

NON-PHARMACOLOGICAL REMEDIES AND OVER THE COUNTER DRUGS FOR COVID-19 PROPHYLAXIS: A QUESTIONNAIRE BASED SURVEY

Pharmacology

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ABSTRACT

OBJECTIVE: Since the beginning of the COVID-19 pandemic, like many countries, the general population in India adopted some traditional methods with the belief and hope that these methods are effective in the prevention of SARS CoV-2 virus infection. The objective of this study was to capture data on such non pharmacological remedies and over the counter drugs used as prophylaxis against the SARS CoV-2 infection by the Indian population.

MATERIALS AND METHODS: An online questionnaire was prepared and distributed using Google form. The questionnaire was shared online via Whatsapp and other social media and the responses from the recipients who were not SARS CoV2 positive or those who had not tested for SARS CoV2 and had been asymptomatic were recorded.

RESULTS: We received responses from 536 participants who did not suffer from COVID19 infection till the time of this survey. Few of the most commonly used home remedies in these people were the following: mask wearing (97.7%), exercising (74.2%), hot tea consumption (55.04%), Vitamin C supplementation (47.38%), gargling (38.6%), zinc supplementation (33.02%), hot lemon drink consumption (31.9%) and vitamin D supplementation (31.79%).

CONCLUSION: In the absence of scientifically proven, directly acting prophylactic drugs, a large number of people are following various common preventive measures many of which may offer some protection from the pandemic as evident from this survey and the review of the literature.

KEYWORDS

non pharmacological remedies over the counter medicines, COVID-19, home remedies

INTRODUCTION:

On 30th January 2020, the World Health Organization (WHO) declared the Coronavirus Disease 2019 (COVID-19) outbreak to be a global public health emergency and on 11th March 2020, COVID-19 was declared a pandemic. Since then various pharmacological and non-pharmacological measures are being tried for prevention of the infection. However, the infection has spread at an epic proportion. As of mid-November 2020, there were about 8.8 million COVID-19 cases in India with more than 40000 positive cases reported every day. By November 2020, India had the largest number of confirmed cases in Asia, and second number of confirmed cases in the world after the United States.(1)

A large number of people however have not shown any signs and symptoms of infection even though they have been in proximity to COVID-19 patients in some ways.(2) Many of these people probably remained asymptomatic and without any residual consequences. Many people have followed various preventive measures and probably some of these may have helped them in this COVID pandemic situation. Through this survey, we attempt to find out the various non-pharmacological remedies and over the counter (OTC) medicines taken by these people which may have helped them in a positive way against the COVID-19 pandemic. The result of the survey should be beneficial to the general population.

METHODS:

The study was conducted after obtaining Institutional Ethics

Committee approval. Using Google form, a standardized online questionnaire was shared via Whatsapp and the responses from the participants who never contracted Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) infection, never showed signs or symptoms or were tested negative for SARS-CoV2 were recorded after taking their online consent for the survey. Participants who were tested positive for SARS-CoV2 were excluded from the analysis. The list of questionnaires, excluding the demography details are given in Table 1.

Table 1: Standardised questionnaire used for the online survey with the options (the participants was expected to mark the most suitable response or write in brief).

Do you have a history of diabetes?	Yes / No
Do you have a history of Hypertension?	Yes / No
Do you have a history of respiratory problems like allergic rhinitis (recurrent cold due to allergy), asthma or COPD (Chronic Obstructive Pulmonary Disease)?	Yes / No
Do you have a history of any other co-morbidities?	Yes / No
Were you tested positive for SARS CoV2?	Yes / No
Was there any case of SARS CoV2 positive in your family?	Yes / No

What are your dietary habits?	Vegetarian Non Vegetarian Both	Do you take any other ayurvedic medicine specifically to prevent COVID-19?	Yes / No
Do you take steam inhalation?	No. I don't take steam inhalation Yes. Once a day Yes. Twice a day Yes. 3 or more times a day	Do you take homeopathic medicine specifically to prevent COVID-19?	Yes / No
Do you practise Gargling?	No. I don't gargle Yes. Once a day Yes. Twice a day Yes. 3 or more times a day	Do you wear a mask regularly?	Yes / No
What do you use for gargling	Nothing, I don't gargle Salt water solution Povidone Iodine Gargle Chlorhexidine solution Others.....	If yes, what type of mask do you wear?	2 plier surgical mask 3 plier surgical mask N95 mask Cloth mask Other.
How many times per week do you exercise?	No. I don't exercise Once or twice a week 3-6 days a week Everyday	Do you avoid going to crowded places?	Yes / No
Exercise duration per session	Less than 30 mins 30 mins to one hour More than one hour	Do you stay at home as much as possible?	Yes / No
Do you consume hot lemon drink specifically to prevent COVID-19?	No Once a day Twice or more per day	Do you drink plenty of water in order to prevent COVID?	Yes / No
Do you consume Indian gooseberry (amla) specifically to prevent COVID-19?	No Yes. Once a day Yes. Twice or more per day	Do avoid touching eyes, nose or mouth to prevent yourself from getting the infection?	Yes / No
Do you consume honey specifically to prevent COVID-19?	Yes / No	Is there any other habit that you follow to prevent COVID-19?	
Do you consume hot tea to prevent COVID-19?	No Once or twice per day Thrice or more per day		
Do you consume Chyavanprash (Ayurveda preparation) to prevent COVID-19?	Yes / No		
Do you take any other remedy to prevent COVID-19?			
Do you take any of the following OTC drugs?			
Probiotics:	Yes / No		
Vitamin C:	Yes / No		
Vitamin D:	Yes / No		
Zinc:	Yes / No		

RESULTS:

587 people participated in the survey. Out of these, 51 participants who were tested positive for SARS-CoV2 had also responded and were excluded from analysis. Of the remaining 536 participants, 294 (54.85%) were males and 242 (45.15%) were females. The mean age of the participants was 34 years. The comorbidities present in the participants were: 56 (10.44%) had hypertension, 33 (6.15%) people had diabetes, 14 (2.61%) had both diabetes and hypertension and 42 (7.38%) had some respiratory conditions (Table 2). Eighty (14.92%) responders replied that at least one person in their family was tested positive for SARS-CoV2.

