SHORT REPORT

Efficacy of sarilumab and dexamethasone co-administration for lowering multiple blood biomarkers in the treatment of cytokine release syndrome in hospitalized COVID-19 patients

Ishtiaq Ahmad, Hamidullah

Abstract

The current study was planned to explore the potential synergistic role of the co-administration of sarilumab and dexamethasone in reducing blood biomarkers associated with cytokine release syndrome in hospitalised patients of coronavirus disease-2019. The sample comprised 22 patients hospitalised with severe and critical severity levels and who were treated with sarilumab and dexamethasone. Positive responses were seen in blood biomarkers, including decreased interleukin-6 alpha levels and improved oxygen saturation. Tumour necrosis factor, D-dimer, C-reactive protein, ferritin and lymphocyte count also showed positive responses in patients who survived than those who died. Lactate dehydrogenase levels fluctuated with improvement among the survivors, but had limited effectiveness in those who died. The findings suggested promising avenues for future treatment strategies in patients with severe coronavirus disease-2019 and cytokine release syndrome.

Keywords: Sarilumab, Dexamethasone, Biomarkers, Cytokine release syndrome, COVID-19.

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Introduction

The novel coronavirus disease-2019 (COVID-19) became a global pandemic, with devastating health, societal and economic impacts since its outbreak in late 2019. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and is often associated with significant morbidity and mortality, particularly in severe cases. One of the factors contributing to the severity of COVID-19 illness is cytokine release syndrome (CRS), an overwhelming systemic inflammatory response associated with high levels of circulating cytokines.[1]

CRS is thought to be a significant player in the pathogenesis of severe COVID-19, leading to multiple organ dysfunction syndrome (MODS) and acute respiratory distress syndrome (ARDS). Therefore, managing this overactive inflammatory response is an essential part of COVID-19 treatment strategy. CRS in the context of COVID-19 entails an uncontrolled release of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and others.[2] These cytokines coordinate immune cell activation and start a cascade of inflammatory mediators that leads to systemic inflammation, tissue damage, and organ dysfunction over time. When immune responses are dysregulated, it can cause a cytokine storm that worsens the inflammatory environment and exacerbates the clinical symptoms seen in severe COVID-19 patients.

Sarilumab (SAR), a human monoclonal antibody against the IL-6 receptor (IL-6R), has been used in rheumatoid arthritis (RA) treatment[3] and has shown promise in modulating the immune response in severe COVID-19 by inhibiting IL-6 signalling.[4] Dexamethasone (DEX), a long-standing anti-inflammatory glucocorticoid, was proven effective in reducing mortality in severe and critical COVID-19 patients in a recovery trial.[5]

The current study was planned to explore the potential synergistic role of the co-administration of SAR and DEX in reducing blood biomarkers associated with CRS in hospitalised patients of COVID-19.

Methods and Results

The open-label study was conducted at Mardan Medical Complex (MMC) in Khyber Pakhtunkhwa, Pakistan, from January to May 2021. After approval from the ethics review boards of MMC and Bacha Khan Medical College (BKMC), the sample was raised using convenience sampling technique. Those included were patients aged 18 years or older who were hospitalised after testing positive for COVID-19 on real-time polymerase chain react on (PCR) using (QIAGEN kits and QIAGEN Roter-Gene Q5 plex system). Patients meeting the inclusion criteria received co-administration of SAR and DEX. Patients with at least 50% data regarding dosage and blood biomarkers values available were included. The patients were split into two

Department of Medicine, Mardan Medical complex, Bacha Khan Medical College, Mardan, Pakistan.

Correspondence: Hamidullah. e-mail: dr.hamidullah2013@gmail.com

ORCID ID. 0009-0008-1796-1816

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Severe and Critical groups. The Severe group had patients with respiratory distress equivalent to 30 breaths per minute (bpm), oxygen saturation <93% at room air, and arterial oxygen partial pressure (PaO_2) or fraction of inspired oxygen (FiO_2) of 300mmHg corresponding to 0.133kPa. Patient needing mechanical ventilation (MV), had a septic shock, or required to be admitted to an intensive care unit (ICU) were in the Critical group.[6]

Patients with contraindications for either medication, such as pregnant or lactating women, individuals with severe liver or kidney disease, and those previously administered with SAR-DEX combination during the current illness episode were excluded.

