



## Review Article

## An Ayurvedic personalized prophylactic protocol in COVID-19

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## ABSTRACT

The current COVID-19 pandemic brought about by the SARS-CoV-2, a novel  $\beta$  coronavirus is creating intense health havoc globally. Researchers suspect the situation to stay for long in the community, considering this virus's pathogenesis, high rate transmission and tendency to provoke uncontrolled immune response activation. Immune mechanisms are highly individualistic. We put forward a hypothetical model of *prakruti* (Ayurvedic body phenotyping character) based personalized prophylactic-therapeutic strategies aiming at a better immunomodulation and quicker resolution of host immune mechanisms. We propose this model in symptomatic, mild to moderate, COVID-19 diagnosed cases and in cases quarantined for high to low risk primary contact with a positive case. We also suggest a community level personalized Ayurvedic prophylactic-therapeutic strategy based on the DOTS model.

Person-centered body purificatory measures (*panchakarma* procedures) like therapeutic purgation (*virechana*) and medicated enema (*basti*) are suggested in this hypothetical protocol with justification on evidence-based links between immune responses and *prakruti* along with specific *jwara* (fevers of varied origin as per Ayurvedic sciences) and COVID-19 symptomatology. The paper also appraises the importance of *pitta dosha/ama dosha* in the manifestation of inflammation driven destructive phase of immune responses along with its stage-wise intervention. This hypothetical model intends to open up discussions on significance of *prakruti* assessment as a predictive marker to screen people who are at risk of succumbing into deteriorating states if infected with COVID-19. It also intends to discuss the predictive personalized medicine measures based on *prakruti* in yielding individual host immune homeostasis which may positively reduce the chances of untoward events of an aggravated immune responsiveness and subsequent inflammation driven tissue destruction – the candidate causes for COVID-19 related casualties. Testing this model may give insight towards emphasizing personalized host immune coping mechanisms that may prove crucial in any infectious outbreaks in near future too.

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## 1. Background

Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), a novel  $\beta$  corona virus (CoVs) which is responsible for the pandemic pneumonia of 2020 is continuing its wrath worldwide [1]. The family of CoVs lately, have been the pathogens of emerging respiratory disease outbreaks in humans [2]. Scientists from various global health research organizations are desperately putting efforts into research on SARS-CoV-2 pathogenic mechanisms for developing prophylactic-therapeutic measures that would contain the

transmission of this highly contagious virus and effectively reduce the number of casualties. Also, the pathological mechanism that is leading to severe stages of pneumonia is under scrutiny.

The symptoms and mortality associated with COVID-19 outbreak is supposed to be because of derangement in host immune homeostasis [3]. Further, it is assessed that asymptomatic cases of COVID-19 account for pervasive transmission of the virus globally [4]. In summary, replication, widespread transmission and threatening the host immune homeostasis is the evident mode of attack of this virus. As vaccine development process is experiencing an undue delay in this pandemic scenario; creating an effective host response in the form of eliminating pathological microbes, avoiding untoward responses which produce excessive tissue damage and creating a pro-environment to establish tissue homeostasis is the key to sustain now, or as a matter of fact while

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any such highly contagious microbial attack in near future. Thus, pre-post exposure prophylactic strategies that aim at improving host response mechanisms are decisive to contain the mortality rates associated with such pandemics [4].

Immune homeostasis is distinctive or individualistic [5]. Factors such as genes, gender, nutrient status, age, gut flora, dietary habits, physical activity, alcoholism and other substance abuse, pregnancy etc. highly determine the cross-sectional immune status of individuals. Hence, personalized medicine is the key for achieving better host homeostasis in pan immune system ailments afflicting humans, infectious or otherwise. Now, if we can predict the extent of insult that could possibly happen in an infected case and then adopt personalized prophylactic treatment measures, it would be phenomenal.

We present a hypothetical model which emphasizes that predictive immune responsiveness based on Ayurvedic concept of fundamental bodily constitution, namely the 'prakruti'; and subsequent personalized prophylactic-therapeutic measures in diagnosed cases of COVID-19 and in cases quarantined for high to low risk primary contact with a COVID-19 case may generate promising evidence conversely to general administration of immunomodulators (*Vimanasthana*) [6]. Our hypothesis is based on the fact that the initial host response, adaptive immune mechanisms, immune homeostatic physiology and other arms of immune phenotyping are significantly derived and influenced by *prakruti* of individuals [7,8]. Also, the influential model of healthcare practice termed as '*dasa vidha pareeksha*' revealed by *Charaka* wherein *prakruti*, pathological examination (*vikruti*; with regards to causative factors, *dosha* status, *prakruti*, seasonal, geographical factors and immune factors), tissue related homeostasis (*saara*), physique (*samhanana*), psychological state (*satva*), acclimatization to environmental variations (*satmya*), metabolic wellness (*ahara shakti*) physical endurance (*vyayama shakti*) and age (*vaya*) are critically analyzed to achieve the predictive personalized therapeutic efficacy; stands as a significant background to our hypothesis [6]. This hypothetical model intends to discuss the significance of *prakruti* assessment in screening/predicting those who may fall into deteriorating states if afflicted with COVID-19 infection. Also, we discuss the predictive and planned process of yielding individual host immune homeostasis through *prakruti*-based personalized therapies which may have the potential of reducing chances of untoward events of an aggravated immune responsiveness and subsequent inflammation driven tissue destruction which are candidate causes for COVID-19 related casualties.