Table 2: List Of Co-morbidities In The Patients Participating In The Survey

Comorbidities	N (percentage)
Diabetes	33 (6.15%)
Hypertension	56(10.44%)
Diabetes and Hypertension	14(2.61%)
Respiratory Problems	42(7.38%)
Family H/O COVID-19	80(14.92%)
Vegetarian food habit	211(39.36%)
Non Vegetarian food habit	325(60.63%)

Apart from the usual expected measure of avoiding crowd, staying at home, drinking plenty of water, the following are few of the most commonly used home remedies in decreasing order: mask wearing (97.7%), exercising (74.2%), hot tea consumption (55.04%), vitamin C supplementation (47.38%), gargling (38.6%), zinc supplementation (33.02%), hot lemon drink consumption (31.9%), Vitamin D supplementation (31.71%), and others as in Table 3.

Table 3 – Responses regarding the practices and remedies used by the participants

Remedy/ Practice	N (%)	Remedy/ Practice	N (%)
Exercise:		Honey:	
• once or twice a week	141(26.3%)	• Total Yes responses	104(19.5%)
• 3-6 days a week	125(23.32%)	• Total No responses	432(80.5%)
• everyday	132(24.62%)	Chyavanprash:	
• Total yes responses	398(74.2%)	• Total yes responses	78(14.55%)
• Total no responses	138(25.76%)	• Total No responses	458(85.44%)
Hot tea:		Indian Gooseberry (Amla) :	
• once or twice a day	265(49.44%)	• once a day	65(12.12%)
• thrice or more per day	30(5.59%)	• twice or more per day	6(1.11%)
• Total yes responses	295(55.04%)	• Total yes responses	71(13.23%)
• Total no responses	241(44.96%)	• Total no responses	465(86.7%)
Vitamin C:		Homeopathic medicine:	
• Total Yes responses	254(47.38%)	• Total Yes responses	64(11.94%)
• Total no responses	282(52.61%)	• Total no responses	474(88.05%)
Gargling:		Ayurveda medicine:	
• once a day	170(31.71%)	• Total Yes responses	60(11.9%)
• twice a day	26(4.9%)	• Total no responses	476(88.8%)
• thrice or more a day	11(2.5%)	Probiotics:	
• Total yes responses	207(38.6%)	• Total Yes responses	51(9.51%)
• Total no responses	329(63.24%)	• Total no responses	485(90.48%)
Zinc:		Mask:	
• Total Yes responses	177(33.02%)	• Total yes responses	524(97.7%)
• Total no responses	359(66.9%)	• Total No responses	12(2.3%)
Hot lemon drink:		Avoided going to crowded places:	
• once a day	153(28.54%)	• Total yes responses	481(89.74%)
• twice or more per day	18(3.58%)	• Total No responses	55(10.26%)

• Total yes responses	171(31.9%)	Drank plenty of water:	
• Total no responses	365(68.1%)	• Total yes responses	399(74.4%)
Vitamin D:		• Total No responses	137(25.6%)
• Total Yes responses	170(31.72%)	Stayed at home as much as possible:	
• Total no responses	366(68.28%)	• Total yes responses	469(87.5%)
Steam inhalation:		• Total No responses	67(12.5%)
• once a day	112(20.9%)		
• twice a day	15(2.7%)		
• thrice or more per day	3(0.5%)		
• Total yes responses	130(23.3%)		
• Total no responses	406(75.7%)		

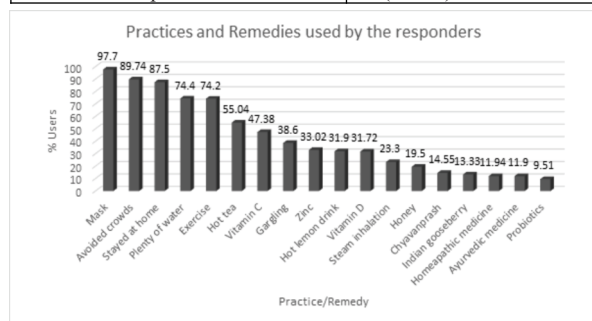


Figure 1: Responses regarding practices and remedies used by the responders

DISCUSSION:

The survey had started in September 2020 and continued till the November 2020. The average age of participants was 34 years which correlated well with the presence of fewer co-morbidities like hypertension and diabetes in the survey population. It is important to note that the incidence of COVID-19 is comparatively higher in the younger population.(3)

The following is the overall review of the non-pharmacological measures followed by the participants.

