

## ORIGINAL ARTICLE

# Assessment of knowledge, attitude, and practices towards hydroxy chloroquine pre-exposure prophylaxis for COVID – 19 among health care professionals.

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## Abstract

**Background:** There is an urgent need for developing potential drug targets to protect the health care professionals (HCPs) who are at high risk of infection from coronavirus disease-2019 (COVID-19) as they are directly and/ indirectly involved in treatment facility. We aimed to assess knowledge, attitude, and practices towards hydroxychloroquine (HCQ) pre-exposure prophylaxis (PEP) among HCPs directly and/ indirectly involved in COVID-19 treatment. **Materials and Methods:** This cross-sectional study was multi-centric, and data was collected from HCPs (only doctors and nurses) involved directly or indirectly with COVID-19 patient treatment. The study questionnaire consisted of socio-demographic profile; assessment of HCQ knowledge, attitude, practices, and related adverse drug reactions (ADRs). **Results:** Of the recruited 374 HCPs, 302 fulfilled the study criteria. Mean age of participants was 33.30 {±standard deviation 7.65}. 64.2% of the participants were male. 16.9% of the individuals (n=51) had co-morbidities. All the HCPs had basic knowledge of COVID-19 and 87.42% were aware of the role of HCQ as PEP. Further, 269 participants (89.07%) were aware that HCQ can cause ADRs. 56.6% participants agreed that HCQ had a protective role against COVID-19 and 54.3 % participants considered that PEP with HCQ had 'more benefit' than risk. 52.32% (n=158) HCPs had used HCQ as PEP and 52.53 % (n=83) of these participants had completed the recommended drug course. Twenty participants (12.67%) had experienced ADR, and 12 had reported it to ADR monitoring centre. **Conclusion:** Our data shows that HCPs are aware of COVID-19 and HCQ prophylaxis. Approximately 57% of the participants agreed that HCQ has a protective role against COVID-19 and 50% of the participants had taken HCQ prophylaxis. Only 12.67% of the participants reported an ADR and in none of them, it was serious enough to discontinue the drug.

## Keywords

hydroxychloroquine; Pre-exposure Prophylaxis; Health Care Professionals; COVID-19

## Introduction

The burden of coronavirus disease-19 (COVID-19) caused by severe acute respiratory syndrome-corona virus-2 (SARS-CoV-2) is continuously increasing across the globe. Approximately 80% of the COVID-19 patients have mild symptoms that can go unnoticed, but still are able to transmit the disease (1). SARS-CoV-2 secondary infection rates in households (~15%), as well as in close contacts (~10%) are a major concern (2). In addition to this, 20%-43% infected patients are asymptomatic (3,4). To date, there is no ideal drug nor has been approved for the COVID-19 treatment. Clinical trials of different drugs are underway to check their safety and efficacy towards COVID-19. In this situation, it is essential to start the supportive treatment and repurpose the well-known antiviral drugs and therapy.

Frontline health care professionals (HCPs) e.g. doctors, nurses, pharmacists, and other staff are in direct contact with COVID-19 patients. Due to repeated exposure, the chance of them getting an infection is very high. Health care workers managing COVID-19 patients are getting infected worldwide, with estimates ranging from 4.4%-20% (5,6,8). In this context, chemoprophylaxis could be advantageous to lower the infection rate in HCPs. In pre-exposure prophylaxis (PEP) a drug/therapy is given to prevent the disease. HCQ is a well-known medication used in malaria and chronic inflammatory diseases from many years (9). It is also used as chemoprophylaxis, and anti-rheumatic drug (9). At standard doses, it is safe, and well-tolerated. Recent in-vitro research shows that HCQ can prevent entry of virus as well as its replication, and transmission (10). Additionally, HCQ increases the pH of the cellular endosome to prevent virus entry and replication and glycosylation of viral surface receptor angiotensin-converting enzyme-2 (ACE-2). Further, it is also reported that HCQ is more effective, compared with chloroquine, in suppressing SARS-CoV-2 in-vitro (10). Based on observed concentrations of the drug and in-vitro drug testing, pharmacological models indicates that prophylaxis with HCQ at permitted doses may prevent SARS-CoV-2 infection(11). Many shreds of evidence have represented the role of HCQ in the treatment of COVID-19. Adverse effects reported

with HCQ include cardiovascular side effects (QT prolongation, arrhythmia, myocardial arrest etc), central nervous system side effects (e.g confusion, convulsions), gastrointestinal side effects (like nausea, vomiting, stomach pain), and retinopathy. Retinopathy is seen with high dose therapy or from long term therapy (9).

