

**LETTER**

# COVID-19 and immunosuppressants: An opinion pool of practicing dermatologists of India

Dear Editor,

Coronavirus disease 2019 (COVID-19) cases continue to increase with increasing morbidity among immunocompromised. There were no definitive guidelines for immunosuppressants in India during the initial months of the pandemic, so we conducted a survey of dermatologists about immunosuppressants. A total of 550 dermatologists answered an online questionnaire and responses were analyzed using Microsoft Excel. Recommendations later made by the Indian Association of Dermatologists have also been added<sup>1</sup> (Table 1). Our survey provided a bird's view of decisions regarding immunosuppressant prescription among dermatologists (Figures 1-4).

Innate immunity is the first line of defense in viral infections. Previous coronavirus outbreaks have demonstrated the action of tumor necrosis factor-alpha (TNF- $\alpha$ ), B cell antibodies, and cytokines in infection control.

Most immunosuppressants comprehensively affect multiple inflammatory pathways by reducing the dendritic activity. On entry, the virus affects the type 1 interferon responses, causing the first wave of replication and subsequent B cell activation neutralizes the virus. Classic immunosuppressants (steroids, cyclosporine, mycophenolate mofetil, azathioprine, and methotrexate) smother most mediators of immune response. For these drugs, dermatologists must be vigilant for any

**TABLE 1** Questionnaire of the survey

No.	Question	Options	Results	IADVL recommendation
1.	Years of dermatology practice?	(1) <10 y	(1) 327/550 (59.45%)	N/A
		(2) 10 to 20 y	(2) 124/550 (22.54%)	
		(3) 20 to 30 y	(3) 61/550 (11.09%)	
		(4) >30 y	(4) 38/550 (6.9%)	
2.	Are you running your OPD services?	(1) Running normal OPD services	(1) 238/550 (43.27)	Recommend seeing patients by appointment only
		(2) Running limited OPD services	(2) 209/550 (38%)	
		(3) OPD is closed	(3) 103/550 (18.72%)	
3.	How do you prefer to follow-up your patients on immunosuppressants?	(1) Personally in the OPD.	(1) 319/550 (58%)	Prefer telephonic and online consultation, avoid outpatient department visits
		(2) Verbally over the phone	(2) 57/550 (10.36%)	
		(3) Over digital media (such as email, WhatsApp and online consultation)	(3) 174/550 (31.63%)	
4.	If a patient has stable disease activity, while already on immunosuppressants, what is your next step?	(1) Continue the same drug at same dose	(1) 216/550 (39.27%)	No specific recommendation. Advise a conservative approach for classical immunosuppressants
		(2) Decrease the dose of same drug	(2) 232/550 (42.18%)	
		(3) Switch to relevant topical medication	(3) 102/550 (18.54%)	
5.	If a patient shows flare of disease activity, while already on immunosuppressants, what is your next step? (multiple answers)	(1) Increase dose of same immunosuppressant drug	(1) 181/550 (32.9%)	Decide on a case-by case-basis. Consider other drugs such as dapsone and apremilast

(Continues)