Exercise: In our survey, 398 (74.2%) people were exercising once or twice a week to everyday. Exercises provide overall health benefits and has been recognized since long with around 5,000 published papers. During each bout of exercise, an enhanced recirculation of immunoglobulins, neutrophils, and natural killer cells occurs that persists for up to 3 hours post exercise.(4) Exercise seems to enhance macrophage phagocytosis and oxidative burst, neutrophil oxidative burst, increase the percentage of TCD4 lymphocytes, and reduce circulating TNF- α and IL-6, followed by an increase in IL-1 β .(5)

It is interesting to note that the probability of people continuing exercise during lockdown and the probability of people freshly starting exercise are both high.(6) Promoting exercises of any type can be an important preventive measure in this pandemic.

Consumption of Hot Tea: 295 (55.04%) participants said that they consume hot tea at least once a day and 30 responders consumed it at least three or more times a day with the intention to prevent COVID-19 infection. Tea is almost the integral part of Indian culture hence it is not surprising that a large number of people use this measure. One of the perceptions in the general population is that drinking hot tea more frequently can clear the throat off the viruses. There are however no direct clinical studies justifying the same.

Tea contains many polyphenols which has several health benefits(7) including having potential antimicrobial effects.(8) Polyphenols exhibit antiviral activities against various viruses, especially RNA viruses. These polyphenols target the Main Protease (Mpro) of SARS-CoV-2, which is a key component of viral replication and a prime target for anti-COVID-19 drug development.(9) One study evaluated eight polyphenols against Mpro using molecular docking and found all these exhibited good binding affinity toward Mpro. Three polyphenols (epigallocatechin gallate, epicatechingallate and gallic acid) interacted strongly with one or both catalytic residues of Mpro of the SARS-CoV-2 and appears to be promising drug candidates for COVID-19 treatment. Another study showed that tannins present in tea, has some antiviral effects.(10) More studies are needed to understand the role of these in SARS-CoV-2 infection.

Regarding the temperature effects, studies on other coronaviruses have reported that infectivity of SARS-CoV was lost after heating at 56°C for 15 minutes.(11) Similar another study showed that the virus viability was rapidly lost at higher temperatures and higher relative humidity (e.g., 380C, and relative humidity of 95%).(12) Further research is needed to evaluate temperature effect of hot beverages like tea on the current SARS-CoV2.

It is however recommended as a general rule that all the remedies should be applied with moderation. In somewhat older articles consumption of hotter tea or coffee (medians 62.0 and 56.0 Celsius temperature) was associated with chronic gastritis.(13) On the other hand, a relatively newer study showed that Green tea, but not black or Oolong tea, was associated with a 37% reduced risk of chronic atrophic gastritis.(14)

Vitamin C (Ascorbic acid): Vitamin C was used by 254 (47.4%) people in our survey. Vitamin C has been historically introduced as an antiviral in 1951(15) with its immunity boosting properties. The recommended daily allowance for Vitamin C is 90 mg for adult men and 75 mg for adult women with an additional daily 35 mg for smokers of either gender.(16) Though indirect, several mechanisms have been implicated in support of its antiviral properties including antioxidant properties, enhanced antibody production, high phagocytic activity, chemotaxis, etc. It is also involved in proliferation and differentiation of B- and T-cells, which play a pivotal role in immune mediated reactions.(15) Recent scientific reports suggest that Vitamin C inhibits the lipopolysaccharide (LPS) induced TNF- α and IL-1 β expression and reduced the malondialdehyde (MDA) levels, increased the Glutathione (GSH) levels and acts as an anti-inflammatory agent.(15) Additionally, Vitamin C inhibits the lung fibrosis by reducing IL-17 secretion and induced superoxide dismutase (SOD) levels.(17) Clinical evidence supported the protective effect of ascorbic acid supplementation in stressful conditions like common cold(15) infection, trauma, surgery and burns, when serum ascorbic acid levels decline rapidly.(18)

However, most of the articles on immune system benefits are older and the recent articles have found that the benefits of Vitamin C are seen only at very high doses. A meta-analysis of six trials showed administration of oral Vitamin C 1-3g/day for 1-5 days significant ($p=0.003$) reduced the length of ICU stay only by 8.6%.(19) Short term administration of Vitamin C is considered to be safe however more studies are needed to evaluate Vitamin C against the current SARS-CoV2.

Gargling: In our study, 270 (38.6%) people practiced gargling (with warm water, cold water, vinegar, etc.) to prevent COVID-19, ranging from once a day to thrice or more per day. Studies have shown that patients infected with SARS-CoV-2 had highest salivary viral load in the oropharyngeal saliva swab sample during the first week, especially on day 4 (20) or starting from the first day of the symptom onset.(21) Hence it is thought that reducing the amount of virus in the body tissue at the initial stage of infection might positively influence the course of disease.

Gargling may physically wash out the viruses and infected cells or cause the chemical inactivation of the virus.(22) A randomized study from Japan showed that gargling with tap water 3 times a day significantly reduced the incidence of upper respiratory tract infection (URTI) by 36%.(23) Another randomized study showed that nasal cavity irrigation and throat gargling with hypertonic saline during 48 hours after symptom onset in patients with URTI significantly reduced viral load, the period of illness by 1.9 days, use of medications by 36% and household contact transmission by 35%.(24) Chloride ions in hypertonic saline have been shown to have direct antiviral effects.(25) More studies are needed to determine the chloride concentration and gargling frequency. Since throat gargling with tap water or saline is

practically free, there hold a lot of economic benefits. Care should be taken by patients with hypertension and kidney disease and ingestion of excessive saline should be avoided. People with abnormal swallowing reflexes should also avoid gargling to prevent unexpected choking and aspiration pneumonia.(26)

