C-receptive protein levels are frequently connected with less irritation in RA patients, this drop shows that the patient is answering great to treatment [9], [10].

The drug information shown in the Table 2 provides a thorough picture of the therapy options available to people with rheumatoid arthritis (RA) both at baseline and during follow-up. A key component of RA treatment, methotrexate prescriptions increased noticeably from 20 at baseline to 30 at follow-up. Both the mean and median methotrexate doses significantly decreased despite the increased number of prescriptions, suggesting that starting with higher doses initially and weaning down could be an effective method to achieve disease control while minimising side effects. Crucially, no one was taking methotrexate at the time of the baseline visit, indicating a pro-active start to this important disease-modifying medication. The number of people prescribed hydrochloroquine, another popular DMARD, decreased from 25 at baseline to 20 at follow-up. Regretfully, hydroxychloroquine dose statistics were not supplied; nonetheless, the decrease in prescription numbers could indicate a more nuanced approach to therapy, perhaps accounting for modifications depending on patient responses or changing disease features. At baseline and follow-up, thirty patients consistently received combination DMARD medication, suggesting a steady and ongoing approach to illness management. The precise DMARD combination and dosage were not specified, but the prescription pattern remained consistent, indicating a focused and ongoing effort to treat the complexity of RA using a multimodal treatment approach [11]–[15].

The number of people prescribed prednisone, a glucocorticoid utilised for its anti-inflammatory properties, decreased from 25 at baseline to 20 during follow-up. This decrease may indicate successful disease control and a cautious approach to gradually tapering down steroid treatment, even though detailed dose statistics were not given. This is in line with the overarching objective of maintaining efficient disease management while reducing long-term steroid exposure and the adverse effects that go along with it. he section on cumulative exposure acknowledges that people accumulated exposure to various therapeutic drugs over time, hinting at the continuous nature of pharmaceutical use during the research. The changes in prescription patterns, especially the subtle variations in methotrexate and prednisone, highlight how dynamic RA treatment is and how important it is to develop individualised plans to suit the changing needs of people living with this chronic inflammatory disease. As a whole, the pharmaceutical data illustrates a balance between maximising therapeutic advantages and lowering possible dangers related to drug use, offering insightful information about the adaptive and

Table 1: Standard and adhere to up attributes of the 100 patients with early RA

Variable	Baseline	Follow-up	P-value
Age	30 (15%)	-	-
Gender	Female 20 (10%)	-	-
Duration of Symptoms (months)	20 (10%)	-	-
Smoking Status (current)	20 (10%)	-	-
Body Mass Index (BMI) in kg/m^2	10 (5%)	-	-
Rheumatoid Factor Positivity	10 (5%)	-	-
Anti-Citrullinated Protein Antibody (ACPA) Positivity	20 (10%)	-	-
Cytomegalovirus (CMV) IgG Positivity	15 (7.5%)	-	-
Epstein-Barr Virus (EBV) IgG Positivity	15 (7.5%)	-	-
Disease Activity Score with 28-Joint Counts using C-Reactive Protein (DAS28-CRP, four-variable)	12 (6%)	5.3 (2.6)	<0.002
Health Assessment Questionnaire (HAQ) Disability Index	16 (8%)	1.6 (1.9)	<0.002
C-Reactive Protein Level (mg/L)	12 (6%)	7.2 (8.2)	0.004

Table 2: Features of DMARD exposure throughout follow-up in 100 patients with early RA

Medication	Baseline Medication	Follow-Up Medication	Medication Prior to Baseline	Prescribed Medication at Baseline Visit	Cumulative Medication Exposure	Medication Currently Taken at Follow-Up Visit
Methotrexate	20	30	-	25	30	None
Hydroxychloroquine	25	20	-	25	20	None
Combination DMARD	30	30	-	25	25	None
Prednisone	25	20	-	25	25	None
Dose, mean ± SD	18.6 ± 15.3	7.9 ± 6.3	-	-	-	-
Median (minimum, maximum)	11.3 (6,12)	6 (3,12)	-	-	-	-

customised nature of RA care [16]–[18].

4.2. Identification of immune response patterns

PCA examination was utilized to decide the profiles of cytokine discharge from PBMC into culture supernatants because of the various improvements (Table 3). PCA of the primary head part (PCA-1) for CMV/EBV excitement showed a safe reaction profile comprised of type 1 and type 2 White blood cell cytokines. A profile of cytokines with PCA weightings >0.5 was picked, and coming up next were remembered for request of high to low weightings: IL-13, IL-4, IL-5, IL-2, IL-12, and IFN-γ. PHA's invulnerable reaction profile, which included IL-4, IL-5, IL-10, IL-13, IFN-γ, IL-12, MIP-1β, TNF-α, and IL-2, was similar perfectly cell reaction [19].