## 2. Ayurveda and predictive medicine in COVID-19 symptomatology

### 2.1. COVID-19 symptomatology and *jwara* principle

*Jwara* (fevers of varied origin) is detailed in *chikitsa sthana*, *nidana sthana* and *uttara sthana* of *Brihatrayee* (*Charaka Samhita*, *Susruta Samhita* and *Ashtanga Hrudaya*) and in subsequent textbooks of Ayurveda. Seeing the amplitude of classification of *jwara* symptoms into different subsets, and its positioning in the initial pages of therapeutics in relevant classic *Ayurvedic* literatures, it is inferred that the disease manifestation and progression into deteriorating states termed as *sannipata avastha* in *jwara* may be implied to different disorders explained subsequently to *jwara* as well. Understanding *jwara* symptomatology is important in assessing any disease progression and severity with respect to clinical and biochemical host responses.

### 2.2. Sickness behaviour and *jwara poorvarupa* principle

Sickness behaviour with respect to behavioural immune system refers to behavioral, cognitive and emotional symptoms that go along with infection, such as fatigue, loss of appetite and social interest. This is believed to eventually reduce the direct and indirect contact between an infected host and his nearest relations. There is also an emotional reaction termed as 'disgust' towards peculiar sights and smells, body secretions etc. These changing behaviours represent an early anti-pathogenic defense system [9].

These sickness features of behavioural immune responses are detailed as prodromal phase (*jwara poorvarupa* state) in Ayurveda. *Jwara poorvarupa* state diagnosis is clinically important clinically. Prophylactic-therapeutic measures are advocated from the *poorvarupa* state in *jwara* (eg. internal administration of medicated ghee (*snehapana*) in *vatika jwara poorvarupa*, therapeutic purgation (*virechana*) in *pittaja jwara poorvarupa*) and administering such measures in this phase may positively decelerate the disease progression and initiate an early tissue homeostasis. Table 1 represents the *jwara poorvarupa* symptoms and its comparison with COVID-19 symptoms [10–12]. Whether this sickness behaviour can be systematically measured in COVID-19 positive cases or in cases quarantined for an evident primary contact with a positive case in their respective incubation periods, is debatable. But if it's achieved, this shall be the appropriate phase to initiate prophylaxis or treatment. The *poorvarupa* stage diagnosis needs a detailed history taking along with emotional, cognitive and behavioural analysis.

### 2.3. Differential understanding of specific types of *jwara* w.r.t COVID-19 symptoms

Fig. 1 represents COVID-19 disease progression in an Ayurvedic parlance. Tables 2–4 correspond to the comparison of specific *jwara* subsets mentioned in Fig. 1 with COVID-19 symptoms [10–15]. Thus, while analyzing different subsets of *jwara* based on site of manifestation, symptoms and severity, COVID-19 or as a matter of fact any infectious fever emerging as a respiratory illness reflects features of *Kaphaja jwara/Vatakaphaja jwara* or *Pralepaka* (Table 2); *Vishama jwara* (*Anyedyu/Anyedyu vipryaya/Chaturthaka/Chaturthaka viparyaya/Triteeyaka*), *Asthi majja gata jwara* (Table 3); and *Sama Sannipata jwara* (Table 4) [6, 16,17]. Fig. 1 explains how the differentiation of *jwara* into different subsets is individualistic, which is influenced by one's *prakruti*, *agni* (primary metabolism and cellular energy transfer) and *sara* (internal tissue homeostasis).