**TABLE 1** (Continued)

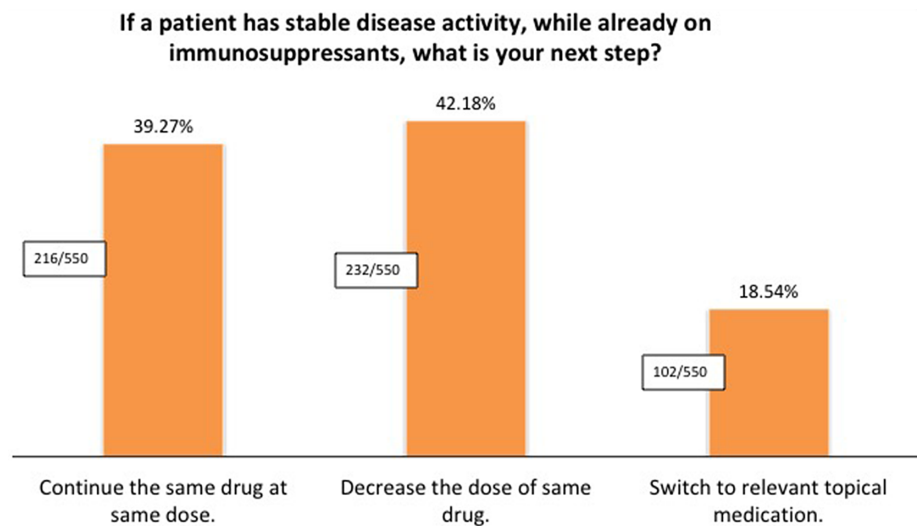
No.	Question	Options	Results	IADVL recommendation
		(2) Add a relevant topical medication	(2) 261/550 (47.45%)	
		(3) Switch over to other relevant cytotoxic drug	(3) 126/550 (22.9%)	
		(4) Switch to smaller molecules like apremilast	(4) 179/550 (32.5%)	
6.	In a patient on immunosuppressants, if you suspect COVID-19 infection, what is your next step?	(1) Stop medication and recommend testing	(1) 254/550 (46.18%)	Stop the drug, decide on the severity of primary disease
		(2) Decrease dose and recommend testing	(2) 114/550 (20.72%)	
		(3) Continue medication and recommend testing	(3) 182/550 (33.09%)	
7.	In a patient showing disease flare during the COVID-19 pandemic, which of the following have you observed to be a likely underlying cause? (multiple choices)	(1) Irregularity in drug intake due to unavailability of medications	(1) 337/550 (61.2%)	N/A
		(2) Patient is unable to access the health care facilities due to lockdown	(2) 262/550 (47.63%)	
		(3) Personal stress, depression, or anxiety due to COVID-19 pandemic	(3) 277/550 (50.36%)	
		(4) Underlying cause could not be detected	(4) 80/550 (14.54%)	
8.	For which patient group, would you recommend self-quarantine? (multiple choices)	(1) On immunosuppressant, $\leq 14$ and $\geq 65$ y of age	(1) 216/550 (39.27%)	No recommendation
		(2) On immunosuppressants, with comorbidities (asthma, DM, HTN, renal disease, and others)	(2) 323/550 (58.72%)	
		(3) All patients on immunosuppressants	(3) 357/550 (64.9%)	
		(4) Not advising self-quarantine to patients on quarantine	(4) 25/550 (4.54%)	
9.	At this time, will you prescribe regular immunosuppressants to new patients?	(1) No, I will wait till the COVID-19 situation improves	(1) 172/550 (31.55%)	No specific recommendation
		(2) Yes, I will start regular immunosuppressants	(2) 44/550 (8.07%)	
		(3) I will decide on a case-by-case basis	(3) 329/550 (60.39%)	
10.	Would you advise prophylactic HCQS to your patients on immunosuppressants (after necessary baseline investigations)?	(1) Yes	(1) 92/550 (16.72%)	Should be prescribed if patient on immunosuppressants is in contact with the laboratory-confirmed cases
		(2) No	(2) 458/550 (83.27%)	

Abbreviations: COVID-19, coronavirus disease 2019; DM, diabetes mellitus; HCQS, hydroxychloroquine; HTN, hypertension; IADVL, Indian association of dermatologists, venereologists and leprologists; OPD, outpatient department.

