

## **“E survey of hydroxychloroquine (HCQ) prophylaxis against COVID-19 among health care professionals in Gujarat, India.”**

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## **Abstract**

### **1. Introduction:**

The virus that causes COVID-19 diseases is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has generated pandemic which requires preventive measures, vaccines and pharmacological interventions. Some studies showed effectiveness of Chloroquine and Hydroxychloroquine for the treatment and prophylaxis. HCQ acts mainly by modulating cellular metabolism of coronaviruses. Due to cost-effectiveness and availability ICMR also recommended its use for prophylaxis and found effective. So, this study was carried out to document perceived effectiveness and adverse effects of HCQ as prophylaxis.

### **2. Methodology:**

A cross-sectional e-survey was carried after ethical approval and validated questionnaire had been sent to 500 health care professionals via google form online. In 3 months of duration, 193 responses were received (who had taken HCQ prophylaxis), data collected and analyzed.

### **3. Results:**

Among 193 responses, 109 from government and 84 were from private set up. The most common reason(s) to take prophylaxis was direct contact with positive cases, selected by 94 (50.5%) responders and 133 (70%) had completed the course as per ICMR guideline. 86.5% participants didn't have infection while others were positive cases and among them 69% had mild to moderate symptoms. Nausea was most common adverse effects followed by dizziness, vomiting, abdominal pain, hypoglycemia, hypersensitivity, etc. No any cardiovascular effect was noticed and 62.8% agreed to recommend HCQ as prophylaxis to others.

### **4. Statistical analysis:**

Data analyzed using descriptive statistics with SPSS 1.0.0.1406 version

## 5. Conclusion:

HCQ prophylaxis against COVID-19 among health care professionals showed perceived effectiveness without any serious adverse effects here which is shown by other studies also and so it is considered as complementary strategies for prophylaxis with vaccination.

**Key Words:** HCQ, Prophylaxis, COVID-19, Health Care Professionals

**Type of Article:** Original research article

### Introduction:

The virus that causes Coronavirus disease 2019 (COVID-19) is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which has generated a worldwide pandemic.<sup>[1]</sup> The peak of the first wave of the pandemic was in mid-September with more than 10 lakh active cases in the country and the highest single-day spike of 97,894 new cases recorded on September 16, 2020. Later on, there was a steady decline in the number of new cases per day for some time. But again on February 16, 2021, the country reported a mere 9,000 new cases and an active caseload of 1.36 lakhs. The vaccination program in India began on January 16, 2021, and it was widely believed that the battle against the virus was about to end. By the end of February 2021, there was a sharp rise in the number of daily reported cases, declaring the second wave of the pandemic had already set. With second wave of the pandemic, health systems of India was getting overwhelmed in most parts of the country.<sup>[2]</sup> The second wave of the pandemic has changed the global scenario in every aspect, presented with wide disparities in geographical distribution, with a few states peaking much ahead of others. It has not only affected millions of individuals across the globe but also flipped the lives of countless people who are combating to survive COVID-19.<sup>[1, 2]</sup>

During initial phase of pandemic, social distancing, face mask, hand hygiene was the mainstay of prevention of infection. But along with prevention some pharmacological intervention was also required. Vaccine could be the most important mode of treatment for COVID-19 but the repurposing of conventional medicines for short-term prophylaxis would be immediate option at that time.<sup>[3]</sup> According to information by Lu, in 2020, treatment in COVID-19 patients with antiviral drugs like human immunodeficiency virus (HIV)-protease inhibitors, neuraminidase inhibitors, ribonucleic acid (RNA) synthesis inhibitors and nucleoside analogues could be rather weak.<sup>[4]</sup> Additionally, a number of drugs like remdesivir, galidesivir, lopinavir/ritonavir combination, favipiravir, and several vaccines, plasma therapy, tocilizumab etc. received emergency clearance or in pipeline in both preclinical as well as early and late phase clinical

trials.<sup>[5]</sup> Some studies have showed effectiveness of Chloroquine and Hydroxychloroquine (HCQ) for the treatment and prevention of infection by different microorganisms, including SARS-CoV-2.<sup>[6]</sup> Hydroxychloroquine can inhibit replication of SARS-CoV-2 in vitro.<sup>[7,8]</sup> In the Journal, Boulware et al. reported the results of a randomized trial testing hydroxychloroquine as a post exposure prophylaxis for COVID-19.<sup>[9]</sup>