*Vishama jwara* refers to a chronic existence of morbid factors in the body post inappropriate management of any type of *jwara*, leading to derangement in tissue homeostasis (*dhathu pra-dooshana*) [17]. External causative agents like microbes (*Bhutabhishanga*) almost and always may result in *vishama jwara* or *sannipata jwara* where there is insidious provocation of three pathophysiological entities that govern major physiological activities in the human body (*doshas*) namely *vata*, *pitta* and *kapha*, all at once [17, 18]. This precisely impairs primary gut metabolism and manifests as *jwara*. The site of manifestation of symptoms gives clue into diagnosis of *vishama jwara* subsets. For eg, if there is arthralgia (*doshas* at joints) it is *Pralepaka* variety of *jwara* manifestation and if respiratory symptoms primarily manifest (*doshas* at chest region) it is *Anyedyu*. If there is a combination of respiratory and digestive complaints (*doshas* at chest region and upper GIT), it is diagnosed as *Anyedyu-viparyaya*. Differential understanding is important as the internal medication varies accordingly. *Vangasena* explained *Abhinyasa jwara*, where he mentioned it as *sannipata jwara* stage in which a slimy, threadlike

**Table 1**  
Poorvarupa in Jwara Vs COVID-19 symptomatology.

Poorvarupa symptoms	COVID-19 symptoms
<i>Srama (clinical correlation) – fatigue</i>	✓
<i>Arati – malaise</i>	✓
<i>Vivarnatvam– discolouration or various cutaneous changes</i>	✓
<i>Vairasya– bad taste or loss of taste</i>	✓
<i>Nayanaplava – watering of the eyes or epiphora</i>	✓
<i>Ichchadeshoumuhuhu – rapidly changing likings or rapid mood swings</i>	✓
<i>Jrumbha (vata) – yawning (due to fatigue)</i>	✓
<i>Angamarda – bodyache (myalgia or arthralgia)</i>	✓
<i>Guruta – feeling of heaviness</i>	–
<i>Romaharsha – horripilation</i>	–
<i>Aruchi - anorexia</i>	✓
<i>Tamapravesha – appearance of darkness in front of the eyes (due to excessive drowsiness?)</i>	✓
<i>Apraharsha – hypoactive sexual desire</i>	–
<i>Seeta – chills</i>	✓
<i>Anannabhinandana (Kapha) – aversion of food (included in anorexia)</i>	✓
<i>Nayanayordaaha (Pitta) – burning sensation in eyes (due to conjunctivitis)</i>	✓
<i>Alasya – laziness (due to fatigue)</i>	✓
<i>Garagourava– feeling of heaviness in body parts</i>	–
<i>Hitopadeshaakshanti – aversion to good advices (sickness behaviour/depressive mood?)</i>	–
<i>Baladwesa – irritability (sickness behaviour/due to rapid mood swings/depressive mood?)</i>	✓
<i>Vinamana– adopting a sickness posture, head down</i>	–
<i>Pindikodweshatana – calf pain or localized myalgia</i>	✓
<i>Klama – tiredness (due to fatigue)</i>	✓

sputum secretion and obstruction in upper respiratory tract was a clinical manifestation [16]. *Susruta* mentioned *ojonirodhaja jwara*, a severe stage in *sannipata jwara manifestation*, where there is deterioration of internal homeostasis and tissue physiology (*ojo visramsas*) [17]. *Swasanaka jwara* is a cluster of symptoms explained by *Bhavaprakasha* wherein *sannipata jwara* leads to morbid respiratory illness and distress.

Fig. 1 hypothesizes the differential manifestation of aforesaid *jwara* in individuals with different *prakrutis*. A final diagnosis of the diseased state is highly dependent on *doshik* constitution and subsequent symptomatology, general health status, digestive capacity etc. This differential understanding and specificity is important in personalized prophylactic-therapeutic advocacies.

### 3. Immune mechanism and prakruti

Disease susceptibility, and selection of prophylactic and therapeutic measures as per Ayurveda significantly depends upon, *prakruti*. Notably, immune mechanisms (*bala*) are determined by *prakruti* of individuals [6,17,]