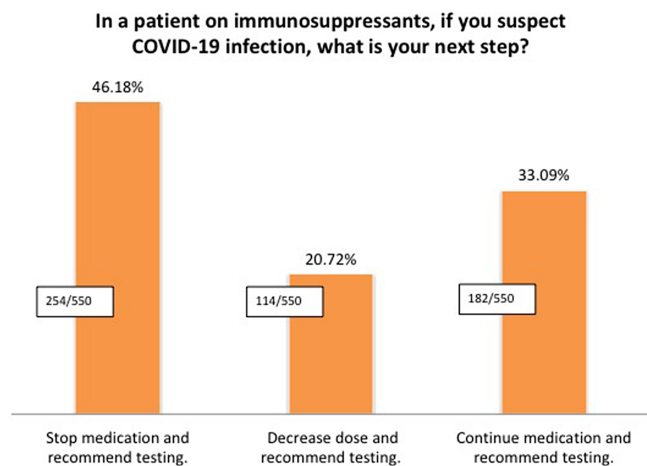
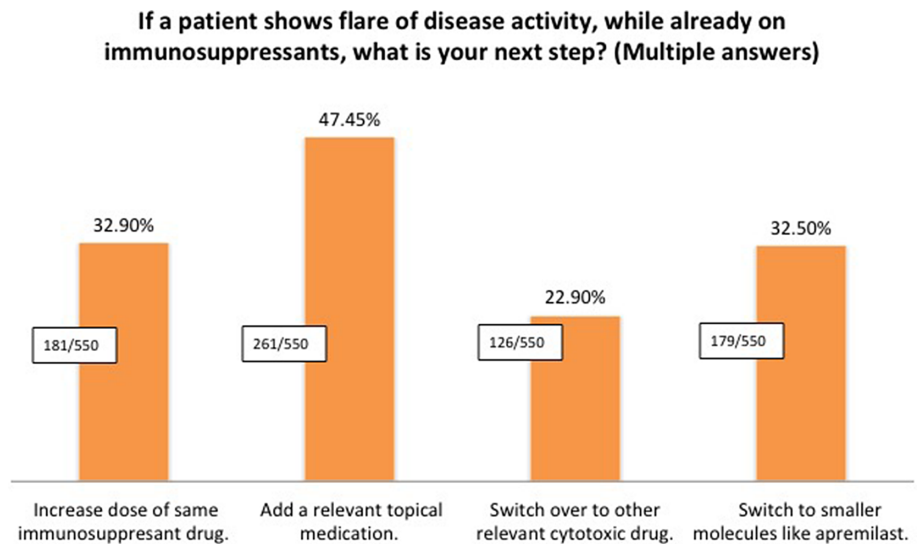
possible infection symptoms. Data suggest no benefits/risks of stopping immunosuppressants in asymptomatic patients.<sup>2</sup> For stable disease, 42.18% of our respondents would decrease the dose.

Among the small molecules, apremilast is more commonly used in India, compared to Janus kinase (JAK) inhibitors like tofacitinib. Apremilast does not target specific cytokines, has no increased risk of

**FIGURE 1** Graph showing opinion regarding immunosuppressants for patients with stable disease activity



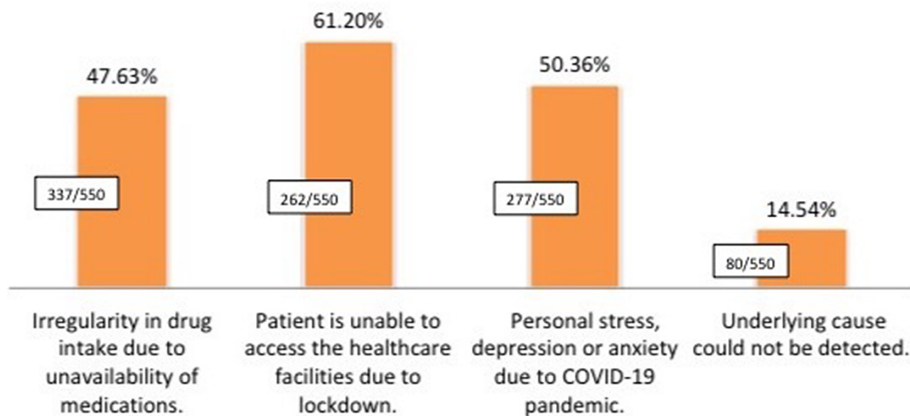
**FIGURE 2** Graph showing opinion regarding immunosuppressants for patients with flare in disease activity