Hydroxychloroquine sulfate is a chloroquine analogue frequently used for malaria, rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE). It possesses anti-inflammatory and immunomodulatory properties such as inhibition of cytokines (IL-1 and IL-6) production, inhibition of phospholipase A2 and metalloproteinases and modulation of B and T cell function. It increases lysosomal pH and modulates the cellular metabolism of iron, thus reduces its intracellular concentration, which in turn inactivates glycosyltransferases and glycosylating enzymes, further suppressing glycosylation of SARS-coronaviruses. Cost-effectiveness and easy availability of HCQs make it more prone to use in large scale particularly in low- or middle-income countries (LMIC) settings.<sup>[10]</sup>

In India, The National Taskforce (NTF) for COVID-19 constituted by Indian Council of Medical Research (ICMR) recommended the use of HCQ for prophylaxis of SARS –CoV-2 infections for asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19 and also to asymptomatic household contacts of laboratory confirmed cases in March 2020. Revised advisory on 22nd May 2020, by The National Taskforce (NTF) reviewed the use of HCQ in health care workers. In which they reported that healthcare workers involved in COVID-19 care with HCQ prophylaxis, were less likely to develop SARS-CoV-2 infection compared to those who were not on it. This was an investigation of three central government hospitals in New Delhi. Another observational prospective study of healthcare workers at AIIMS, New Delhi showed lower incidence of SARS-CoV-2 infection in health care workers with HCQ prophylaxis (median 6 weeks of follow up).<sup>[11, 12]</sup> Thus, this study was carried out with aim and objective to document perceived effectiveness and any adverse effects observed during study period of HCQ as prophylaxis against COVID-19 among health care professionals of Gujarat, India.

### **Materials and Methods:**

A cross-sectional, observational E-survey was carried out at the tertiary care hospital, Gujarat, India. Ethical approval from IRB (Institutional Review Board) of Government Medical College

and New Civil Hospital (Approval number- GMCS/STU/ETHICS/APPROVAL/21082/20) was taken. The questionnaire was prepared for data collection including questions about medicines taken for prophylaxis, duration of prophylaxis, exposure to COVID-19 infection after HCQ prophylaxis etc. [Table-1]. Informed consent form & Participant information sheet were part of the form. The questionnaire had been sent to 500 health care professionals (medical doctor, nursing staff, pharmacist and dentist) through instant messaging application. This questionnaire was distributed to the health care professionals of our contacts and others were approached by snow ball sampling. Among them who were willing to participate and had taken HCQ as prophylaxis against COVID-19 were enrolled. In 2 months of duration, 193 responses were received as per inclusion criteria, after confirming they have taken HCQ as prophylaxis in verbal or by telephonic conversation or by mail or message. Data collected and analyzed using descriptive statistics with latest SPSS 1.0.0.1406 version and MS excel 2010.

**Table1: Study Questionnaire**

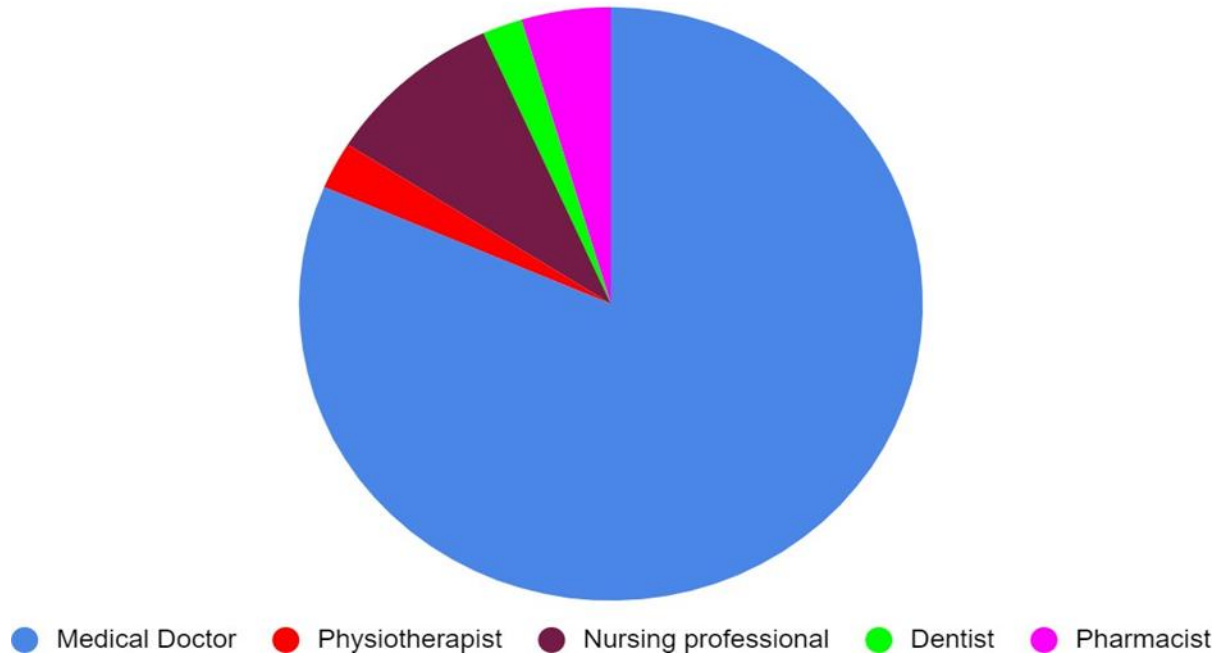
Sr. No.	Questions
1	What was the reason (s) to take HCQ prophylaxis?
2	Have you taken HCQ prophylaxis according to ICMR guidelines?
3	Do you have any co-morbid condition?
4	Has ECG been recorded?
5	After taking HCQ as prophylaxis, did you experience any of the adverse effects given below?
6	Were any of the adverse events serious enough to require?
7	Have you been diagnosed as COVID-19 positive case after taking HCQ prophylaxis?
8	If yes, after how many days of consumption of HCQ?
9	If yes, what was the status as COVID-19 positive case?
10	Will you recommend HCQ as prophylaxis to others?