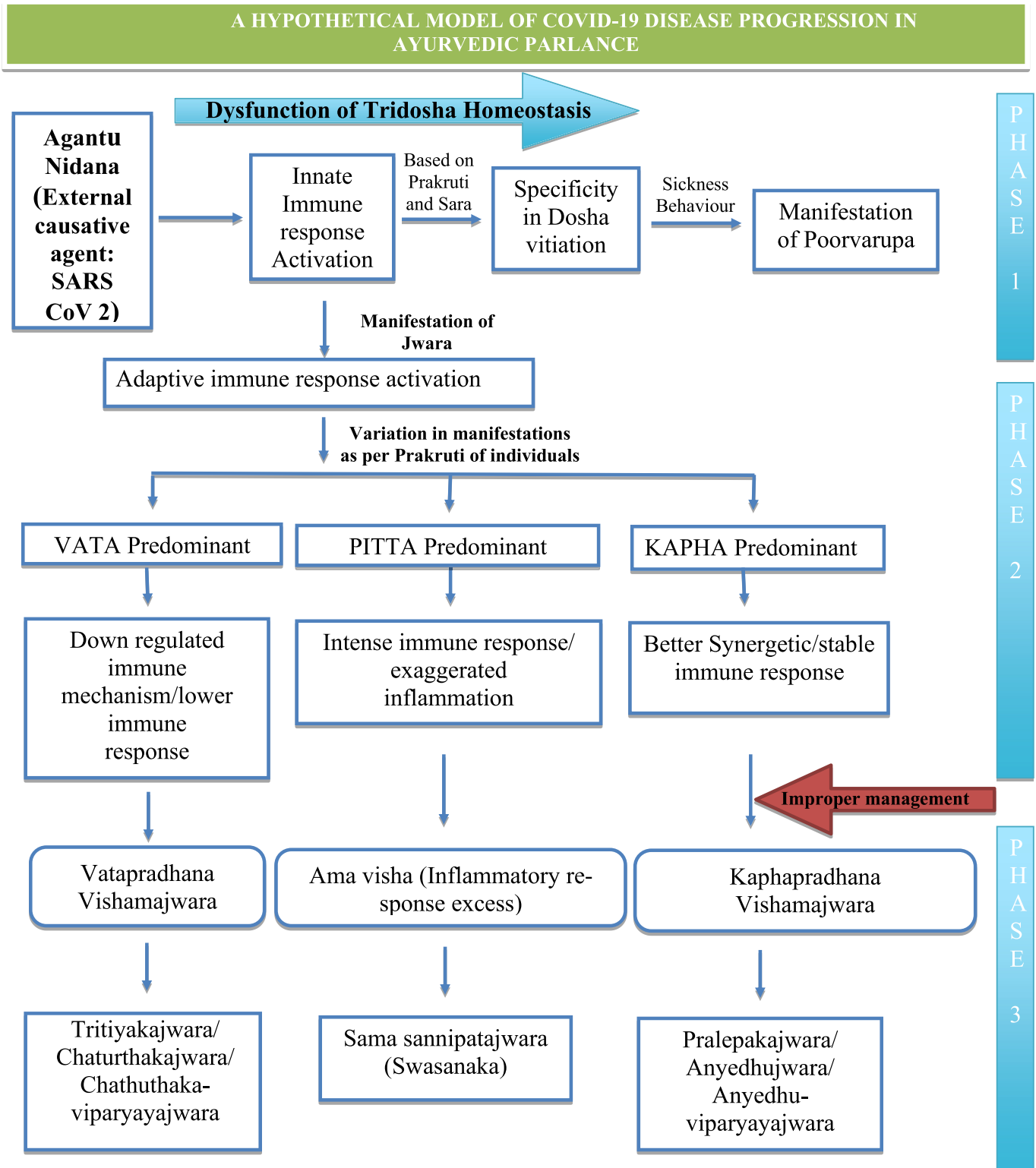
Congruent with this statement, an immunophenotyping study based on CD marker expression (CD14, CD25 and CD56) on different human *dosha prakrutis* concluded that *pitta* predominant *prakruti* individuals exhibited elevated innate immune responses and were hypersensitive. *Kapha* predominant *prakruti* individuals had higher expression of CD25 and CD56 exhibiting stable immune responses. Compared to *kapha prakruti*, *vata* predominant *prakruti* individuals showed compromised/low potential immune responses [7]. Further, another study on genome expression and biochemical correlates of *prakruti* stated that *vata prakruti* individuals exhibited a distinct down regulation of genes involved in response to biotic stimulus and inflammatory response [8]. Also, the cholinergic anti-inflammatory pathway, a function of efferent vagus nerve plays a significant role in controlling systemic and local inflammation paving way to neuronal immunomodulation [19]. A discussion paper, while identifying neurological systems that represent *vata dosha*, formulated hypotheses on links between *vata dosha* and vagus nerve [20]. These leads suggest that *vata dosha* dysfunction or an exaggerated *vata dosha* physiology, as in *vata* predominant *prakruti* may hamper immunomodulation.

Conversely, *pitta* predominant *prakruti* individuals demonstrated over-expression of genes related to immune response based on more pathogen recognition receptors, more inflammation and hypersensitivity. *Kapha prakruti* individuals presented with an overall up-regulation of genes involved in cellular bio-synthesis and purine salvage pathway. B and T cell receptor signaling pathways (for adaptive arm of immune mechanism) [21] were found enriched in over-expressed genes of *kapha prakruti* predominant males. Thus, comparatively, a better synergy between innate and adaptive immunity and better adaptive host immune response is exhibited by *kapha prakruti* predominant individuals whereas intense immune response symptoms that at times result in an exaggerated inflammation driven destructive phase may be substantiated in *pitta* predominant *prakruti* individuals. Fig. 1 represents the basic differences in immune responses with respect to different *prakrutis*.

