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# "Compliance of the Indian National Task Force guidelines for COVID-19 recommendation by Indian doctors — A survey"



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#### ABSTRACT

Background and aims: As the Coronavirus disease 2019 (COVID-19) pandemic unravels rapidly, there is a glut of confusing and divergent scientific information emanating from differing sources, including the Indian National Task Force for COVID-19. Thus, a web-based survey was conducted to decipher the approach of Indian doctors to the various options for treatment of COVID-19.

Methods: A web-based questionnaire among one lakh doctors across India through email and social media was circulated. After data quality and internal validation, 826 responses were included for analysis. Basic demographic and comparative analysis were performed using the Python3.8.2 software (Windows 10 64 bit, USA).

Results: Amongst all the states of India most respondents hailed from the top ten affected states. Overall 76.15% of doctors would either prescribe or consider prescribing hydroxychloroquine (HCQ) as prophylaxis for health-care providers (HCP). Doctors with experience of managing COVID-19 were more likely to advocate use of HCQ as prophylaxis for HCP ( $\chi 2=4.357$ , P=0.037). Intensivists were more likely to advocate HCQ as prophylaxis ( $\chi 2=14.588$ , P<0.001) as well as for management of mild to moderate COVID-19 ( $\chi 2=3.91$ , P=0.048). In COVID-19, 65.8% doctors overwhelmingly preferred using anti-viral agents in severe cases, continuing ACEi/ARB (60.9%), and routinely screening for COVID-19 as a preoperative strategy (73.85%).

*Conclusions:* Indian doctors are largely following the scientific guidance provided by Indian National Task Force for COVID-19 and would consider prescribing HCQ as prophylaxis for COVID-19. They would also consider using it in mild to moderate COVID-19.

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#### 1. Introduction

Coronavirus disease 2019 (Covid-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has taken the shape of a worldwide pandemic. Although most patients have minor symptoms, the case fatality rate is around 5.6% as of 9th June 2, 020 [1], which is even higher in people with comorbidities [2]. However, till date, the cure for this disease evades us and the treatment is largely supportive [3]. Multiple therapeutic agents have been examined in observational studies in COVID-19 with confusing results. The most prominent amongst these has been

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HCO, which has recently been at the centre of controversy [4]. HCO has been in use for several decades for multiple conditions but has recently been studied for its possible action against COVID-19. HCQ has in vitro activity against SARS-CoV-2 and has been postulated to impair the terminal glycosylation of the angiotensin-converting-enzyme 2 (ACE2) receptor, which is the binding site for the SARS-CoV-2 [5]. Although some observational studies have suggested a beneficial effect of HCQ, others have not [6,7]. A recent meta-analysis of the observational studies did not find any reduction in viral clearance rate and actually showed a significant increase in death with HCQ, compared to the control arm [8]. A recent multinational registry analysis involving 96032 patients had suggested decreased in-hospital survival but this article was subsequently retracted because of concerns with respect to the veracity of the data and analyses [4]. Nevertheless, the ministry of health in India on March 31, 2020 had considered

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HCQ in combination with azithromycin (AZ) as an off label indication in patients with severe disease requiring intensive therapy unit (ITU) management [9].

In the light of lack of definitive curative treatment of COVID-19, it is important to break the chain of transmission particularly as the risk of secondary household transmission is around 10–15% [10]. The long half-life and high lung concentration (500-times the blood concentration) of HCO are ideally suited for prophylactic use and this attractive strategy for prevention of COVID-19 is being assessed in 60 out of the 203 COVID-19 trials registered at clinicaltrials, gov [11,12]. Some nonrandomised cohort studies have suggested that the use of HCQ might reduce or even eliminate this risk [13–15]. However, yet again the opinion regarding HCQ as a prophylactic agent is divided in light of studies which have been unable to replicate the benefits shown in previous studies [12,16,17]. In India, a recent observational study revealed that consumption of four or more maintenance doses of HCQ by HCP was associated with a significant reduction in the chances of getting infected with COVID-19 [18]. The National Task force for COVID-19 in India have recommended chemoprophylaxis with HCQ for high risk populations including asymptomatic HCP and household contacts of COVID-19 patients [19].