**Results:**

In this study, we received 193 responses from various cities of Gujarat. Among 193 responses, average age was 36 years (minimum 19 years and maximum 65 years) and 113 (58.5%) were male while 80 (41.5%) were female.

Figure 1 shows health care professionals from different health care fields in the study.

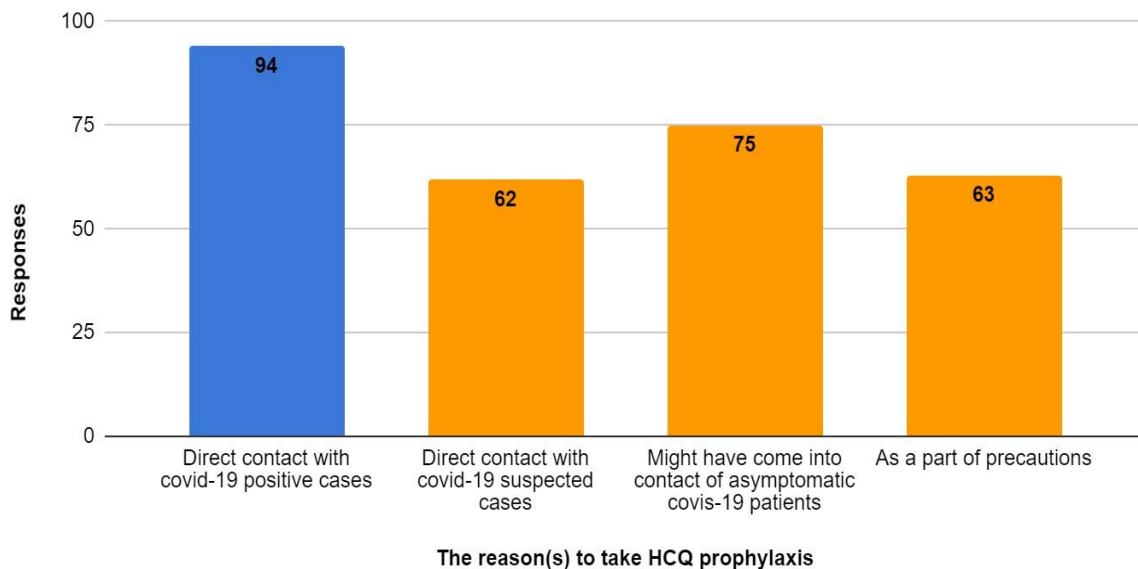
Figure 1: Different type of health care professionals



Out of 193 responses, 109 (57%) were from government and 84 (44%) were from non-government set up.

Figure 2 shows that the most common reason(s) to take HCQ prophylaxis was direct contact with COVID-19 positive cases which was selected by 94 (50.5%) responders with other reasons.

Figure 2: The reason(s) to take HCQ prophylaxis among HCPs (n=186)



As per ICMR guideline of HCQ prophylaxis against covid19, 133 (70%) had completed the course.

Table 2 shows different adverse effects observed after HCQ prophylaxis, in which nausea was most common followed by dizziness, vomiting, abdominal pain, and others like hypoglycemia, hypersensitivity, photosensitivity, body ache, nonspecific headache, malaise were reported without any cardiovascular effect. Those who developed ADR, among them 14 required symptomatic treatment and 5 required hospital administration.