Informed consent was obtained from each patient. The duration of the study extended over a period of 10 days for each patient, during which patients received treatment according to the attending physician's recommended dosages. As there were no standard recommended dosage for SAR-DEX co-administration, the attending physician made dosage decisions based on the individual patient's response and preference. Patients received a random variety of dosages for SAR (150mg) and DEX (6mg) on random days, and antimicrobials when needed.

The key outcome measure was the change in the levels of various blood biomarkers indicating CRS severity, such as IL-6, TNF-α, C-Reactive protein (CRP), ferritin, lymphocyte,

Table-1: Patient characteristics, treatment regimen, and clinical outcomes in hospitalised coronavirus disease-2019 (COVID-19) patients with cytokine release syndrome (CRS).

Patients No.	Age (years)	Gender	Weight (Kg)	Severity	Treatment Days 1	2	3	4	5	6	7	8	9	10	Doses	Nosocomial Infection
1	50	Male	65	Severe	SAR DEX	***	DEX	***	SAR DEX	DEX	CPS DEX	CPS DEX	CPS	CPS	SAR:2 DEX:6 CPS:4	*S. Aureus* (Mssa)
2	43	Female	79	Critical	SAR DEX	***	DEX	DEX	DEX	DEX	***	DEX	***	DEX	SAR:1 DEX:7	None
3	56	Male	90	Critical	SAR DEX	DEX	DEX	SAR	***	DEX	DEX	MER	MER	MER DEX	SAR:2 DEX:6 MER:3	*Klebsiella Pneumoniae*
4	59	Female	100	Severe	SAR DEX	DEX	DEX	***	DEX	DEX	***	DEX	DEX	DEX	SAR:1 DEX:8	None
5	59	Male	69	Critical	SAR DEX	DEX	DEX	DEX	***	DEX	†††	†††	†††	†††	SAR:1 DEX:5	None
6	56	Male	105	Critical	SAR DEX	***	DEX	DEX	***	DEX	***	SARDEX	***	DEX	SAR:2 DEX:6	None
7	51	Female	93	Critical	SAR DEX	DEX	***	DEX	DEX	SAR DEX	DEX	MER DEX	MER DEX	MER	SAR:2 DEX:8 MER:3	*Klebsiella Pneumoniae*
8	52	Male	85	Severe	SAR DEX	DEX	***	DEX	DEX	SAR DEX	DEX	†††	†††	†††	SAR:2 DEX:6	*S. Aureus (MRSA)*
9	44	Male	81	Critical	SAR DEX	DEX	***	DEX	DEX	***	DEX	DEX	***	DEX	SAR:1 DEX:7	None
10	45	Female	77	Critical	SAR DEX	DEX	DEX	***	***	DEX	***	DEX	DEX	DEX	SAR:1 DEX:7	None
11	49	Male	79	Critical	SAR DEX	DEX	DEX	***	DEX	SAR DEX	DEX	CEF	CEF	CEF	SAR:2 DEX:6 CEF:3	*S. Pyogenes*
12	47	Male	93	Critical	SAR DEX	***	DEX	DEX	DEX	***	***	***	DEX	DEX	SAR:1 DEX:6	None
13	29	Female	94	Critical	SAR DEX	DEX	DEX	DEX	SAR DEX	†††	†††	†††	†††	†††	SAR:2 DEX:5	*Klebsiella Pneumoniae*
14	38	Male	69	Critical	SAR DEX	DEX	DEX	DEX	DEX	DEX	DEX	DEX	***	***	SAR:1 DEX:7	None
15	55	Female	73	Severe	SAR DEX	DEX	DEX	DEX	***	***	DEX	***	DEX	DEX	SAR:1 DEX:7	None
16	51	Male	102	Critical	SAR DEX	***	DEX	***	DEX	DEX	DEX	***	***	DEX	SAR:1 DEX:6	None
17	44	Female	69	Critical	SAR DEX	DEX	DEX	***	DEX	SAR DEX	DEX	AMP	AMP	AMP DEX	SAR:2 DEX:7 AMP:3	*Candida Species*
18	66	Male	77	Severe	SAR DEX	DEX	DEX	DEX	DEX	DEX	***	***	DEX	DEX	SAR:1 DEX:8	None
19	54	Male	84	Critical	SAR DEX	***	DEX	DEX	DEX	DEX	SAR	AMP DEX	AMP DEX	AMP	SAR:2 DEX:7 AMP:3	*Candida Species*
20	51	Male	89	Severe	SAR DEX	DEX	***	DEX	***	DEX	***	DEX	DEX	DEX	SAR:1 DEX:7	None
21	69	Male	88	Critical	SAR DEX	***	DEX	DEX	DEX	SAR DEX	DEX	AMP DEX	†††	†††	SAR:1 DEX:7 AMP:1	*Candida Species*
22	52	Female	96	Critical	SAR DEX	DEX	***	DEX	DEX	***	DEX	DEX	DEX	DEX	SAR:1 DEX:8	None