The other pharmacological agents proposed for the treatment of COVID-19 have also revealed mixed results. For AZ, the initial success in the French study [20] was not mirrored in subsequent trials [21]. Regarding antivirals, although the initial randomised control trial in Wuhan did not reveal any benefit, a subsequent study confirmed superiority to placebo in shortening recovery time in patients with Covid-19 and evidence of lower respiratory tract infection [22]. This, however was not replicated in another trial involving COVID patients not requiring mechanical ventilation [23]. Another antiviral agent Lopinavir, in combination with Ritonavir, has had mixed results [24].

Vitamin C by virtue of its possible efficacy against influenza virus has been used in some centres as supportive treatment and has been shown to improve oxygenation index in one study [24]. Convalescent plasma transfusion has shown promise but is currently limited by small sample size and larger studies are awaited [25].

The role of corticosteroids (CS) in critically ill COVID-19 patients has also revealed diverse results [26]. A recent meta-analysis found absence of benefit of CS in critically ill COVID-19 patients but signalled a trend towards benefit in patients with acute respiratory distress syndrome (ARDS) which did not reach statistical significance [26].

As SARS-CoV-2 uses the angiotensin converting enzyme inhibitors 2 (ACE2) receptor to enter target human cells, theoretical concerns were initially raised regarding angiotensin converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) as animal models had revealed that they upregulate ACE2 receptors [27]. However a recent meta-analysis of observational studies have revealed that ACEi/ARB use in patients subsequently affected with COVID-19 may reduce the odds of death [27].

Studies on currently used pharmacological modalities against COVID-19 have produced an assortment of confusing signals. This has been compounded by the lack of concordance amongst august bodies regarding their use, leaving the treating doctors with their own perception of the various studies and meta-analyses. Hence it is imperative to understand the current perception amongst the medical fraternity regarding pharmacological approach to COVID-19. To this end we designed a questionnaire based survey amongst doctors all over India cutting across all specialties.

#### 2. Materials and methods

#### 2.1. Conceiving the survey

KKG conceived the idea of conducting the survey in view of the controversies surrounding the prophylaxis and therapeutic management related to SARS-CoV-2 infection. The key questions to be included in the survey were prepared by KKG (Table 1). It was then converted into an e-platform and circulated to one lakh physicians identified from a verified directory during the period of 4th May to May 25, 2020.

#### 2.2. Data collection and analytical techniques

The e-platform was designed to filter out all incomplete attempts, automatically. There was no scope for completing the survey without filling up all the components. The e-platform was also made IP address sensitive, thereby preventing multiple entries. It was made available to the physicians through email and social media prompts. The completed questionnaire was automatically uploaded into an excel sheet. The target was to collect the first 1000 responses and perform an in-depth analysis.

The excel sheet was converted into a comma separated-values (CSV) file and uploaded in Jupyter notebook. Analysis was performed using the Python3.8.2 software (Windows 10 64 bit, USA). The plan was to analyse the entire data identifying important trends and patterns before embarking on a comparative analysis.

#### 2.3. Quality assessment and internal consistency of the survey

The robustness of the thought process in the questionnaire as well as its internal validity was carried out using the principle component analysis (PCA) with factor loadings and Cronbach's Alpha (CA), respectively. The python software was used to conduct these analyses. The Mahalanobis Distance test was performed to identify the outliers.

#### 2.4. The final database for analysis

Having performed all the data cleaning techniques, as well as quality checks, 826 responses were finally included for the analysis.

#### 3. Results

The results of the analysis (n=826) is divided into two sections-basic demographics and comparative analysis.

#### 3.1. Demographic analysis

The responses could be traced to 26 states, with approximately 90% contribution from the top 10 affected states (Fig. 1). The activity was predominated by males (79%) with the predominant age group being 31–60 years (78.94%) (Table 2). From a specialty point of view, 15.13% of the doctors in the survey had experience in managing patients in the intensive therapy unit (ITU), whereas 17.43% doctors were from the surgical specialty. 21% of the total respondents had experience in managing patients diagnosed with SARS-CoV-2.