Povidone-iodine (PVP-I) is another widely used antiseptic having broad spectrum of antimicrobial activity.(27) PVP-I (0.23%) was shown to rapidly inactivate SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in *in-vitro* studies after a 15-second exposure.(28)

There have been reports of use of vinegar for treatment of URTI. However, there are no structured clinical studies. One *in-vitro* study evaluated the stability of SARS coronavirus against many chemicals including wine vinegar. The study showed $>3 \text{ Log}_{10}$ reduction of virus with 60 seconds of contact.(27)

Zinc supplement was taken by 177 (33.02%) participants. Zinc ions (Zn) are closely involved in the normal development, differentiation and function of immune cells.(29) Zinc deficiency is associated with reduced antibody production, reduced function of the innate immune system, decreased cytokine production by monocytes, and decreased chemotaxis and oxidative burst of neutrophil granulocytes.(30) Multiple antiviral effects of Zn have been demonstrated in a variety of viral species, including several Nidoviruses, to which SARS-CoV-2 belongs.

Other studies showed Zn supplementation may offer preventive as well as adjuvant therapeutic benefit for COVID-19 through modulation of antiviral and antibacterial immunity, reducing inflammation, improvement of mucociliary clearance, prevention of ventilator-induced lung injury, etc.(31, 32) Studies evaluating prophylactic role of lower doses of Zinc were continued for as long as one year indicating continued long term benefits. Apart from the tablets, multiple small doses of zinc lozenges also seem to be beneficial in URTI. Zinc lozenges coats the oral cavity and were helpful in mitigating the duration of rhinovirus infections.(33, 34)

The recommended dietary allowance (RDA) of zinc in Europe is 11mg/day for men and 8mg/day for women and the tolerable upper intake level (UL) is 40mg/day.(35) However, it is stated that in case of adults, 30–50 mg/day for a short duration might be helpful in coronavirus infection.(36)

Lemon Drink: Lemons also contain Vitamin—C, which is an antifibrotic, antioxidant as well as an immunomodulator(37). Lemon essential oils have shown dose dependant reduction of human ACE2 levels and Transmembrane Protease Serine 2 (TMPRSS2) mRNA levels in HT-29 cells.(37) Inhibiting TMPRSS2 significantly blocks SARS-CoV cell entry and can be a potential targets for anti-viral intervention.(37) In our survey, 171(31.9%) participants said that they consumed hot lemon drink once, twice or more per day.

Vitamin D deficiency is seen in about 50–90% in Indian population as per various studies.(38) Apart from its effects on bone, (38) vitamin D also reduces the pro-inflammatory cytokines and increases the anti-inflammatory cytokines. Vitamin D plays a significant role in local “respiratory homeostasis” either by stimulating the antimicrobial peptides or by directly interfering with replication of respiratory viruses.(39)

Several articles have established the connection of Vitamin D deficiency and COVID19 infection.(40) Vitamin D deficiency increases the susceptible to COVID-19's deadly “cytokine storm”, mortality rates and illness severity.(41) One study demonstrated that fatality rate was high in Vitamin D deficient (21% vs 3.1%) patients compared to patients with normal Vitamin D levels.(42)

Vitamin D's Tolerable Upper Intake Level (UL) is 4,000 IU per day, which is more suitable for Vitamin D deficient people. However, the preventive and/or therapeutic dose for Vitamin D in COVID-19 has not been defined. Some health groups recommended taking 800 to 2,000 IU Vitamin D per day.(40) Various weekly, monthly and 6 monthly doses are also defined in the deficient cases. Overall, most of the articles have suggested a loading dose in the deficient people and continued with the daily or weekly doses.

One has to keep in mind that since Vitamin D is easily available, there is possibility of over treatment and adverse reactions with high

Vitamin D levels. Prolonged ingestion of excessive amounts of Vitamin D can lead to hypercalciuria, hypercalcemia, calcification of soft tissues including vascular tissue and its complications, and nephrocalcinosis.(43) Consuming adequate amount of water is important in people taking vitamin D and calcium to prevent the calcium deposition in kidneys.

Steam inhalation is traditionally used as a home remedy for common cold and URTI. Theoretically, steam may help congested mucus to drain better and heat may inactivate the viruses as indicated in an *in-vitro* study.(44) Overall, steam inhalation studies are conflicting or have not proven to be beneficial and on the other hand there have been few reports of scalding injuries especially in the children.(45,44,46-49) Steam inhalation however continues to be used because it provides subjective relief of symptoms in COVID-19. In our survey, the number of people using steam inhalations were:- 112 used it once a day, 15 people used it twice a day, 3 used it thrice or more per day.

Honey was used by 104 (19%) people in our survey. Honey is known for its anti-inflammatory, antioxidants and anti-viral properties.(50, 51) Phenolic acids, flavonoids, sugars, protein, amino acids, carotenes, organic acids and other components are well known for their antioxidant and other properties.(52-54) In an *in-silico* analysis, honey demonstrated ligand binding properties to SARS-CoV-2 proteins.(55) Appropriately designed trials are a need of the hour for translating these evidences in human subjects with COVID-19.

Chyawanprash, an Ayurvedic health supplement, was used by 78 (14.6%) people in this survey. Chyawanprash is formulated by processing around 50 medicinal herbs and their extracts, including the prime ingredient, amla (Indian gooseberry), mixed with honey and herbs (namely clove, cardamom, and cinnamon). Chyawanprash has been a consistent part of Indian tradition for the past 5000 years.(56) A regular intake of Chyawanprash may help to improve overall health and the immunity.(56) Results of an ongoing clinical study on Chyawanprash, in the pandemic of COVID-19 is awaited.