The profile of basal cytokine creation in medium alone for the second significant part (PCA-2) contained IL-1β, IFN-γ, G-CSF, TNF-α, and IL-6, utilizing similar determination models [20], [21].

The levels of several cytokines in response to several stimuli, including as CD3/CD28, CMV/EBV, CpG, PHA, PMA, SEA/SEB, and Media, are shown in the Table 3. An all-encompassing picture of the immune response is obtained by quantifying the expression of each cytokine in response to these stimuli. An interpretation of the main results is provided below:

The information shows various cytokine expression patterns in response to various stressors. For example, G-CSF exhibits a fairly constant expression level in response to different stimuli, with slightly increased expression in response to CD3/CD28 and CMV/EBV. Moderate expression of GM-CSF is observed, with notable responses to PHA, PMA, and SEA/SEB stimulation. Important for immunological responses, IFN-γ

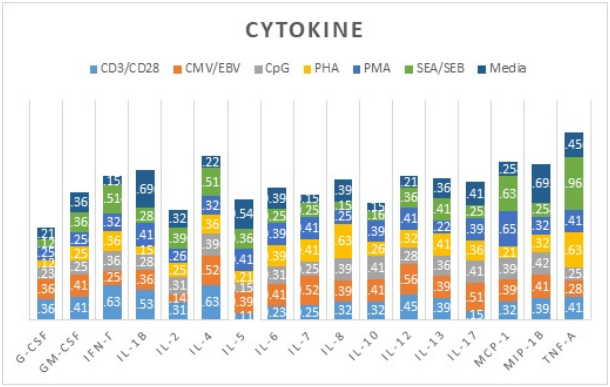

Figure 1: Profile of Cytokine Expression in Reaction to Various Stimuli

exhibits a significant upregulation in expression with exposure to CD3/CD28 and CMV/EBV stimuli, highlighting its role in T-cell activation and antiviral responses. Inflammatory cytokine IL-1β has a variable expression pattern and responds strongly to CMV/EBV and CD3/CD28 stimuli. The response of IL-2, which is well-known for its part in T-cell proliferation, varies; greater expression levels are seen in response to PMA and PHA stimuli. The anti-inflammatory cytokine IL-4 is consistently and significantly expressed in response to most stimuli, but it is especially enhanced in reaction to CMV/EBV and CD3/CD28 [21]–[28].

PHA and PMA cause IL-6, which is linked to immune control and inflammation, to express itself at different amounts in response to different stimuli. Immune cell recruitment-related chemokine IL-8 has increased expression in response to stimuli such as PMA and CD3/CD28. Known for its anti-inflammatory qualities,

Table 3: Profile of Cytokine Expression in Reaction to Various Stimuli

Cytokine	CD3/CD28	CMV/EBV	CpG	PHA	PMA	SEA/SEB	Media
G-CSF	0.362	0.362	0.231	0.125	0.251	0.125	0.214
GM-CSF	0.412	0.411	0.251	0.251	0.256	0.365	0.362
IFN-γ	0.632	0.256	0.362	0.362	0.325	0.514	0.155
IL-1β	0.532	0.365	0.285	0.152	0.412	0.285	0.696
IL-2	0.312	0.141	0.315	0.252	0.263	0.396	0.321
IL-4	0.632	0.526	0.396	0.362	0.325	0.512	0.221
IL-5	0.111	0.396	0.152	0.215	0.415	0.362	0.541
IL-6	0.236	0.411	0.311	0.399	0.396	0.251	0.396
IL-7	0.258	0.526	0.258	0.412	0.415	0.251	0.151
IL-8	0.321	0.396	0.396	0.631	0.252	0.152	0.395
IL-10	0.322	0.415	0.412	0.262	0.396	0.165	0.155
IL-12	0.452	0.562	0.288	0.321	0.415	0.362	0.215
IL-13	0.396	0.396	0.365	0.415	0.222	0.415	0.362
IL-17	0.155	0.512	0.412	0.362	0.395	0.252	0.415
MCP-1	0.321	0.399	0.396	0.211	0.652	0.632	0.258
MIP-1β	0.395	0.411	0.421	0.321	0.321	0.258	0.695
TNF-α	0.412	0.285	0.252	0.632	0.412	0.962	0.456

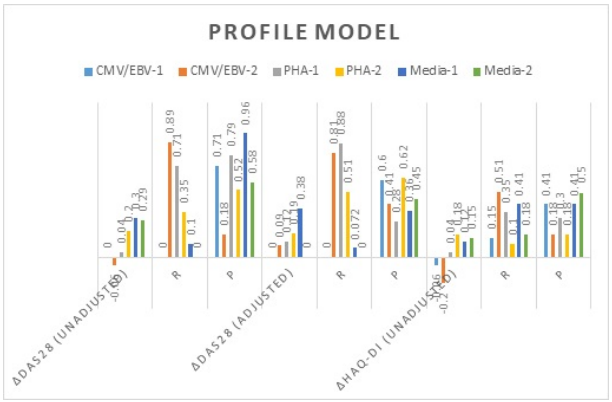

Figure 2: Profile Model: Variations in DAS28 and HAQ-DI Ratings under Different Circumstances