**Table 1** The questionnaire.

|   | Certainly<br>yes | May Undecided as of now | No, not<br>at all | Don't<br>know |
|---|------------------|-------------------------|-------------------|---------------|
| In the context of evidence based medicine, based on the current evidence available, would you consider using HCQ for prophylaxis for HCP against COVID-19?                        |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using HCQ for treatment of mild to moderate COVID-19 patients?             | •                |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using HCQ for treatment of severe COVID-19 patients?                       | •                |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using AZ for treatment of mild to moderate COVID-19 patients?              |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using AZ for treatment of severe COVID-19 patients?                        |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using antiviral drugs for treatment of mild to moderate COVID-19 patients? |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using antiviral drugs for treatment of severe COVID-19 patients?           |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using corticosteroids for treatment of severe COVID-19 patients?           |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using Vit C for treatment of COVID-19 patients?                            |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, would you consider using convalescent plasma for COVID-19 patients?                           |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, do you believe that testing for COVID to be part of routine pre-operative investigation?      |                  |                         |                   |               |
| In the context of evidence based medicine, based on the current evidence available, do you believe that ACEi/ARB  |                  |                         |                   |               |

 $HCQ = Hydroxychloroquine, HCP = Health\ care\ provider,\ AZ = Azathioprine,\ ACEi = Angiotensin\ converting\ enzyme\ inhibitor,\ ARB = Angiotensin\ receptor\ blocker.$ 

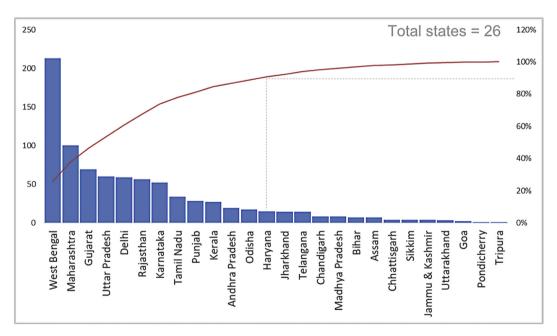


Fig. 1. State-wise pattern of responses from the survey. x-axis: States, y-axis: Count.

#### 3.2. Comparative analysis

## 3.2.1. Overall trends from the questionnaire (Baseline for a comparative analysis)

should be stopped in patients affected with COVID19?

Have you managed any COVID-19 patients?

Do you think vaccine is the ultimate answer to stop this pandemic and not herd immunity

• There was an overall trend towards advocating HCQ both as prophylaxis for HCP (44.55%) as well as those diagnosed with mild-moderate COVID-19 (45.04%) and severe COVID-19 (43.58%) (Table 3).

- A very similar trend was observed with azithromycin use in SARS-CoV-2 patients with mild-moderate (51.94%) and severe disease (46%) (Table 3).
- As far as using anti-vital agents were concerned, a large proportion of doctors (65.98%) preferred its use in cases with severe COVID-19 infection (Table 3).
- There was a clear and definitive trend towards continuing with ACEi/ARB (60.9%) in patients diagnosed with COVID-19, as well as routinely testing all patients for COVID-19 as part of a preoperative assessment (73.85%) (Table 3).

 Table 2

 Demographic characteristics of physicians who participated in the survey.

| Attributes          |                         | Number | Percentage (%) |
|---------------------|-------------------------|--------|----------------|
| Gender              | Male                    | 754    | 79             |
|                     | Female                  | 72     | 21             |
| Age (years)         | <30                     | 34     | 4.12           |
|                     | 31-40                   | 217    | 26.27          |
|                     | 41-50                   | 233    | 28.21          |
|                     | 51-60                   | 202    | 24.46          |
|                     | 61-70                   | 126    | 15.25          |
|                     | >70                     | 14     | 1.69           |
| Speciality          | ITU                     | 125    | 15.13          |
|                     | Non-ITU                 | 701    | 84.87          |
|                     | Surgical                | 144    | 17.43          |
|                     | Non-surgical            | 682    | 82.57          |
| COVID-19 experience | Managed COVID-19        | 172    | 21             |
|                     | Did not manage COVID-19 | 654    | 79             |