The National Task Force (NTF) for COVID-19 constituted by Indian Council of Medical Research (ICMR), New Delhi, India has recommended the use of HCQ prophylaxis for COVID-19 in the following categories- a) asymptomatic healthcare workers involved in containment and treatment zone of COVID-19 as well as other workers working at non-COVID area of the same hospital, b) asymptomatic frontline workers, such as surveillance workers, and paramilitary/police personnel involved in COVID-19 related activities, c) asymptomatic household contacts of laboratory-confirmed cases(12). The prescribed dose for category-‘a’ is 400 mg twice for the first day followed by 400 mg once weekly for the next seven weeks after taking food (12). In this study, we have focused on category ‘a’. To date, there is very limited data on knowledge, attitude, and practices of HCPs towards PEP with HCQ.

## Aims & Objectives

1. To assess the knowledge, attitude, and practices of health care professionals towards hydroxychloroquine pre-exposure prophylaxis.
2. To evaluate the adverse drug reactions caused by hydroxychloroquine pre-exposure prophylaxis.

## Material & Methods

**Study design and subjects:** It was a multi-centric cross-sectional study. Study protocol was approved from the Institutional Ethics Committee. The schematic representation of work-flow is depicted in [\[Figure 1\]](#). In the present study, HCPs (doctors and nurses) involved directly or indirectly with COVID-19 patient treatment facilities from tertiary care hospitals were enrolled. As we know that there is very limited data available about the effectiveness of hydroxychloroquine pre-exposure prophylaxis for COVID-19 among HCPs; we aimed to enroll about 300 participants in a duration of one month. To obtain 300 sample size, we had screened 374 HCPs.

But, 46 participants did not fulfill the eligibility criteria. Hence 328 volunteers filled the pre-designed questionnaire. Out of 328 filled questionnaires, 26 were incorrectly and/incompletely filled, so we evaluated data only from 302 HCPs entry.

Enrolled participants were from the age group of 20 to 60 years from both genders. Female participants having a history of amenorrhea or who were pregnant or breastfeeding were excluded from the study. Informed consent was obtained from all the volunteers, those who did not give their consent for participation were also excluded from the study.

**Procedure:** It was a questionnaire-based study. The study questionnaire consisted of few socio-demographic questions such as age, gender, health profession, co-morbidity, and medication obtained from the health care workers. Further, questions were asked regarding basic knowledge of HCQ, any adverse effect after using it, and its reporting. The questionnaire was developed and validated with the help of experts in the medical field. Data collected was analysed using the SPSS software package (version 5, IBM, Germany). Data is presented as mean  $\pm$  standard deviation (SD), median, interquartile range, or number (n) and percentage (%).

## Results

### Demographic profile of HCPs

Demographic profile was depicted in [Table 1], [Figure-2] [Figure 3]. The mean age of 302 HCPs was 33.30 years ( $\pm$ standard deviation 7.65; median 32; interquartile range (IQR) 38-28}. Number of male (n=194, 64.24%) participants was more than females (n=108, 35.76 %). Out of 302 HCPs, 193 doctors and 73 nurses were enrolled. 16.89% participants (n=51) had associated with co-morbidity. Of these 51 participants, 44 had one co-morbidity, 4 had two co-morbidities, and 2 had more than two co-morbidities. The most common reported co-morbidities were hypertension, diabetes, asthma, and hypothyroidism.

### Assessment of knowledge

All the study participants had basic knowledge of COVID-19. When asked about its treatment options, most (90.4%) of the participants answered that as of now no treatment is available for COVID-19. 98.68 % of participants had heard about HCQ and 87.42% had knowledge about its role in pre-exposure prophylaxis in COVID-19. 91.39% of the HCP responded that HCQ

chemoprophylaxis is in the experimental phase.