Amla (Indian gooseberry; *Syn emblica officinalis*): 65 participants in our survey consumed it once a day and 6 people consumed the fruit at least twice per day. Amla is a good source of Vitamin C (57) and has been used as home remedies for a long time. As per one study, a teaspoon of Amla juice or powder added to a glass of warm milk and consumed daily thrice a day clears an “unpleasant throat”. Adding some ghee (clarified butter) to this decoction seems to clear the cough as reported in the study.(58) Role of Amla in COVID-19 needs to be evaluated in future studies.

Homeopathic medicines was taken by 64 (11.9%) people in our survey. This percentage appears to be somewhat lesser considering that many organisations had distributed homeopathic medicines (Arsenicum album 30) free of cost with the hope of increasing the innate immunity to a large number of people in the community.(59) However, we could not find clinical evidence through randomized control trials about the efficacy of Arsenicum album 30 in COVID-19 disease.

Ayurvedic medicine was taken by 60 (11.1%) people in our survey with the intention of preventing COVID-19 disease. There appears to be a low usage compared to the large acceptance of Ayurvedic medicines by India. Crude extract or pure compounds isolated from medicinal plants and/or herbs have shown promising inhibitory effect against coronavirus.(60) The *in-silico* study performed on *Tinospora cordifolia* showed that one of its ingredient, berberine can regulate 3CL pro protein function and can control viral replication.(61) Few Ayurvedic medicines like Sadangapaniyam with guduci, Saddharanacurna, Suksmatraphala Kanakasavam, Indukantam Kasayam, are used for respiratory infections.(62)

The AYUSH ministry of India (AYUSH is an acronym for Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy) is formulating ethical national guidelines for integrative management and prevention of COVID 19 for the disease.(63)

Probiotics: Roles of gut microbiota in influencing lung disorders like asthma, chronic obstructive pulmonary disease, chronic bronchitis, emphysema, lung cancer, pneumonia, pleural effusion and viral infection has been established through many studies.(64) It is also recognized that viral infections in the respiratory tract cause a disturbance in the gut microbiota.(65) Moreover, regulation of the immune response by probiotics is also established through relevant

studies.(66) In a recent study, it was reported that the proportion of patients with COVID-19 who suffered from antibiotic-related diarrhea could reach 36%.(67) These studies indicate the urgent need to support the balance of microbiota in patients with COVID-19 using some probiotics.(67,68)

COVID19 infection has been reported with gastrointestinal symptoms. Probiotics may be beneficial in reducing signs and symptoms of these patients with GI symptoms. Moreover patients with SARS-CoV-2 infection have viral RNA or live infectious virus present in faeces which is present for a longer duration even after clearance from the respiratory tract.(69) Whether faecal-oral transmission occurs is not confirmed yet.

Probiotics have an important role in the maintenance of immunologic equilibrium in the gastrointestinal tract through direct interaction with immune cells against many gastro-intestinal diseases.(70, 71, 66) In 2008, a study demonstrated that higher butyrate-producing bacteria in the fecal microbiota is associated with increased resistance against respiratory viral infection.(72)

More so, in early February, The Guidance (version 5) established by the China's National Health Commission and National Administration of Traditional Chinese Medicine recommended that in the treatment of patients with severe COVID-19 infection, probiotics may be used to maintain the balance of intestinal microecology and prevent secondary bacterial infection.(73, 74)

Masks: This part is dealt in the end because expectedly it is the most commonly used preventive methods promoted and enforced by the government authorities. In our survey 524(97.7%) participants used masks of various types.

Various types of masks are available since the beginning of the COVID pandemic. Wearing even a simple cloth mask is far better than not wearing a mask, to safeguard the wearer and the others' health. Surgical face masks and N95 respirators however appear to be the best option, if available, for protecting a healthy person in a high-risk environment.(75)

Cloth masks are cheap, easily available, washable and reusable. The Office of the Principal Scientific Advisor to the Government of India has recently released a manual for home-made cloth masks.(76) The manual gives advice on how to make homemade cloth masks using an old T shirt or cotton vest (the fabric must be 100% cotton). Depending on the thickness of the fabric, two or three layers are appropriate. A meta-analysis showed that wearing a mask protected individuals against influenza-like illness. Maximum protection from catching the infection from others is offered by the N95 mask (99%), whereas the surgical mask offers 75-80% protection and the cloth mask by around 50-70%. A cloth mask is however not recommended for use by any health care worker in a hospital setting.(77) Also one should take care that using any type of mask should not give a false sense of security and other measures of social distancing and hygiene must also be followed. Apart from these there were measures in the survey like avoiding going to crowded places, drinking plenty of water, etc. These are general measures hence we have not evaluated these in details.

In conclusion, even though a large number of drugs are under investigation and newer drugs are receiving approval, there is a need for establishing preventive measures. It is to be considered that since the beginning of the COVID pandemic, only lockdown, social distancing, hand hygiene and sanitization have been promoted as preventive measures. There are still a large number of measures which can be followed as seen in the above survey, many of which may offer some protection from the current pandemic.