**FIGURE 3** Graph showing opinion regarding immunosuppressants for patients with suspected coronavirus disease 2019 (COVID-19) infection

infection, or reactivation of latent infections. A short  $t_{1/2}$  makes it easier to stop and restart within a few days. Other than psoriasis, off-label uses include alopecia, aphthous stomatitis, lichen planus, and Behçet's disease. Limited immunosuppression makes them a safer therapeutic choice.<sup>3</sup> A reported case of psoriasis on apremilast contracted COVID-19 and did not develop any serious symptoms.<sup>4</sup> Only 32% of respondents would switch to smaller molecules depending on the case and 47.45% chose topical medications. Biologics, with a longer  $t_{1/2}$ , are not easy to stop and do not have a broad immunosuppressive effect due to specific targets. Nevertheless, monoclonal antibody like rituximab, targeting B-cells, can be a cause for concern during a viral outbreak. Biologic trials in psoriasis demonstrated an increased infection risk with most of them being TNF- $\alpha$  blockers except etanercept.<sup>5</sup> Dermatologists must be cautious if patients on monoclonal antibodies show any symptoms of COVID-19 infection. Regular follow-up is highly advisable. While most respondents said they would prefer meeting patients in the outpatient department, this might increase the risk of infection exposure. When asked about suspicious

**In a patient showing disease flare during the COVID-19 pandemic, which of the following have you observed to be a likely underlying cause? [Multiple choices]**



**FIGURE 4** Graph showing opinion regarding possible causes of diseases flare during present coronavirus disease 2019 (COVID-19) pandemic

symptoms and drug modulation, 47% of respondents would stop medications and 33% would continue at same dose.

Conforti et al state that psoriasis patients on immunosuppressants, in areas with high infection rate, need therapeutic reassessment with limitation of time and duration of doses, with preferred topical therapy and lower impact drugs.<sup>6,7</sup> During previous influenza outbreaks, both the British and Australian Rheumatology Association guidelines suggested stopping all immunosuppressants and biologics for at least a week in areas with certain exposure. In suspected cases, immunosuppressant therapy should be stopped, while continuing antiviral treatment till remission. The guidelines were for a future larger pandemic with more virulent strains, like the present scenario.<sup>8</sup> While most guidelines recommend against changing doses in stable disease activity, 42.18% of respondents opted for decreasing doses and 39.27% wanted the same dose.

Hydroxychloroquine has been suggested as chemoprophylaxis in susceptible individuals, but the data are limited. The Indian Dermatology Association recommends it for patients in contact with confirmed cases.<sup>1</sup> In our survey, 85% of respondents would not prescribe hydroxychloroquine to patients on immunosuppressants.

Several authors advise caution against new immunosuppressant prescriptions presently. The Australian-New Zealand consensus advises against new immunosuppressant prescriptions with case-by-case judgment.<sup>9</sup> In our survey, 60.36% would decide by case and 31.55% would wait till the situation improves. Higher risk people needing self-quarantine include those over 65 years of age, with chronic systemic illness or immunosuppressed.<sup>10</sup> 64.9% respondents would advise home quarantine for all patients.

Stress and anxiety can aggravate disease and needs counseling and reassurance. Problems such as irregularity in drug intake and health care inaccessibility do not warrant a change in drug or dosage. Clinicians can recommend yoga and meditation, which are available on Ministry of Health and Family Welfare portals. The present pandemic demands prudent decisions about prescribing immunosuppressants. Our observations throw light on the clinical decisions taken by

dermatologists for prescribing immunosuppressants, and so far no such survey has been conducted regarding the use of immunosuppressive drugs during the present pandemic.

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