### 4. Concept of pitta dosha, ama and inflammation driven damaging phase of immune response

*Pitta dosha*, one among the three *doshas* is causally linked with inflammation and immune mechanism [17]. Notably, *pitta dosha* is responsible for digestion, metabolism, thermoregulation and energy homeostasis and is causally associated with *jwara* as well [16]. *Pitta dosha* manifests as *agni*. The concept of *agni* is appropriately translated in a study as the primary entity responsible for metabolic and transformative processes at physiological and cellular levels [22]. *Ama* or *ama dosha* refers to substance formed as a result of improper metabolism at varied physiological levels and hence, it is non-homogenous to the bodily tissues [6].

*Ama dosha* is at times referred to as *ama visha* or a toxic substance which is capable of tissue damage [6]. *Ama* also serves as a candidate causative agent for *jwara*. It is therefore not surprising if it is inferred that recognition of *ama* by host cells may be as a ‘non-self’ which triggers host immune responses. Elaborating this statement, *ama* thus may also be inferred as an excess accumulation of endotoxins and other inflammatory mediators. *Pitta dosha* predominant *prakruti* refers to an increased physiological activation of *pitta dosha* compared to *vata* and *kapha* at varied levels. Accordingly and from evidence generated from above cited studies



**Fig. 1.** Legend: Schematic diagram representing COVID-19 disease progression in Ayurvedic parlance. Antigen invasion (*agantu nidana*), is causally linked with dysfunction of host *dosha* homeostasis that fundamentally affects primary metabolism (*agni*), manipulates thermoregulation (*swedavaha srotorodha*) and induces *poorvarupa* (sickness behaviour). *Poorvarupa* symptoms cluster is a candidate factor to assess the dysfunctional *dosha* constitution. If not appropriately intervened, *poorvarupa* state advances to *Jwara*. The type and severity of *jwara* manifested is significantly dependent on *prakruti* and *saara* (endurance and tissue homeostasis).

**Table 2**  
Vatakaphajjwara/Kaphajjwara Vs COVID-19 symptomatology\*.

Kaphaja/Vatakaphaja jwara symptoms	COVID-19 symptoms
Tapahani- Low grade fever (mild and moderate cases) <sup>4</sup>	✓
Aruchi- anorexia	✓
Parvashiroruk – arthralgia <sup>5</sup> & headache	✓
Peenasa – rhinorrhoea	✓
Swasana – dyspnea	✓
Kasa – cough	✓
Vibandha – constipation	–
Seeta– chills	✓
Jadya – stiffness	✓
Timira - appearance of darkness in front of the eyes (due to excessive drowsiness?)	✓
Bhrama – dizziness <sup>6</sup>	✓
Tandra – drowsiness	✓
Hritlepa – pressure in the chest or chest tightness <sup>6</sup>	✓
Chardana – vomiting	✓
Seetapitika/Udarda– urticaria <sup>1</sup>	✓

**Table 3**  
Chathurthaka Jwara/Asthi-majjagata Jwara Vs COVID-19 symptomatology\*.

Chathurthaka Jwara	COVID-19 symptoms
Tamapravesha - appearance of darkness in front of the eyes (due to excessive drowsiness?)	✓
Kasa – cough	✓
Mahaswasa – dyspnea	✓
Antardaha – burning sensation inside the body	–
Asthimajjagata jwara	
Asthibhedha – arthralgia	✓
Swasa – dyspnea	✓
Vireka– diarrhoea	✓
Chardi– vomiting	✓