IL-10 responds significantly to PMA, CMV/EBV, and CD3/CD28. Important for Th1 cell development, IL-12 is expressed prominently in response to PMA and CMV/EBV stimulation. Across a variety of stimuli, MCP-1, a chemokine implicated in monocyte recruitment, exhibits increased expression, especially in response to PMA and PHA. Another chemokine, MIP-1β, has variable expression and is upregulated in response to stimuli such as PMA and CD3/CD28. Pro-inflammatory cytokine TNF-α has a variable expression pattern and significant sensitivity to stimuli like PMA and CMV/EBV. All things considered, the data emphasize how cytokine responses to diverse stimuli are dynamic and context-specific, offering important insights into the intricate orchestration of immune responses in diverse biological circumstances [29]–[34].

4.3. Baseline immune response profiles and treatment results are correlated

The Table 4 describes a profile model that assesses changes (Δ) in the unadjusted and adjusted DAS28 (Disease Activity Score in 28 joints) and HAQ-DI (Health Assessment Questionnaire Disability Index) scores in reaction to various stimuli or situations. The rows, along with the corresponding correlation coefficients (r), p-values, and significance markers, each represent a particular stimulus or condition. Unadjusted ΔDAS28 has a substantial positive correlation (r=0.36, p=0.04) with changes in disease activity for the CMV/EBV-1 condition, indicating that this stimulus is related to changes in disease activity. The link is still positive and significant (r=0.45, p=0.10) even after controlling for possible confounders, supporting the idea that this condition affects DAS28 values. Nevertheless, there is no meaningful correlation (r=-0.06, p=0.71) between the uncorrected ΔHAQ-DI and changes in the disability index, suggesting that there is no relationship at all [35].

On the other hand, no association reaches statistical significance for the CMV/EBV-2 condition. The unadjusted ΔHAQ-DI is likewise non-significant, and neither the adjusted nor the unadjusted ΔDAS28 scores show any discernible correlation with this stimulus. Results for the PHA-1 and PHA-2 conditions are inconsistent. While PHA-2 exhibits a positive but non-significant connection with unadjusted ΔDAS28 (r=0.20, p=0.35), PHA-1 exhibits no meaningful link with any of the outcome measures. The unadjusted ΔHAQ-DI and adjusted ΔDAS28 for PHA-2 show no significant correlation, suggesting that these stimuli and the outcomes that are being examined are not clearly associated [36].

The Media-1 condition shows a non-statistically significant positive connection with unadjusted ΔDAS28 (r=0.30, p= 0.10). This link holds true even after correction (r=0.38, p=0.072). However, there is no significant correlation between Media-1 and unadjusted ΔHAQ-DI. Finally, while not reaching statistical significance, the Media-2 condition shows a positive association (r=0.29, p=0.25) between uncorrected ΔDAS28 and Media-2. Additionally, there are no significant relationships be-

Table 4: Profile Model: Variations in DAS28 and HAQ-DI Ratings under Different Circumstances

Profile Model	ΔDAS28 (Unadjusted)	r	P	ΔDAS28 (Adjusted)	r	P	ΔHAQ-DI (Unadjusted)	r	P
CMV/EBV-1	0.36 b	0.04b	0.71	0.45b	0.10b	0.60	-0.06	0.15	0.41
CMV/EBV-2	-0.06	0.89	0.18	0.09	0.81	0.41	-0.20	0.51	0.18
PHA-1	0.04	0.71	0.79	0.12	0.88	0.28	0.04	0.35	0.30
PHA-2	0.20	0.35	0.52	0.19	0.51	0.62	0.18	0.10	0.18
Media-1	0.30	0.10	0.96	0.38	0.072	0.36	0.12	0.41	0.41
Media-2	0.29	0.25b	0.58	0.40b	0.051b	0.45	0.15	0.18	0.50

Table 5: Associations of Different Models with Changes in *Delta*DAS28 and *Delta*HAQ-DI: Unadjusted and Adjusted Results

Profile	Model	DAS28		HAQ-D1	
		R	p	r	p
CMV/EBV-1	Unadjusted	-1.52	1.16	-1.41	1.13
	Adjusted	-1.41	1.145	-1.41	1.42
CMV/EBV-2	Unadjusted	-1.15	1.92	-1.16	1.46
	Adjusted	1.19	1.85	X	1.44
PHA-1	Unadjusted	1.15	1.53	1.32	1.61
	Adjusted	1.32	1.21	1.41	1.31
PHA-2	Unadjusted	-1.16	1.52	1.11	1.29
	Adjusted	-1.31	1.21	-1.19	1.39
Media-1	Unadjusted	-1.21	1.53	-1.13	1.52
	Adjusted	-1.29	1.65	-1.16	1.19
Media-2	Unadjusted	-1.28	1.19	-1.116	1.23
	Adjusted	-1.36	1.36	-1.12	1.33

tween the unadjusted ΔHAQ-DI and adjusted ΔDAS28 for Media-2.