Once daily: SAR: Sarilumab 150mg; Twice daily: DEX : Dexamethasone 6mg, AMP: Amphotericin B50mg, MER: Meropenem 1gm, CEF: Cefotaxime 2g, CPS: Cefoperazone + Sulbactam; Doses: Represent how many days a patient received the mentioned doses; *** no drug administrated at that day, †††Death.

lactate dehydrogenase (LDH) and D-Dimer (D-D). These blood biomarkers were randomly assessed for 10 days using fully automated ElectroChemiLuminescence (ECL) technology for immunoassay analysis (Roche Cobas E411), a semi-automated enzyme-linked immunosorbent assay (ELISA) microplate reader (RT-6000,Rayto), fully automated analyzer for clinical chemistry assays (Roche Cobas C501), and haematology analyser (Es 60, Horiba ABX).

Blood sample was drawn within 24-48 hours of admission for a blood culture test. The secondary outcome markers of the study included age, weight, oxygenation levels, the 10-day mortality rate, and the occurrence of nosocomial infections. A fingertip pulse oximetre by (Masimo) was used to measure peripheral capillary oxygen saturation (SpO_2) for each patient.

Data was collected using standardised case report forms to ensure consistency and accuracy. The collected data was analysed according to the intention-to-treat principles, meaning all patients who received at least one dose of the treatment were analysed. Data was statistically analysed using SPSS 26. The primary analysis involved comparing the biomarker levels on the day of admission versus the 10th day of the study. The percentage change in biomarker levels from the initial measurement at admission to the final measurement day was calculated for each patient. Improvement or exacerbation of CRS severity over the 10-day period was measured based on SpO_2 levels. The clinical status of patients was classified into four groups: SpO_2 95-100%=stabilisation, SpO_2 85-95% = improvement, SpO_2 <85% = exacerbation, and death.

Of the 22 patients, 14 were males and 8 were females. The overall age range was 29-69 years, and bodyweight ranged 65-105kg. There were 16 patients in the Critical group and 6 in the Severe group. The SAR-DEX combination was used in the treatment regimens, with additional medications given where needed. Nosocomial infections observed included methicillin-susceptible staphylococcus aureus (MSSA), methicillin-resistant staphylococcus aureus (MRSA), Klebsiella (K.) pneumoniae, Candida species, and streptococcus (S.) pyogenes, highlighting the vulnerability of hospitalized patients (Table 1).

Overall, 4 patients died during the study, 5 patients were in the stabilisation category, 10 patients in the improvement category, and 3 patients in the exacerbation category. IL-6 alpha levels reduced substantially throughout treatment, with 66.43% improvement on average. Notably, stabilization patients had the highest average improvement percentage 67.48%, followed by improvement 66.91%, exacerbation 46.32%, and dead 4.35%.

Changes in TNF demonstrated significant gains, notably in the stabilization and improvement categories 85.23% and 77.83%, respectively. However, the exacerbation category had an average deteriorating percentage of -48.73%, while the dead category had a substantial average fall of about -226.33%.

The D-D transformation showed positive patterns, with an average improvement percentage of 45.52% for stabilisation and 40.64% for the improvement category. The exacerbation category showed a slight average decline

Table-2: Changes in different biomarkers following sarilumab and dexamethasone co-administration and their clinical out come in hospitalised coronavirus disease-2019 (COVID-19) patients with cytokine release syndrome (CRS)