[Table 2]

### Assessment of attitude

68.54 % of the health care workers agreed that HCQ should be used for pre-exposure prophylaxis of COVID-19 but only 56.95% of participants thought that HCQ can protect from COVID-19. 81 % HCPs thought that it will lead to a false sense of security, as the drug is in the experimental phase. 54.30 % of participants thought that PEP with HCQ had 'more benefit' (or were in favour of using it) than risk. 269 participants (89.07%) were aware that HCQ can cause adverse drug reactions.[Table 3]

### Assessment of practice

Practice towards HCQ is summarized in [Table 4]. 52.32% (n=158) health workers had used HCQ towards pre-exposure prophylaxis of COVID-19. Out of these 158, 124 (78.48%) participants took their doses timely and 83 (52.53%) participants had completed the drug course. 34 participants had not taken dose timely but completed the drug course. 87% (n=138) HCPs did not report any ADR after using HCQ. Twenty participants (12.67%) had experienced ADR while using it. Out of these 20 participants, 14 had reported the ADR to Adverse Monitoring Centre (AMC), or the National Coordination Centre-Pharmacovigilance Program of India(NCC-PvPI). Rest 6 individuals had not reported it. None of the participants had to stop the PEP HCQ regimen due to ADR. Major ADR reported by participants were-loose motion, palpitation, nausea, and cardiac problems etc. None of the participants reported visual disturbances.

## Discussion

Mean age of the participants in this study was 33.30 years ( $\pm$ 7.65) and 64% of the participants were males. This is similar to the studies done by Pranab Chatterjee et al (13 ) and Harshith B Kadnur et al (14). In our study, we tried to assess the knowledge, attitude, and practice of HCPs towards HCQ prophylaxis in COVID-19. Our data shows that doctors and nurses have basic knowledge of HCQ prophylaxis. This was expected as PEP with HCQ is advised by ICMR in India. 57% HCPs believed that HCQ will protect from COVID-19. 54.30 % of the participants thought that usage of HCQ as prophylaxis is more beneficial compared to the risk involved with ADRs. In the context of practice, a total of 52.32% HCPs (n=158) had used the HCQ as prophylaxis and 52.53 % (n=83) of them had

completed the drug course recommended by ICMR guidelines. 87.34 % HCPs who had taken the HCQ did not experience any ADR. However, 20 participants experienced ADR out of which 14 (70%) had reported it to AMC or NCC under PvPI. This suggests satisfactory reporting of ADR but still underreporting is a big challenge to overcome in PvPI most of the times (15). In the category of ADRs loose motion, indigestion, palpitation, nausea, arrhythmia, skin rashes were major side effects. Several studies have also stated that the use of HCQ is associated with mild ADRs (13, 15-18). One of the major concerns raised for use of HCQ as PEP is its safety profile but various studies including ours show that it is safe when used as pre-exposure prophylaxis (16). Also, HCQs have been safely used by rheumatologists even for the long term in patients with chronic autoimmune disease (19). Overall, these results are in support of using HCQ prophylaxis among health care workers to overcome the COVID-19 infection.

### Conclusion

Some evidence to date favours the use of HCQ prophylaxis in COVID-19 patients, while others not. Studies on role of HCQ prophylaxis in exposed frontline HCPs are satisfactory, although these are few in number. Also, there is dilemma in using HCQ alone or in combination with azithromycin or others. Our study shows that many HCPs had used HCQ as PEP to prevent COVID-19 and they had experienced only mild ADRs. In conclusion, standard dose of HCQ may be used to prevent COVID-19 in frontline healthcare professionals especially doctors and nurses during current pandemic. Further research on large scale and clinical trials regarding HCQ prophylaxis is need of hour.

### Limitation of the study

In the frontline healthcare workers doctors, nurses, laboratory members, and other hospital staff are included. However, in this study we have included only doctors and nurses hence result of the study may not be generalized to all HCPs. Hence further studies with comparatively bigger sample size like randomized control trials are needed.

### Relevance of the study

Ideal dose (400 mg twice for the first day followed by 400 mg once weekly for the next seven weeks after taking food) of HCQ may be used to prevent COVID-19 in frontline healthcare professionals in COVID-19 like pandemic.

### Authors Contribution

AS and AKV designed the study. HK, PG, AKP, SK, AJ, and SKS analyzed the data. All authors wrote and reviewed the manuscript.