### 3.2.2. Comparison between those who have managed COVID-19 versus those who did not

- Those who have experience in managing COVID-19 were more likely to advocate use of HCQ as prophylaxis for HCP than as treatment ( $\gamma$ 2 = 4.357, P = 0.037) (Supplementary Table 1).
- Those who have experience in managing COVID-19 and were involved in ITU care, were more likely to advocate use of HCQ both as prophylaxis for HCP ( $\chi 2 = 14.588$ , P < 0.001), as well as for treatment of mild-moderate COVID-19 ( $\chi 2 = 3.91$ , P = 0.048) (Supplementary Table 1).
- There was no difference between those who had experience in management of COVID-19 and involved in ITU management versus the rest as far as using corticosteroids for severe disease was concerned ( $\chi 2 = 0.007$ , P = 0.933). A very similar trend was seen among those with surgical specialty versus their non-surgical counterparts when it came to performing routine preoperative COVID-19 testing ( $\chi 2 = 0.048$ , P = 0.827) (Supplementary Table 1).

## 3.2.3. Comparison between doctors involved in ITU management versus the rest (irrespective of experience with managing COVID-19) on HCQ use

• Doctors involved in ITU management were more likely to advocate HCQ as prophylaxis for HCP ( $\chi 2 = 14.588$ , P < 0.001), as well as for treatment of mild-moderate COVID-19 ( $\chi 2 = 3.91$ , P = 0.048) (Supplementary Table 1).

#### 4. Discussion

To our knowledge, this is the first questionnaire based survey which attempts to gauge the perception amongst doctors regarding therapeutic management of COVID-19 given the uncertainties surrounding it (Table 1). A survey over a longer period of time would be ideal, but due to the changing dynamics of therapeutic management of COVID-19, it was thought prudent to terminate the survey within a short time span so that the medical fraternity in general and the concerned authorities in particular have an understanding of the doctors predilection towards management of COVID-19, which would then help formulate appropriate steps in that direction.

Interestingly, most of the respondents came from the top 10 COVID-19 affected states (Fig. 1). Though this survey was open to doctors of all specialties, surgical specialties had lesser representation probably due to the fact that the COVID-19 patients are predominantly managed by internal medicine and allied specialties (Table 2).

Regarding HCQ prophylaxis, around three quarter of the doctors would either prescribe or at least consider prescribing HCQ as prophylaxis, which is in keeping with the recommendation by the Indian National Task Force for COVID-19<sup>19</sup> (Table 3). This could have been influenced by the recent ICMR study, suggesting a significant decline in getting infected with COVID-19 with HCQ prophylaxis (AOR: 0.44; 95% CI: 0.22–0.88) [18]. However, another study from the United States and Canada testing HCQ for post exposure prophylaxis failed to replicate the results [16]. Interestingly doctors who have already been managing COVID-19 and/or were involved in ITU care were more likely to offer HCQ as prophylaxis to HCP than the rest of the doctors (Supplementary Table 1).

As far as treatment is concerned, majority of the doctors would prescribe or consider prescribing HCQ, although the current evidence for the same have been mixed [6,7] (Table 3). This is also notwithstanding the fact that safety concerns have been flagged with HCQ use as treatment for COVID-19, and is currently considered as an off label indication in severe disease [8,9]. One may hypothesise that this could be due to the fact that longstanding experience with HCQ in treating inflammatory arthropathy and its related drug chloroquine in treating malaria, may have instilled enough confidence amongst the doctors in India to tilt the benefit risk ratio in favour of HCQ, particularly as till date there is no definite curative treatment of COVID-19.

There was a similar trend in using AZ, perhaps emboldened by the initial success of the French study [13]. Doctors were more likely to use antiviral medications in the severe cases than the milder cases. Given the diverse and confusing results of antiviral