**Table 4**  
Symptoms of Sama-Sannipata- Jwara Vs COVID-19 symptomatology<sup>a</sup>.

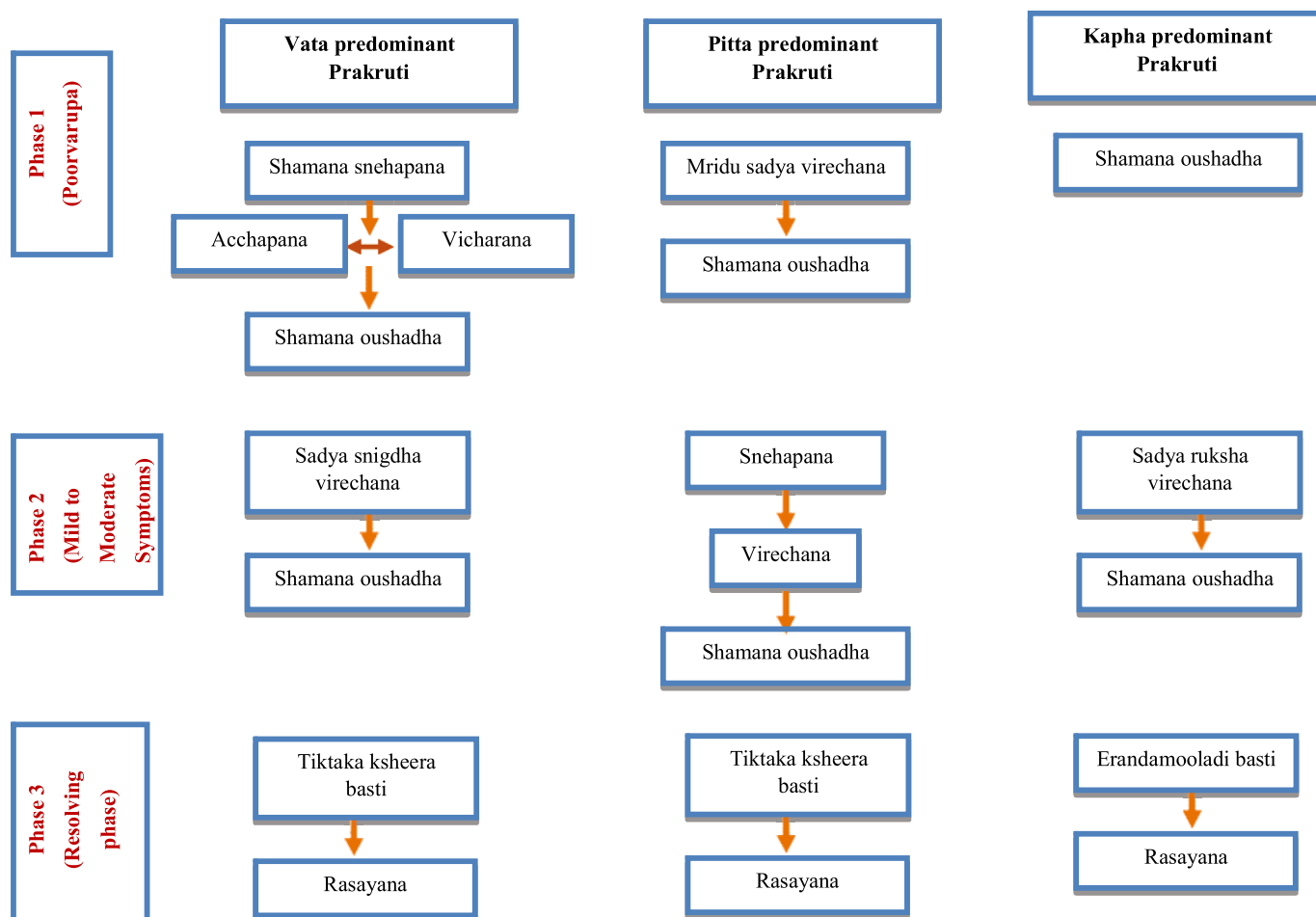
Sama-Sannipata-Jwara	COVID-19 symptoms
Kshanedaha & Kshanesheeta - Dysfunctional thermoregulation	–
Asthisandhiruja- arthralgia	✓
Shirotuja- headache	✓
Saasraavekalusheraktelochane– epiphora and conjunctival congestion	✓
Saswanaukarnau & Karnarija	–
Kanthashookairiva– sore throat	✓
Tandra– drowsiness	✓
Moha– coma (septic shock)	✓
Pralaapa–loss of orientation	✓
Kaasa– cough	✓
Shwaasa– dyspnea	✓
Aruchi– anorexia	✓
Bhrama– dizziness	✓
Paridagha, Kharasparshajihwa – changes in tongue texture	–
Srastaangata – feeling of fatigue/laxity in body parts	–
Kaphayuktaraktsheetevanam– sputum production <sup>6</sup>	✓
Shiraslothanam	–
Trishna– excessive thirst (may occur due to diarrhea)	✓
Nidraanaasha – sleeplessness	–
Hridayadha– chest tightness	✓
Chiraat and alpasweda, mutra and purisha – dysfunctions in thermoregulation, urinary output, constipated bowels	–
Pratatamkathakoojanam – moaning/howling	–
Shyaava, Raktakotha and mandala – Livido reticularislesions? <sup>1</sup>	✓
Mookatwam- mute (sickness behaviour, depressed mood)	–
Srotopaaka- inflamed auricle/ear canal	–
Udaragauravam – heaviness in the abdomen	–
Chiraatpaakashchadoshaanaam – chronic nature	–
Maranam- impending death	✓
Upadrava – Karnamoolashotha – inflammation and oedema over mastoid process (skull)	–