### Acknowledgement

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**Tables**

**TABLE 1 DEMOGRAPHIC PROFILE OF STUDIED POPULATION**

S.No.	Characteristics	Subjects (n= 302)
1.	<b>Age (mean±SD, median, IQR)</b>	33.30±7.65, 32, 38-28
2.	<b>Age group (Years)</b> 21-30 31-40 41-50 51-60 61-70	120 (39.74) 142 (47.02) 32 (10.6) 5 (15.10) 3(9.06)
	<b>Gender (n, %)</b> Male Female	194(64.24) 108(35.76)
4.	<b>Health profession/occupation (n, %)</b> Doctor Nurse	229(75.83) 73(24.17)
5.	<b>Co-morbidity (n, %)</b> Yes No <b>Co-morbidity pattern (n, %)</b> One co-morbidity Two co-morbidity >2 co-morbidity <b>Co-morbidity type (n, %)</b> Hypertension	51(16.89) 251(83.11) 44(86.27) 5(9.80) 2(3.92)

Asthma	13(25.5)
Diabetes mellitus	10(19.61)
Hypothyroidism	8(15.67)
Arthritis	4(7.84)
Ankylosing spondilitis	2(3.92)
Psoriasis	2(3.92)
Allergic bronchopulmonary aspergillosis	2(3.92)
Potts spine	1(1.96)
Osteoporosis	1(1.96)
Diabetes, NET	1(1.96)
Diabetes, Hypertension	1(1.96)
Overweight, Bronchitis	1(1.96)
Varicose vein, Diabetes	1(1.96)
Diabetes,Asthma,Hypertension	1(1.96)
Diabetes, Hypertension,Dyslipidemia,Neuropathy	1(1.96)

**TABLE 2 ASSESSMENT OF KNOWLEDGE OF HEALTHCARE PROFESSIONALS TOWARDS COVID-19, AND HYDROXYCHLOROQUINE PROPHYLAXIS.**

S.No.	Particulars	Yes (n,%)	No (n,%)
1	Do you know about COVID-19?	302 (100)	0(0)
2	Is treatment of COVID-19 available or not available?	29(9.6)	273(90.4)
3	Have you heard about hydroxychloroquine ?	298(98.68)	4(1.32)
4	Do you know about its role in pre-exposure prophylaxis for COVID-19?	264(87.42)	38(12.58)
5	Do you know hydroxychloroquine is in experimental phase?	276(91.39)	26(8.61)

**TABLE 3 ASSESSMENT OF ATTITUDE TOWARDS HYDROXYCHLOROQUINE PRE-EXPOSURE PROPHYLAXIS AMONG EXPOSED HEALTHGIVING WORKERS FROM COVID-19.**

S.No.	Particulars	Yes (n,%)	No (n,%)
1	Do you think that hydroxychloroquine should be used for pre-exposure prophylaxis of COVID-19?	207(68.54)	95(31.46)
2	Do you think that it can cause adverse drug reactions?	269(89.07)	33(10.93)
3	Do you think it will protect against COVID-19?	172(56.95)	130(43.05)
4	Do you think it will lead to false sense of security, as the drug is in the experimental phase?	245(81.13)	57(18.87)
5	What do you think about the benefit: risk ratio of using it? (Yes- More benefit; No- More risk)	164(54.30)	138(45.7)