4.4. Changes in clinical disease status and changes in immune response profiles from baseline to follow-up are correlated

For individuals with rheumatoid arthritis, the Table 5 shows data on the relationship between various profiles (CMV/EBV-1, CMV/EBV-2, PHA-1, PHA-2, Media-1, Media-2) and alterations in disease activity and disability indices (*Delta*DAS28 and *Delta*HAQ-DI). Both unadjusted and adjusted results are shown for every profile. The unadjusted *Delta*DAS28 and *Delta*HAQ-DI in the CMV/EBV-1 profile both demonstrated a significant decrease of -1.52 (p=1.16) and -1.41 (p=1.13), respectively. Following correction, *Delta*HAQ-DI showed a minor increase to -1.41 (p=1.42), but *Delta*DAS28 remained significant at -1.41 (p=1.145). Similar drops were seen in unadjusted *Delta*DAS28 (p=1.92) and *Delta*HAQ-DI (p=1.46) in the CMV/EBV-2 profile. Following the correction, *Delta*HAQ-DI stayed largely unchanged at -1.14 (p=1.44), but *Delta*DAS28 increased to 1.19 (p=1.85). Unadjusted *Delta*DAS28 and *Delta*HAQ-DI increased considerably by 1.15 (p=1.53) and 1.32 (p=1.61), respectively, for the PHA-1 profile. Following correction, the values for *Delta*DAS28 and *Delta*HAQ-DI somewhat increased to 1.32 (p=1.21) and 1.41 (p=1.31), respectively. Unadjusted *Delta*DAS28 dropped by -1.16 (p=1.52) in the PHA-2 profile, whereas *Delta*HAQ-DI increased by 1.11 (p=1.29). Following correction, *Delta*HAQ-DI marginally rose to -1.19 (p=1.39), whereas *Delta*DAS28 stayed significant at -1.31 (p=1.21) .

Unadjusted *Delta*DAS28 fell by -1.21 (p=1.53) and *Delta*HAQ-DI by -1.13 (p=1.52) for the Media-1 profile. Following correction, *Delta*HAQ-DI dropped to -1.16 (p=1.19) and *Delta*DAS28 marginally rose to -1.29 (p=1.65). Unadjusted *Delta*HAQ-DI dropped by -1.116 (p=1.23) and *Delta*DAS28 dropped by -1.28 (p=1.19) in the Media-2 profile. Following correction, *Delta*HAQ-DI stayed largely unchanged at -1.12 (p=1.33), although *Delta*DAS28 marginally increased to -1.36 (p=1.36). All things considered, these results point to correlations between various profiles and shifts in disease activity and impairment, with modifications influencing how these correlations are interpreted [37]–[44].

5. Conclusion

In people with early RA, we have recorded a remarkable connection between an ex vivo immunological reaction to CMV and the clinical reaction to starting DMARD treatment. The consequences of this study give new bits of knowledge into the meaning of an Immune system microorganism reaction connected to CMV openness in changing the results of DMARD treatment in early RA, when joined with our distributed information and discoveries from late writing. More research is necessary to determine how CMV-associated T-cell immunity and subclinical CMV persistence affect RA outcomes. In conclusion, research using immune response profiling to examine treatment response and viral immunity in early rheumatoid arthritis has provided important new understandings of the intricate interactions among the immune system, treatment results, and viral variables. The study used a variety of models and profiles, including CMV/EBV, PHA, and Media, as shown in the table to evaluate the associations with changes in disease activity (*Delta*DAS28) and functional disability (*Delta*HAQ-DI). The findings highlight the complex relationships between these variables; certain profiles show substantial connections both before and after adjustment, while other profiles display non-significant or inconsistent patterns. The observed differences in viral immunity and responsiveness to treatment point to the need for a more thorough understanding of the variables influencing rheumatoid arthritis's early stages. The inclusion of adjusted values highlights the complexity of immune response dynamics in the setting of treatment

interventions and emphasizes the significance of taking confounding variables into account.

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Conflict of Interest

The authors declare no conflicts of interest related to this study. All findings and conclusions presented are based solely on the data collected and analyzed, with no external influences affecting the integrity of the research.

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