<sup>a</sup> Citation in Bibliography.

on immune mechanisms and *prakruti*, it is hypothesized here that *pitta dosha* predominant individuals shall be more prone to an earlier inflammation driven damaging phase of immune response

termed as the 'cytokine storm'– the phenomena observed in certain individuals infected with SARS-CoV-2 which is causally linked with casualties of COVID-19 [4]. The cytokine storm and





**Fig. 2.** Legend: Schematic diagram representing proposed Ayurvedic personalized prophylactic protocol in COVID 19 positive cases. Phase 01 represents the *poorvarupa* state (sickness behaviour phase), wherein *shamana snehapana* (internal administration of sneha i.e., medicated ghee/oil), *virechana* (therapeutic purgation) and specific *shamana oushadha* (disease/*dosha* specific medicaments) are proposed based on predominant *prakruti* as a prophylactic measure. *Vicharana snehapana* refers to lesser doses of *sneha* administration either admixed with food or through specific non-oral routes like enema. *Acchapana* refers to higher doses of direct *sneha* administration. *Mridu sadya virechana* refers to instant induction of mild purgation. Phase 02 represents the onset of symptoms, wherein different types of *virechana* are proposed like *snigdha* or *ruksha* based on *prakruti* and *dosha* status. Phase 03 depicts the resolving phase of immune response wherein different *bastis* (therapeutic enema) and specific *rasayanas* are highlighted considering a better and a quicker immunomodulation after the viral attack. *Shamana oushadha* shall be tailored to subjective day-to-day symptom presentation. Severe cases or cases reporting any complication shall not be considered for *Panchakarma* therapy.

subsequent immunological reactions and toxicity may be understood in terms of *ama visha* induced *jwara*.

Further, the study on genome expression and *prakruti*, found that expression of genes which affected hemoglobin levels namely HBA1, HBB, NOV were found high in *pitta* dosha predominant individuals compared to *vata* and *kapha* types indicating higher hemoglobin levels in the former [8]. Hemoglobin and other components of erythrocytes are potential constituents of innate immunity, competent of generating reactive oxygen species (ROS) that perturb the immune homeostasis by inducing inflammation driven immune reactions, sepsis and shock [23]. *Prakruti* is assessable [8]. Hence, identifying the *prakruti* of people diagnosed with COVID-19 or who are known to have a primary contact with a positive case, shall help to screen (predict) those individuals who can fall into deteriorating states and also may prove crucial in adopting timely and *dosha* specific prophylactic-therapeutic measures.

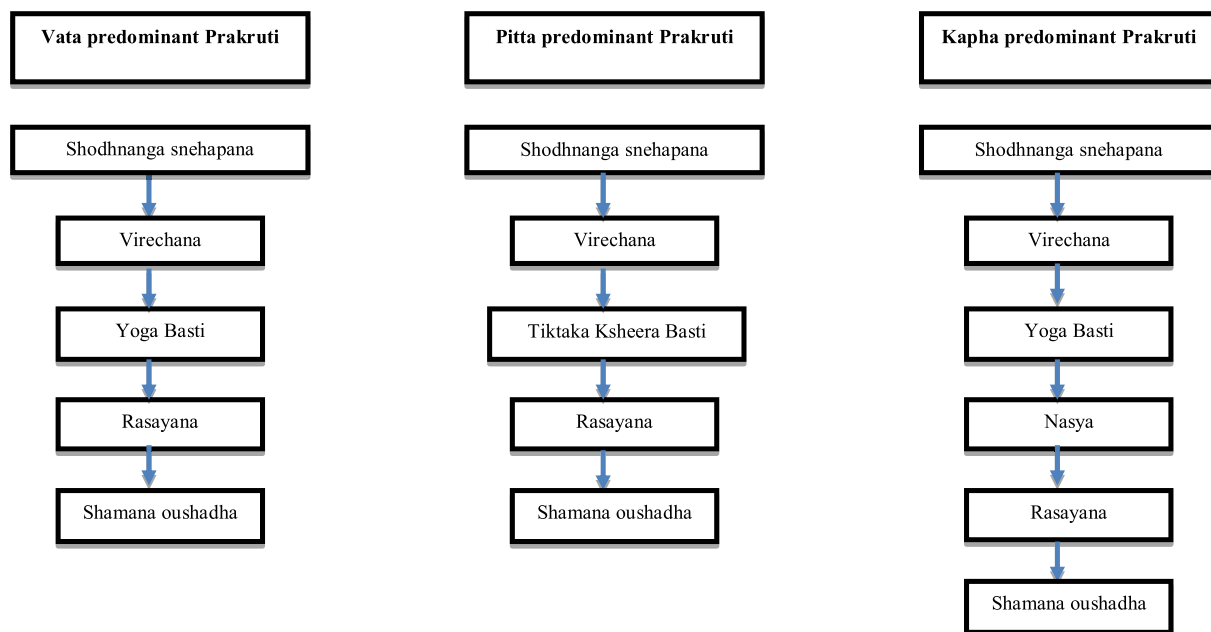
**5. Virechana, basti and rasayana in regulating host immune responses**