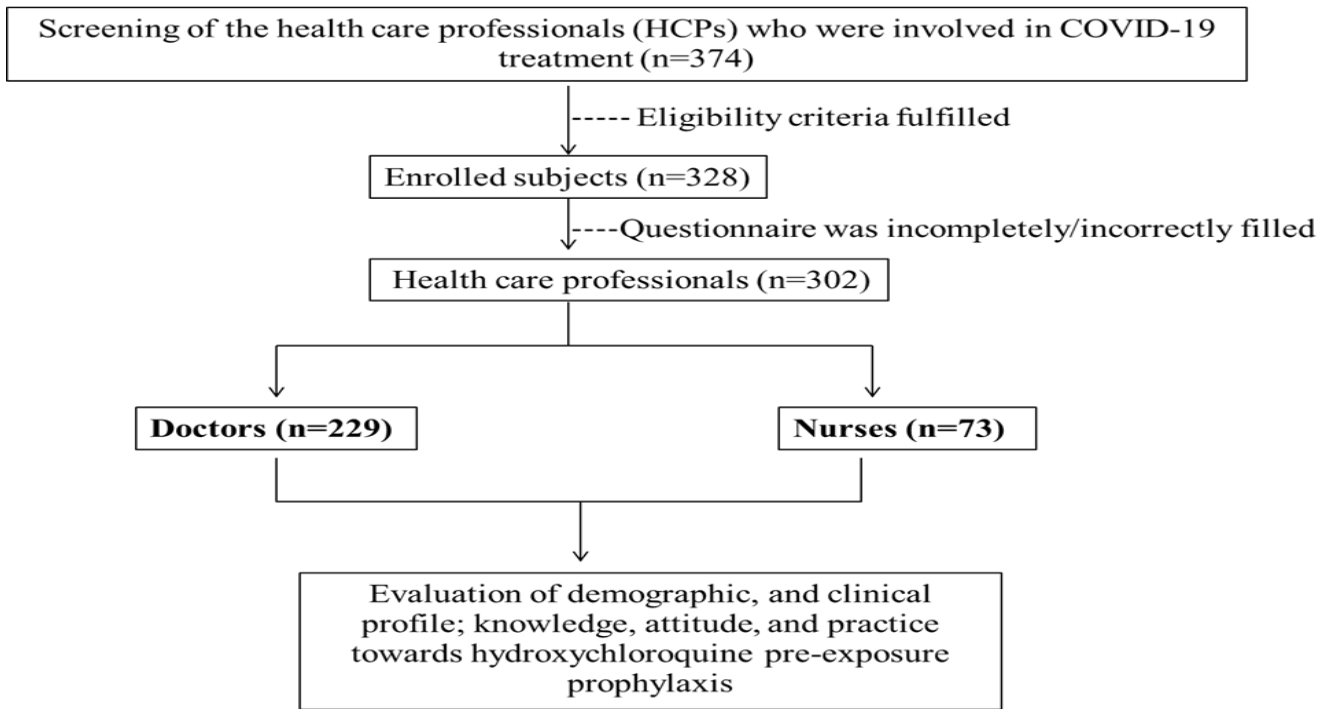
**TABLE 4 ASSESSMENT OF PRACTICE OF HYDROXYCHLOROQUINE PRE-EXPOSURE PROPHYLAXIS AND ITS CONSEQUENCES ON DOCTORS AND NURSES.**

S.No.	Particulars	Yes (n, %)	No (n, %)
1	Have you used hydroxychloroquine as pre-exposure prophylaxis?	158(52.32)	144(47.68)
2	If yes, have you taken all the doses in the time?	124(78.48)	34(21.52)
3	Have you completed the drug course? (400 mg BD on first day, followed by 400 mg once weekly for seven weeks)	83(52.53)	75(47.47)
4	Have you experienced any adverse drug reactions (ADRs) after using it?	20(12.67)	138(87.34)
5	If yes, what is the ADR you experienced?		
	Gastric acidity	2(10)	
	Allergic reactions	1(5)	
	Arrhythmia	1(5)	
	Cardiac abnormalities	1(5)	
	Indigestion	1(5)	
	Diarrhoea	1(5)	
	Indigestion, weakness	1(5)	
	Itching rashes, nausea	1(5)	

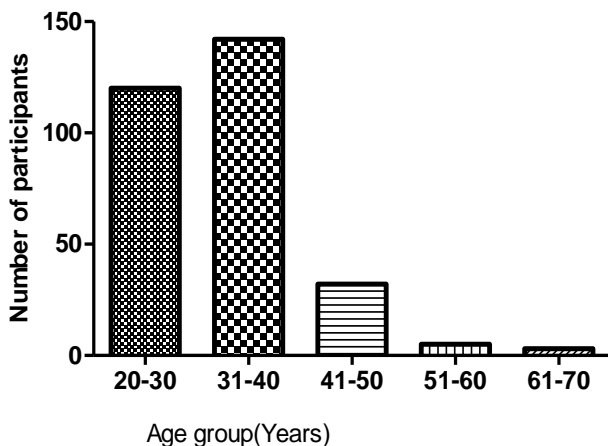
	Skin rashes	1(5)	
	Loose motion	3(15)	
	Nausea, palpitation	1(5)	
	Tinnitus	1(5)	
	Palpitation	2(10)	
	Palpitation, ECG changes	1(5)	
	Palpitation, anxiety	1(5)	
	Palpitations, uneasiness	1(5)	
6	If yes, have you reported the ADRs to Adverse Monitoring Centre, or National Coordination Centre-Pharmacovigilance Programme of India.	14(70)	6(30)

**Figures**

**FIGURE 1 SCHEMATIC REPRESENTATION OF THE WORK-FLOW**



**FIGURE 2 AGE GROUP OF STUDIED POPULATION**



**FIGURE 3 ASSOCIATED CO-MORBIDITIES IN THE PARTICIPANTS**