Patient No.	SpO_2 at admission	Biomarkers at admission				Biomarkers after 10 days				Improvement				SpO_2 after 10 days	Clinical out come
		IL-6	TNF	D-D	CRP	IL-6	TNF	D-D	CRP	IL-6	TNF	D-D	CRP		
1	62	77.8	96.0	997	112	18.1	13.5	588	51	76.73	86.46	42.40	54.46	95	Stabilization
2	57	91.0	50.3	1501	102	23.9	7.3	701	39	73.73	84.00	41.63	61.76	95	Stabilization
3	59	128.4	96.5	1787	98	39.5	35.4	1121	52	69.23	63.54	37.26	50.47	89	Improvement
4	57	83.5	89.0	2345	91	70.2	177.8	1299	34	15.62	-201	39.44	62.63	74	Exacerbation
5	63	77.0	74.2	2478	86	†††	†††	†††	†††	22.72	-241	14.36	31.39	†††	Dead
6	65	98.1	81.9	993	93	34.5	64.6	645	41	64.83	20.98	35.04	55.91	77	Exacerbation
7	60	123.9	179.0	980	104	31.5	39.5	601	55	74.57	78.21	38.67	47.11	86	Improvement
8	60	71.9	60.2	2184	87	†††	†††	†††	†††	-7.92	-448	29.39	8.04	†††	Dead
9	60	79.0	62.1	1603	118	22.1	16.9	801	86	72.02	74.19	50.03	21.81	91	Improvement
10	61	82.1	115.6	950	108	31.2	19.8	729	48	61.99	83.47	23.26	55.55	96	Stabilization
11	64	109.4	145.0	2231	126	39.7	29.5	1298	54	63.71	80.00	41.81	57.14	87	Improvement
12	59	90.8	158.2	2162	125	19.5	46.4	1170	51	78.52	70.88	45.55	59.52	81	Improvement
13	59	81.0	70.2	950	97	†††	†††	†††	†††	-10.24	-217	9.15	37.11	†††	Dead
14	64	90.7	171.0	1768	94	39.6	31.5	899	44	56.33	81.87	49.15	53.19	91	Improvement
15	62	75.5	87.1	2352	83	31.0	19.5	1151	27	58.94	78.16	51.10	67.46	97	Stabilization
16	55	110.8	72.8	1499	95	31.5	9.9	801	45	71.57	87.5	46.56	52.63	83	Improvement
17	67	117.4	143.9	1511	101	68.6	66.3	1601	54	58.53	45.45	-5.95	46.53	78	Exacerbation
18	62	70.5	188.7	1354	106	24.1	84.1	609	68	65.81	55.31	55.02	35.84	82	Improvement
19	58	93.8	87.8	1440	105	30.9	16.5	729	57	67.05	81.60	49.37	47.71	96	Stabilization
20	65	123.9	171.5	1213	95	53.2	32.1	444	44	42.93	81.28	63.39	53.68	85	Improvement
21	59	116.4	125.7	1404	96	†††	†††	†††	†††	14.86	-200	29.41	36.45	†††	Dead
22	65	125.6	96.5	2393	128	43.5	21.9	1101	71	65.36	78.12	53.99	44.53	88	Improvement

IL-6: Interlukine-6 alpha normal range: 5-10 pg/ml/, TNF: Tumour necrosis factor normal range 8-10 pg/ml, D-D: D-Dimer normal range 550-500ng/ml/, CRP: C-reactive protein normal range: 8-10mg/l; SpO_2: Peripheral capillary oxygen saturation normal range 95%-100%; Pt no: Patient number. Improvement is expressed as a percentage and improvement percentage is calculated after 10 days of hospitalisation, while for the deceased patients it was calculated on their last day of death. Patient No 5 died on day 7th, Patient No 8 died on day 8th, Patient No 13 died on day 6th, Patient No 21 died on day 9th. ††† = Death.

Table-3: Changes in different biomarkers following sarilumab and dexamethasone co-administration and their clinical outcome in hospitalised coronavirus disease-2019 (COVID-19) patients with cytokine release syndrome (CRS).