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REFERENCES:

- WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. [cited 2021 Jan 6]. Available from: <https://covid19.who.int/table>
- Zhang J, Tian S, Lou J, Chen Y. Familial cluster of COVID-19 infection from an asymptomatic. *Crit Care*. 2020 Mar 27;24(1):119
- Boehmer TK, DeVies J, Caruso E, van Santen KL, Tang S, Black CL, Hartnett KP, Kite-Powell A, Dietz S, Lozier M, Gundlapalli AV. Changing Age Distribution of the COVID-19 Pandemic - United States, May-August 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Oct 2;69(39):1404-1409
- Niemann DC. Moderate Exercise Improves Immunity and Decreases Illness Rates. *American Journal of Lifestyle Medicine*. 2011;5(4):338-345.
- Leandro CG, Ferreira E Silva WT, Lima-Silva AE. Covid-19 and Exercise-Induced Immunomodulation. *Neuroimmunomodulation*. 2020;27(1):75-78
- Brand R, Timme S, Nosrat S. When Pandemic Hits: Exercise Frequency and Subjective Well-Being During COVID-19 Pandemic. *Front Psychol*. 2020 Sep 24;11:570567
- Ghosh R, Chakraborty A, Biswas A, Chowdhuri S. Evaluation of green tea polyphenols as novel corona virus (SARS CoV-2) main protease (Mpro) inhibitors - an *in silico* docking and molecular dynamics simulation study. *J Biomol Struct Dyn*. 2020 Jun 22:1-13
- Bansal S, Choudhary S, Sharma M, Kumar SS, Lohan S, Bhardwaj V, et al. Tea: A native source of antimicrobial agents. Vol. 53, Food Research International. 2013. p. 568-84.
- Mhatre S, Srivastava T, Naik S, Patravale V. Antiviral activity of green tea and black tea polyphenols in prophylaxis and treatment of COVID-19: A review. *Phytomedicine*. 2020 Jul 17:153286
- Chung KT, Wong TY, Wei CI, Huang YW, Lin Y. Tannins and human health: a review. *Crit Rev Food Sci Nutr*. 1998 Aug;38(6):421-64
- Lai MY, Cheng PK, Lim WW. Survival of severe acute respiratory syndrome coronavirus. *Clin Infect Dis*. 2005 Oct 1;41(7):e67-71
- Chan KH, Peiris JS, Lam SY, Poon LL, Yuen KY, Seto WH. The Effects of Temperature and Relative Humidity on the Viability of the SARS Coronavirus. *Adv Virol*. 2011;2011:734690
- Pearson RC, McCloy RF. Preference for hot drinks is associated with peptic disease. *Gut*. 1989 Sep;30(9):1201-5
- Shibata K, Moriyama M, Fukushima T, Kaetsu A, Miyazaki M, Une H. Green tea consumption and chronic atrophic gastritis: a cross-sectional study in a green tea production village. *J Epidemiol*. 2000 Sep;10(5):310-6
- Leibovitz B, Siegel BV. Ascorbic acid and the immune response. *Adv Exp Med Biol*. 1981;135:1-25
- Simonson W. Vitamin C and coronavirus. *Geriatr Nurs*. 2020 May-Jun;41(3):331-332
- Zhang XY, Xu ZP, Wang W, Cao JB, Fu Q, Zhao WX, et al. Vitamin C alleviates LPS-induced cognitive impairment in mice by suppressing neuroinflammation and oxidative stress. *Int Immunopharmacol*. 2018 Dec;65:438-447
- Hunt C, Chakravorty NK, Annan G, Habibzadeh N, Schorah CJ. The clinical effects of vitamin C supplementation in elderly hospitalised patients with acute respiratory infections. *Int J Vitam Nutr Res*. 1994;64(3):212-9
- Hemilä H, Chalker E. Vitamin C Can Shorten the Length of Stay in the ICU: A Meta-Analysis. *Nutrients*. 2019 Mar 27;11(4):708
- To KK, Tsang OT, Leung WS, Tam AR, Wu TC, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis*. 2020 May;20(5):565-574
- Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020 May;581(7809):465-469
- Liu Y, Liao W, Wan L, Xiang T, Zhang W. Correlation Between Relative Nasopharyngeal Virus RNA Load and Lymphocyte Count Disease Severity in Patients with COVID-19. *Viral Immunol*. 2020 Apr 10
- Satomura K, Kitamura T, Kawamura T, Shimbo T, Watanabe M, Kamei M, Takano Y, Tamakoshi A; Great Cold Investigators-I. Prevention of upper respiratory tract infections by gargling: a randomized trial. *Am J Prev Med*. 2005 Nov;29(4):302-7