**Table 2: Adverse effects after taking HCQ prophylaxis**

Sr. No.	Adverse effect	Total number
1	Nausea	35
2	Vomiting	13
3	Abdominal pain	18
4	Hypoglycemia	5
5	Hypersensitivity	2
6	Photosensitivity	3
7	Cardiovascular effects	0
8	Dizziness	19
9	Others	3

Figure 3 shows that after taking HCQ prophylaxis, 167(86.5%) participants didn't have COVID-19 infection while others were diagnosed as COVID-19 positive cases.

Figure 3: Have you been diagnosed as Covid-19 positive case after taking HCQ prophylaxis?

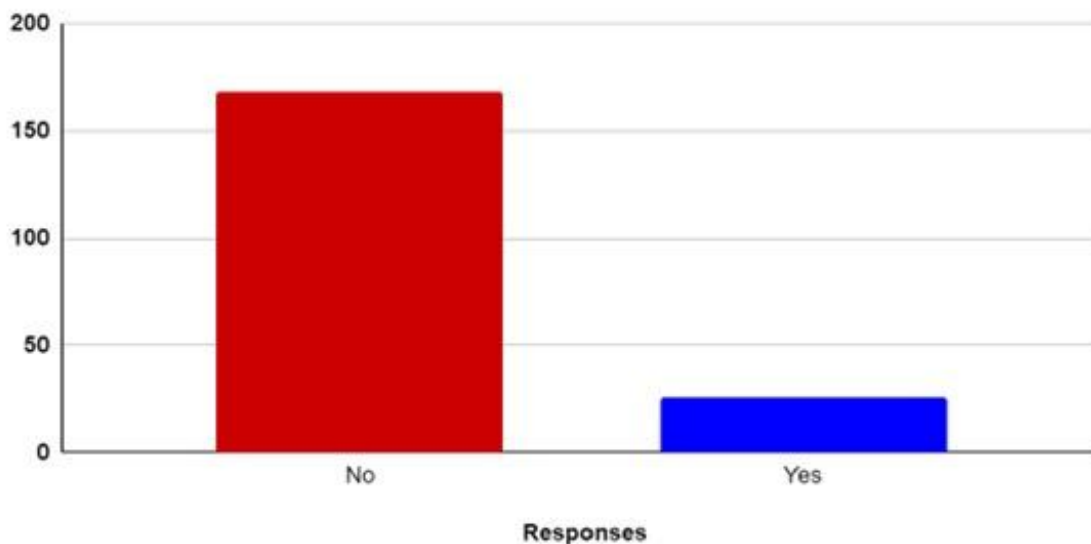
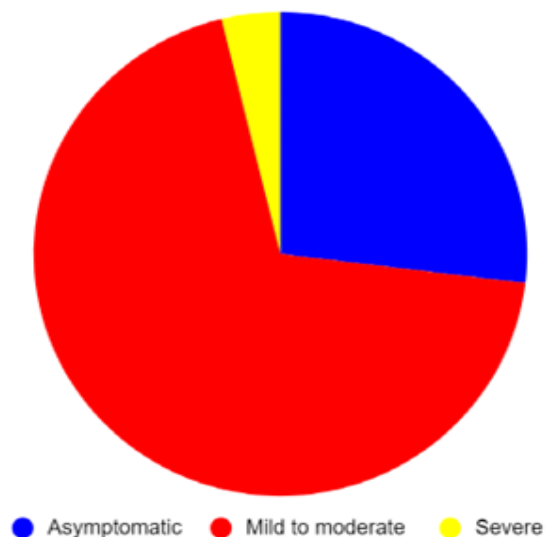


Figure 4 shows among the COVID-19 positive cases, majority became positive after taking HCQ for more than 21 days and 69% had mild to moderate symptoms. From 193 responses, 62.8% agreed to recommend HCQ as prophylaxis to others.

Figure 4: Severity of Covid 19 infection after HCQ prophylaxis



## Discussion

The pandemic of COVID-19 imposes a substantial burden on individuals, communities, healthcare facilities, markets, and government globally<sup>[13]</sup> Till now no definite pharmacotherapy

has been established for cure and so vaccination with other preventive measures and some agents can still have roles for prophylaxis. Vaccines have limitations of efficacy against emerging SARS-CoV-2 variants, long-term efficacy and safety. There is no conclusive evidence for pre-exposure prophylactic use of HCQ in HCWs. A systematic review advises caution while interpreting studies.<sup>[14]</sup> Most studies have limitations of insufficient sample size and the absence of risk stratification.<sup>[14, 15, 16]</sup> Hydroxychloroquine was reported to inhibit acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replication and shown effectiveness for prophylaxis more as compared to treatment.<sup>[17]</sup> Therefore, it has been recommended for prophylaxis of COVID-19 in healthcare workers (HCWs).