Pt no.	SpO_2 at admission	Biomarkers at admission			Biomarkers after 10 days			Improvement			S1p02 after 10 days	Clinical outcome
		FER	LYM	LDH	FER	LYM	LDH	FER	LYM	LDH		
1	62	1963	5.28	851	931	15.99	321	52.57	202.84	62.27	95	Stabilization
2	57	1590	7.67	893	706	17.01	402	55.59	121.51	54.98	95	Stabilization
3	59	1739	5.13	1232	1056	8.99	807	39.27	75.24	34.49	89	Improvement
4	57	2280	9.67	1071	1433	13.07	841	37.14	30.83	21.47	74	Exacerbation
5	63	2117	12.99	1035	†††	†††	†††	19.93	-42.57	-5.79	†††	Dead
6	65	1666	11.03	1288	1125	15.12	1007	32.47	37.08	21.81	77	Exacerbation
7	60	1476	8.88	1037	909	12.76	583	38.41	43.69	43.78	86	Improvement
8	60	1901	3.67	1319	†††	†††	†††	23.40	35.67	21.45	†††	Dead
9	60	1935	6.68	1154	911	10.24	601	52.91	53.29	47.92	91	Improvement
10	61	1314	9.14	1071	456	14.56	649	65.29	59.29	39.40	96	Stabilization
11	64	2105	6.83	1391	1299	8.91	859	38.28	30.45	38.24	87	Improvement
12	59	1744	9.80	1021	869	14.69	701	50.17	49.89	31.34	81	Improvement
13	59	1910	2.00	1496	†††	†††	†††	-34.18	71.00	-24.46	†††	Dead
14	64	1403	12.47	1258	888	21.69	436	36.70	73.93	65.34	91	Improvement
15	62	1369	5.39	1213	586	15.66	625	58.23	190.35	48.47	97	Stabilization
16	55	1667	11.30	1167	845	22.69	733	49.31	100.79	37.18	83	Improvement
17	67	1806	3.77	976	1069	4.65	1161	35.87	23.34	-18.95	78	Exacerbation
18	62	2026	9.15	1363	1109	12.87	846	45.26	40.65	37.93	82	Improvement
19	58	1451	6.92	1379	705	12.39	631	51.41	79.04	54.24	96	Stabilization
20	65	1418	8.27	971	966	16.56	633	33.42	100.24	34.80	85	Improvement
21	59	1747	7.01	1923	†††	†††	†††	-80.67	14.12	20.12	†††	Dead
22	65	1861	6.37	1331	1029	11.36	866	44.70	78.33	34.93	88	Improvement

FER: Ferritin, normal range 24-336ng/mL for males And 24-307ng/mL for females, LYM: Lymphocytes, normal range >20.00%, LDH: Lactate dehydrogenase, normal range 140-280u/l., SpO_2: Peripheral capillary oxygen saturation, normal range 95%-100%; Pt No: Patient number. Improvement was expressed as a percentage and improvement percentage was calculated after 10 days of hospitalisation, while for deceased patients it was calculated on the day of death. Patient No 5 died on day 7th, Patient No 8 died on day 8th, Patient No 13 died on day 6th, Patient No 21 died on day 9th. ††† = Death.

of -2.57%, while the dead category showed an average decline of -6.15%.

CRP showed the highest average improvement percentage in the stabilisation category 54.46%, followed by the improvement category 50.47%. Patients in the exacerbation category had an average improvement percentage of 55.91%, suggesting a difficult response to therapy, while those in the dead category had the lowest average improvement percentage 31.39% (Table 2).

Ferritin levels showed variation at the beginning of treatment, ranging from 1103ng/ml to 2021ng/ml, and fluctuated throughout the treatment. Among patient categories, stabilization displayed the highest average improvement percentage 52.57%, Followed by improvement 45.97%, exacerbation 36.96%, and the dead category -22.59%.

The lymphocyte levels ranged from 2.00% to 12.99% at admission. The stabilisation category had a substantial average improvement 108.24%, followed by improvement 55.76%, exacerbation 37.78%, and the dead 7.23% categories.

Initial LDH levels ranged from 851u/l to 1923u/l. The stabilisation category showed significant improvement 46.16%, followed by the improvement category 40.41%, exacerbation 24.62% and the dead -16.60% categories (Table 3).

Discussion

To the best of our knowledge, the current study is the first to specifically investigate the SAR-DEX combination in reducing inflammatory markers during CRS and improving clinical outcomes in COVID-19 hospitalised patients.

The results indicated that the combined administration resulted in a notable decrease in various blood biomarkers linked to CRS. Furthermore, the study also brought to attention the prevalence of nosocomial infections within the sample. The presence of these infections further emphasised the need of effective treatment strategies to manage CRS and mitigate the risk of secondary infections.

Excessive production of pro-inflammatory cytokines, such as IL-6, IL-2, IL-17, TNF, IL-10, interferon-gamma-protein 10 (IFN-γ-protein10), and macrophage inflammatory protein 1 (MIP-1), serves as a clinical marker for the severity of certain conditions characterised by intense inflammation in the lungs and the formation of blood clots. These cytokines play a crucial role in the pathogenesis of these conditions.[7] Among the pro-inflammatory cytokines, IL-6 has received considerable attention due to its significant involvement in disease progression. Studies have recognised the therapeutic potential of targeting IL-6, as blocking its activity could help mitigate the harmful effects caused by excessive inflammation.[8] Therefore, inhibiting IL-6 has become an attractive approach in the development of potential treatments. Multiple studies have revealed a correlation between elevated levels of IL-6 and increased mortality rates in affected patients, indicating that the level of IL-6 can serve as a valuable indicator of disease severity and prognosis.[8] Considering this, it is reasonable to assume that solely relying on antiviral treatments may not effectively regulate the immune response in severe and critical patients. Additional strategies targetting the immune dysregulation are required to improve the outcomes.