- Ramalingam S, Graham C, Dove J, Morrice L, Sheikh A. A pilot, open labelled, randomised controlled trial of hypertonic saline nasal irrigation and gargling for the common cold. *Sci Rep*. 2019 Jan 31;9(1):1015
- Tsai CL, Wu PC. Possible beneficial role of throat gargling in the coronavirus disease pandemic. *Public Health*. 2020 Aug;185:45-46
- Anderson DE, Sivalingam V, Kang AEZ, Ananthanarayanan A, Arumugam H, Jenkins TM, et al. Povidone-Iodine Demonstrates Rapid In Vitro Virucidal Activity Against SARS-CoV-2, The Virus Causing COVID-19 Disease. *Infect Dis Ther*. 2020 Sep; 9(3): 669-675
- Rabenau HF, Cinatl J, Morgenstern B, Bauer G, Preiser W, Doerr HW. Stability and inactivation of SARS coronavirus. *Med Microbiol Immunol*. 2005 Jan;194(1-2):1-6
- Blasi C. Iodine mouthwashes as deterrents against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Infect Control Hosp Epidemiol*. 2020 Dec 7;1-2
- Overbeck S, Rink L, Haase H. Modulating the immune response by oral zinc supplementation: a single approach for multiple diseases. *Arch Immunol Ther Exp (Warsz)*. 2008 Jan-Feb;56(1):15-30
- Ibs KH, Rink L. Zinc-altered immune function. *J Nutr*. 2003 May;133(5 Suppl 1):1452S-6S.
- Skalny AV, Rink L, Ajsuvakova OP, Aschner M, Gritsenko VA, Alekseenko SI, et al. Zinc and respiratory tract infections: Perspectives for COVID-19 (Review). *Int J Mol Med*. 2020 Jul;46(1):17-26
- Wessels I, Rolles B, Rink L. The Potential Impact of Zinc Supplementation on COVID-19 Pathogenesis. *Front Immunol*. 2020 Jul 10;11:712
- Mossad SB, Macknin ML, Medendorp SV, Mason P. Zinc gluconate lozenges for treating the common cold. A randomized, double-blind, placebo-controlled study. *Ann Intern Med*. 1996 Jul 15;125(2):81-8
- Hemilä H. Zinc lozenges may shorten the duration of colds: a systematic review. *Open Respir Med J*. 2011;5:51-8
- Maggini S, Pierre A, Calder PC. Immune Function and Micronutrient Requirements Change over the Life Course. *Nutrients*. 2018 Oct 17;10(10):1531
- McCarty MF, DiNicolantonio JJ. Nutraceuticals have potential for boosting the type 1 interferon response to RNA viruses including influenza and coronavirus. *Prog Cardiovasc Dis*. 2020 May-Jun;63(3):383-385
- Thota SM, Balan V, Sivaramakrishnan V. Natural products as home-based prophylactic and symptom management agents in the setting of COVID-19. *Phytother Res*. 2020 Dec;34(12):3148-3167
- Beard JA, Bearden A, Striker R. Vitamin D and the anti-viral state. *J Clin Virol*. 2011 Mar;50(3):194-200
- Zdrenghea MT, Makrinioti H, Bagacean C, Bush A, Johnston SL, Stanciu LA. Vitamin D modulation of innate immune responses to respiratory viral infections. *Rev Med Virol*. 2017 Jan;27(1)
- Grant WB, Lahore H, McDonnell SL, Baggerly CA, French CB, Aliano JL, et al. Evidence that Vitamin D Supplementation Could Reduce Risk of Influenza and COVID-19 Infections and Deaths. *Nutrients*. 2020 Apr 2;12(4):988
- Benskin LL. A Basic Review of the Preliminary Evidence That COVID-19 Risk and Severity Is Increased in Vitamin D Deficiency. *Front Public Health*. 2020 Sep 10;8:513
- Jain A, Chaurasia R, Sengar NS, Singh M, Mahor S, Narain S. Analysis of vitamin D level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers. *Sci Rep*. 2020 Nov 19;10(1):20191
- de Paula FJ, Rosen CJ. Vitamin D safety and requirements. *Arch Biochem Biophys*. 2012 Jul 1;523(1):64-72
- Singh M, Singh M, Jaiswal N, Chauhan A. Heated, humidified air for the common cold. *Cochrane Database Syst Rev*. 2017 Aug 29;8(8):CD001728
- Forstall GJ, Macknin ML, Yen-Lieberman BR, Medendorp SV. Effect of inhaling heated vapor on symptoms of the common cold. *JAMA*. 1994 Apr 13;271(14):1109-11
- Wallis BA, Turner J, Pearn J, Kimble RM. Scalds as a result of vapour inhalation therapy in children. *Burns*. 2008 Jun;34(4):560-4.
- Mathew JL. Steam inhalation in respiratory illnesses--full steam ahead or full stop? A systematic review of randomized controlled trial. *Indian Pediatr*. 2010