**Table 3**Response patterns derived from the completed questionnaire.

| Attributes           |   | Yes (%) | Maybe (%) | Undecided (%) | No (%) | Do not know (%) |
|----------------------|---|---------|-----------|---------------|--------|-----------------|
| HCQ                  | Prophylaxis for health-care providers             | 44.55   | 31.60     | 14.53         | 8.96   | 0.36            |
|                      | For mild-moderate COVID-19                        | 45.04   | 33.78     | 11.62         | 8.84   | 0/73            |
|                      | For severe COVID-19                               | 43.58   | 24.82     | 16.83         | 12.83  | 1.94            |
| Azithromycin         | For mild-moderate COVID-19                        | 51.94   | 29.78     | 9.69          | 7.51   | 1.09            |
| -                    | For severe COVID-19                               | 46.00   | 28.57     | 10.77         | 12.47  | 2.18            |
| Anti-virials         | For mild-moderate COVID-19                        | 28.81   | 39.95     | 15.98         | 14.04  | 1.21            |
|                      | For severe COVID-19                               | 65.98   | 22.88     | 6.54          | 3.15   | 1.45            |
| Corticosteroids      | For severe COVID-19                               | 31.60   | 37.29     | 14.16         | 14.04  | 2.91            |
| Vitamin C            | For COVID-19                                      | 43.83   | 34.87     | 10.41         | 7.99   | 2.91            |
| Convalescent plasma  | For COVID-19                                      | 28.21   | 47.46     | 19.98         | 2.78   | 1.57            |
| Testing for COVID-19 | As a routine pre-operative investigation          | 73.85   | 15.74     | 5.93          | 3.63   | 0.85            |
| ACEi/ARB             | Should be stopped in patients affected with COVID | 8.23    | 11.74     | 16.10         | 60.90  | 3.03            |
| Vaccine              | The ultimate answer                               | 42.74   | 24.94     | 15.98         | 13.56  | 2.78            |

use in COVID-19, one may presume that the use is likely to be compassionate in nature [22]. The possible efficacy of Vit C against influenza viruses together with lack of adverse effects may have prompted more than three quarters of the doctors to prescribe or at least consider vitamin C for COVID-19 treatment. Only 28% of doctors would give convalescent plasma for COVID-19 — this low number could be due to inexperience in using convalescent plasma coupled with only a few small studies supporting its use (Table 3).

Given the mixed response to corticosteroids, less than a third of the doctors would give it in critically ill COVID-19 patients with the doctors involved in ITU not supporting it more than the rest of the doctors (Supplementary Table 1).

The message that ACEI/ARB group of drugs are not detrimental to patients during COVID-19 seems to have percolated down well with more than 60% doctors not agreeing to stop it (Table 3). This is in keeping with several studies and a recent meta-analysis supporting the same [27].

The highest affirmative response was reserved regarding testing for COVID-19 as a pre-operative procedure (Table 3). This is understandable given the high number of asymptomatic cases and the risk of contracting COVID-19 during surgical procedures including endoscopy, bronchoscopy, intubation etc.

The main limitation of this survey was related to the everchanging evidence and recommendations related to COVID-19. The responses from physicians were in accordance with the evidence available up to that point in time. A serial survey could help in overcoming this important limitation. Second, to conduct an objective analysis we had to discount off the responses which could not be ranked, for example "maybe". This resulted in loss of information and resulted in a reduction of reduced the numbers included in analysis. Third, surveys are not ideal for exploring subjective and controversial issues since it fails to bring out the truths behind those controversies. Our survey dealt with controversial issues like use of HCQ, AZ, etc. for prophylaxis and treatment of COVID-19, and hence it is subject to the above-mentioned limitations. Fourth, in view of the COVID-19 pandemic being caused by a novel coronavirus, we do not have a standardized questionnaire to model our survey on.

The main strength of this survey has been the fact that it is the first to explore the mind-set of Indian physicians regarding the management issues related to COVID-19. This would give a robust insight to the health policy makers on their impact on the medical community and the need to focus on specific areas of interest as highlighted by our survey. Second, this was a pan-India survey, with responses recorded from 26 states and hence can be considered as representative of a broad Indian doctor community. In this new-normal era of social distancing, this is possibly the best way to generate data and further develop it with repeat surveys and analysis. Most importantly, the biggest strength of this survey was the absence of observer subjectivity, cost-effective means of data generation, and a robust statistical analysis.

In conclusion, the opinion of the medical fraternity in India seems to be broadly in line with the recommendation by the National Task Force for COVID-19 constituted by Indian Council of Medical Research as well as the revised guideline by the ministry of health [9,28].

#### **Declaration of competing interest**

The authors do not have any conflict of interest to declare for this article.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2020.07.040.

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