However, as with any scientific hypothesis, there are dissenting opinions regarding the use of IL-6 blockade in COVID-19 treatment. Some studies have expressed

scepticism or differing views on the efficacy and safety of this approach. Scientific discourse and debate are common in the field, highlighting the need for further research and clinical trials to determine the true potential of IL-6 blockade as a therapeutic intervention for severe cases of COVID-19. The approach in the current study involved using a humanised monoclonal antibody SAR that specifically targeted IL-6R in COVID-19 patients who were in severe and critical stage of disease, and exhibited elevated levels of IL-6. This antibody aimed at blocking the IL-6 signalling pathway, reducing the harmful effects of the cytokine and potentially mitigating the severity of the disease. Similarly DEX is known to have anti-inflammatory properties and can help regulate the immune response. One of the mechanisms by which DEX exerts its effects is by suppressing the production of pro-inflammatory cytokines, including IL-6. The rationale behind co-administering SAR and DEX was to target different points in the inflammatory cascade, and to achieve a synergistic effect.

The current study yielded promising results in terms of reducing the levels of key inflammatory biomarkers. Specifically, there was a significant decrease in the levels of IL-6 and TNF, which are both pro-inflammatory cytokines that play a crucial role in CRS and the subsequent cascade of inflammation. By inhibiting IL-6R with SAR and utilising the immunosuppressive effects of DEX, the current study was able to effectively dampen the exaggerated immune response, resulting in a reduction of these cytokines.

Furthermore, the current study assessed other important biomarkers associated with CRS and disease severity, including ferritin, D-D, LDH and CRP. These biomarkers have been linked to systemic inflammation in COVID-19 patients.[9,10] In the current study, the combination therapy demonstrated positive outcomes by significantly reducing the levels of ferritin, D-D, LDH and CRP. This suggests a potential improvement in the overall inflammatory state and disease severity in patients receiving the combination therapy. Additionally, an important finding was the increase in the number of lymphocytes. Lymphocytes are a vital component of the immune system, responsible for recognising and eliminating pathogens, including the SARS-CoV-2 virus. The observed increase in lymphocyte levels indicated that the combination therapy could enhance the immune response against the virus, potentially aiding in viral clearance and improving patient outcomes.

The observed significant improvements in these biomarkers and improved outcome, including the survival of patients in the stabilisation or improvement categories, resonated with the efficacy noted in a previous study.[11] However, in some critical patients, marked by exacerbation or mortality in the current study, the efficacy was limited, aligning with the findings reported by an earlier study[12] that questioned the efficacy of SAR in certain hospitalised patients. It should be noted that the two studies[11,12] did not co-administer DEX with DAR. These findings underscored the complexity of treating CRSin COVID-19, highlighting the necessity for individualised approaches. The variability in biomarker responses, particularly in more severe cases, suggested that while SAR and DEX could be effective, their impact was not uniform across all patient categories. This aligned with the broader narrative in current COVID-19 research, emphasising the need for a tailored treatment strategy based on patient-specific factors.

The current study has several limitations. As this was the first study of its kind, there was scarcity of previous research to build upon or compare findings with, limiting the contextualisation and validation of the results. Besides, the study had a small sample size, and due to the smaller sample size sample size was not calculated, which may not accurately represent the broader population of hospitalised COVID-19 patients. The open-label design of the study may have led to bias and placebo effects. Also, the lack of standardized dosages for SAR and DEX co-administration, at the time of the study, further limited the generalisability of the findings. Further, the study relied on limited outcome measures, and was conducted at a single centre, which may not reflect regional or institutional variations. Finally, the study did not include long-term follow-up, making it challenging to evaluate the sustainability of the treatment effects. These limitations should be taken into account when interpreting the results of the study.

Conclusion

The co-administration of SAR and DEX showed promise in stabilising and improving biomarker levels associated with CRS. The combination therapy offered a multifaceted approach to dampen the excessive immune response, reduce inflammation and potentially improve patient outcomes.

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Author Contribution:

IA: Data collection, analysis, interpretation, study design, revision, drafting, final approval.
HU: Data collection, analysis, interpretation, study design, revision, drafting.