- Dec;47(12):1047-50.
48. Sanyaolu L, Javed MU, Eales M, Hemington-Gorse S. A 10 year epidemiological study of paediatric burns at the Welsh Centre for burns and plastic surgery. *Burns*. 2017 May;43(3):632-637
 49. Belmonte JA, Domínguez-Sampedro P, Pérez E, Suelves JM, Collado JM. Quemaduras graves relacionadas con la terapia inhalatoria con vahos [Severe burns related to steam inhalation therapy]. *An Pediatr (Barc)*. 2015 Feb;82(2):95-9. Spanish
 50. Shahzad A, Cohrs RJ. In vitro antiviral activity of honey against varicella zoster virus (VZV): A translational medicine study for potential remedy for shingles. *Transl Biomed*. 2012;3(2):2.
 51. Watanabe K, Rahmasari R, Matsunaga A, Haruyama T, Kobayashi N. Anti-influenza viral effects of honey in vitro: potent high activity of manuka honey. *Arch Med Res*. 2014 Jul;45(5):359-65
 52. Al-Mamary M, Al-Meerri A, Al-Habori M. Antioxidant activities and total phenolics of different types of honey. *Nutr Res*. 2002 Sep;22(9):1041-7.
 53. Nagai T, Sakai M, Inoue R, Inoue H, Suzuki N. Antioxidative activities of some commercially honeys, royal jelly, and propolis. *Food Chem*. 2001;75(2):237-40.
 54. Aljadi AM, Kamaruddin MY. Evaluation of the phenolic contents and antioxidant capacities of two Malaysian floral honeys. *Food Chem*. 2004 May 1;85(4):513-8.
 55. Hashem, H. IN Silico Approach of Some Selected Honey Constituents as SARS-CoV-2 Main Protease (COVID-19) Inhibitors. *ChemRxiv*. 2020. Available online: https://chemrxiv.org/articles/preprint/IN_Silico_Approach_of_Some_Selected_Honey_Constituents_as_SARS-CoV-2_Main_Protease_COVID-19_Inhibitors/12115359/2 (accessed on 18 October 2020)
 56. Gurmule R K. Role of Chyavanprashas a Rasayana in combating an outbreak of COVID-19. *International Journal of Research in Pharmaceutical Sciences*. (2020);11(SPL1):165-170. <https://doi.org/10.26452/ijrps.v11iSPL1.2343>
 57. Variya BC, Bakrania AK, Patel SS. *Emblca officinalis* (Amla): A review for its phytochemistry, ethnomedicinal uses and medicinal potentials with respect to molecular mechanisms. *Pharmacol Res*. 2016 Sep;111:180-200
 58. Dasaroju S, Gottumukkala KM. Current trends in the research of *Emblca officinalis* (Amla): A pharmacological perspective. *Int J Pharm Sci Rev Res* 2014;24:150-9
 59. Talwar S, Sood S, Kumar J, Chauhan R, Sharma M, Tuli HS. *Ayurveda and Allopathic Therapeutic Strategies in Coronavirus Pandemic Treatment 2020*. *Curr Pharmacol Rep*. 2020 Oct 22:1-10
 60. Shree P, Mishra P, Selvaraj C, Singh SK, Chaube R, Garg N, *et al*. Targeting COVID-19 (SARS-CoV-2) main protease through active phytochemicals of ayurvedic medicinal plants - *Withania somnifera* (Ashwagandha), *Tinospora cordifolia* (Giloy) and *Ocimum sanctum* (Tulsi) - a molecular docking study. *J Biomol Struct Dyn*. 2020 Aug 27:1-14
 61. Chowdhury P. In silico investigation of phytoconstituents from Indian medicinal herb '*Tinospora cordifolia* (giloy)' against SARS-CoV-2 (COVID-19) by molecular dynamics approach. *J Biomol Struct Dyn*. 2020 Aug 7:1-18.
 62. Girija PLT, Sivan N. Ayurvedic treatment of COVID-19/SARS-CoV-2: A case report. *J Ayurveda Integr Med*. 2020 Jun 19:S0975-9476(20)30042-5
 63. Priya R, Sujatha V. AYUSH for COVID-19: Science or Superstition? *Indian J Public Health*. 2020 Jun;64(Supplement):S105-S107.
 64. Han MK, McLaughlin VV, Criner GJ, Martinez FJ. Pulmonary diseases and the heart. *Circulation*. 2007 Dec 18;116(25):2992-3005
 65. Dhar D, Mohanty A. Gut microbiota and Covid-19- possible link and implications. *Virus Res*. 2020 Aug;285:198018
 66. Yan F, Polk DB. Probiotics and immune health. *Curr Opin Gastroenterol*. 2011 Oct;27(6):496-501
 67. Mak JWY, Chan FKL, Ng SC. Probiotics and COVID-19: one size does not fit all. *Lancet Gastroenterol Hepatol*. 2020 Jul;5(7):644-645.
 68. Xu K, Cai H, Shen Y, Ni Q, Chen Y, Hu S, *et al*. [Management of COVID-19: the Zhejiang experience]. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2020 May 25;49(2):147-157. Chinese
 69. Hindson J. COVID-19: faecal-oral transmission? *Nat Rev Gastroenterol Hepatol*. 2020 May;17(5):259
 70. Ricci A, Tagliacarne SC, Valsecchi C, Boggini T, Cattaneo F, Licari A, *et al*. Probiotics and inflammatory bowel diseases. *J Biol Regul Homeost Agents*. 2015 Apr-Jun;29(2 Suppl 1):96-113
 71. Underwood MA. Probiotics and Innate and Adaptive Immune Responses in Premature Infants. *For Immunopathol Dis Therap*. 2016;7(1-2):1-15
 72. Haak BW, Littmann ER, Chaubard JL, Pickard AJ, Fontana E, Adhi F, *et al*. Impact of gut colonization with butyrate-producing microbiota on respiratory viral infection following allo-HCT. *Blood*. 2018 Jun 28;131(26):2978-2986
 73. Gao QY, Chen YX, Fang JY. 2019 Novel coronavirus infection and gastrointestinal tract. *J Dig Dis*. 2020 Mar;21(3):125-126
 74. Sniffen JC, McFarland LV, Evans CT, Goldstein EJC. Choosing an appropriate probiotic product for your patient: An evidence-based practical guide. *PLoS One*. 2018 Dec 26;13(12):e0209205
 75. Chua MH, Cheng W, Goh SS, Kong J, Li B, Lim JYC, *et al*. Face Masks in the New COVID-19 Normal: Materials, Testing, and Perspectives. *Research (Wash D C)*. 2020 Aug 7;2020:7286735
 76. Yan J, Guha S, Hariharan P, Myers M. Modeling the Effectiveness of Respiratory Protective Devices in Reducing Influenza Outbreak. *Risk Anal*. 2019 Mar;39(3):647-661
 77. Salvi SS. In this pandemic and panic of COVID-19 what should doctors know about masks and respirators? [Internet]. [cited 2021 Jan 6]. Available from: <https://apiindia.org/wp-content/uploads/pdf/corona-virus/review-article-on-mask.pdf>