In the present cross-sectional survey, perceived effectiveness and safety of hydroxychloroquine has been documented. Among 193 responses we received of different health care professionals, among them average age noted was 36 years (minimum 19 years and maximum 65 years). If we see gender-wise participants, 113 (58.5%) were male and 80 (41.5%) were female. We received responses from health care professionals like medical doctor, physiotherapist, nurses, dentists and pharmacists. In similar studies, consenting doctors, nurses, ancillary staff likely exposed to COVID-19 patients and others from different health care fields were enrolled from various government and non-government institutes.<sup>[17]</sup> Here, among 193 responses, 109 (57%) from government and 84 (44%) from non-government set up were received.

The most common reason(s) to take HCQ prophylaxis was direct contact with COVID-19 positive cases, selected by 94 (50.5%) responders with other options. [Figure 2]. As per ICMR guideline of HCQ prophylaxis against COVID-19, 133 (70%) had completed the course. Others have either taken by their own or as per consultation of other practitioners.

Safety profile of HCQ shows wide variety like life-threatening cardiac arrhythmias, QT prolongation, vision loss due to irreversible retinopathy, hemolysis in patients with G6PD deficiency, hypoglycemia etc. and milder effects like gastrointestinal problems, dizziness. As serious adverse effects are not common in routine practice, HCQ is considered safe even with prolonged use.<sup>[18, 19]</sup> Our survey results mimic this like there were different ADRs observed after HCQ prophylaxis, in which nausea was most common followed by dizziness, vomiting, abdominal pain, hypoglycemia, hypersensitivity, photosensitivity and others like malaise, body ache and nonspecific headache. No any cardiovascular event was mentioned [Table 2]. Those who had developed ADRs, among them fourteen required symptomatic treatment and



five required hospital admission. Another similar study stated the same that it was well tolerable to most of the participants, none of them complained of any serious ADRs. Only three of the participants experienced mild epigastric abdominal discomfort with burning sensation and nausea after the first dose which was self-limiting afterwards. Good compliance was noted among majority of the participants.<sup>[18]</sup> Study conducted by Boulware et al showed contradictory conclusions like the incidence of adverse effects was reported higher with probable explanation of using the higher dose (3800 mg) of HCQ for post exposure prophylaxis for COVID-19.<sup>[9]</sup>

After taking HCQ prophylaxis, 167 (86.5%) participants didn't have COVID-19 infection while others were diagnosed as COVID-19 positive in our study [figure 3]. Among these COVID-19 positive cases, majority became positive after taking HCQ for more than 21 days and 69% had developed only mild to moderate symptoms [figure 4]. These results were comparable with another similar study, in which prophylactic use of HCQ was associated with lesser likelihood of developing COVID-19 positive cases and participants had complained of variety of adverse events with all grades of severity.<sup>[19]</sup> A multicentric cohort study assessing effectiveness and safety with HCQ prophylaxis in healthcare workers has published elaborative data. HCQ prophylaxis given for 2-3 weeks, 4-5 weeks or more than 6 weeks significantly reduced COVID positivity by 34%, 48% and 72% respectively. Among COVID-19 positive cases, 89.28% were mild, 2.6% were moderate and others were requiring ICU admission, out of them few needed assisted ventilation. Some milder and fewer serious AEs had been reported including severe nausea, vomiting, abdominal pain, palpitations, fainting, visual disturbance, hypersensitivity and needing at least one day hospitalization which were more or less in the same line with present study.<sup>[20]</sup>

From our 193 responses 62.8% of the participants agreed to recommend HCQ as prophylaxis to others. These findings indicate real world situation with possibility of generalizability, extrapolation and importance from a public health perspective. These days different vaccines are available and recommended by government and private set up but they have varying levels of efficacy and other many challenges. These findings from present study and other studies worldwide regarding HCQ are important to consider as complementary strategies for prophylaxis.

### **Limitations**

It was a cross-sectional E-Survey, so association doesn't imply causation. The roles of confounders were also not studied.

## Conclusion

Along with vaccination and other preventive strategies, HCQ prophylaxis also has additional importance to be used as preventive measure for COVID-19 which is still persisting in the world more or less without any definite treatment.

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