*Virechana* refers to therapeutic purgation which is indicated in *pitta dosha* related disorders [16,24]. Notably, *virechana* is also

indicated in *jwara*, *ama dosha* and respiratory ailments like, *swasa* (asthmatic conditions) and *kasa* (chronic cough), considering the pathogenesis and site specificity of COVID-19 affliction [6]. Effectiveness of *virechana* in *amavata* (rheumatoid arthritis), and *vicharchika* (atopic dermatitis) is reported where there is evident involvement of deregulated immune homeostasis [25–28]. Anti-inflammatory effects of *virechana* is also reported [25]. Surprisingly, anti-rheumatic treatment strategies have also been factually suggested in COVID-19 [3]. Hence, we propose periodic person-centered *virechana* starting from the *poorvarupa* state itself as a prophylactic measure in diagnosed cases of COVID-19 with mild to moderate symptoms as well as high to low risk primary contact cases (with an infected individual) and essentially who have *pitta* predominant *prakruti*. It is also recommended in other *prakruti* individuals keeping in mind the forthcoming respiratory concerns in COVID-19. Furthermore, the procedural administration of any *panchakarma* procedure like *virechanana* are to be planned following norms specifically mentioned under each procedure.

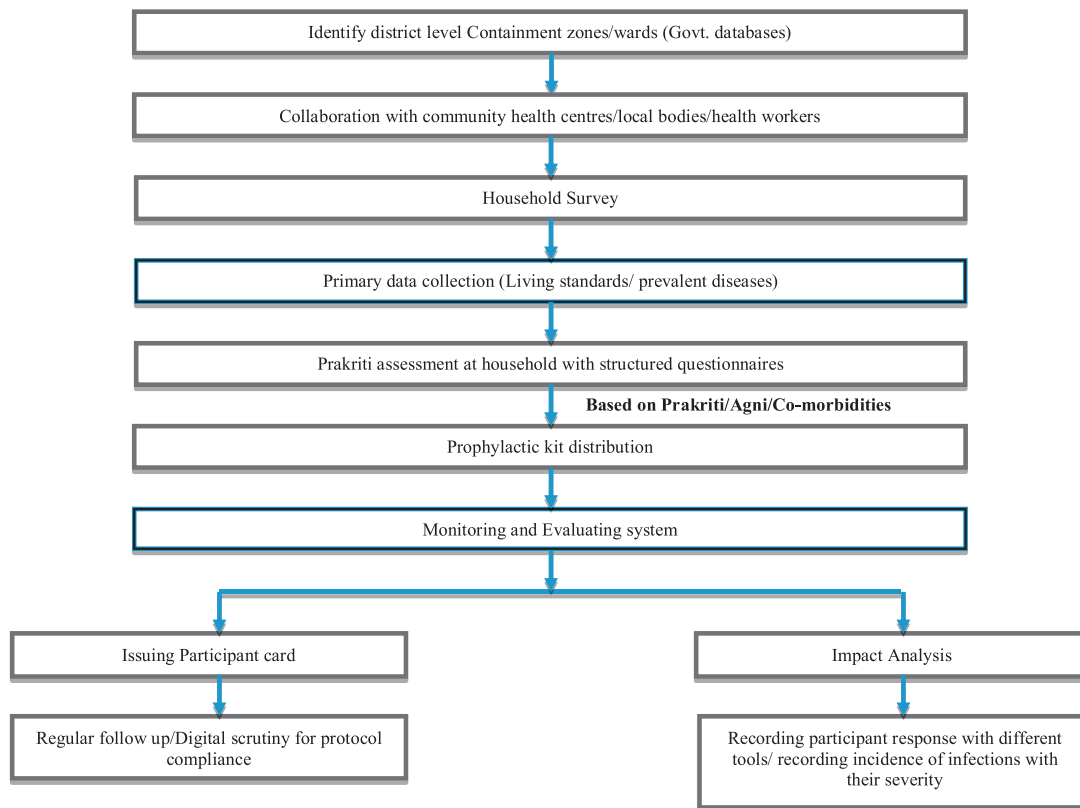
*Vata* predominant *prakruti* individuals are of *alpa bala* (deteriorated health status) [6]. Accordingly, the above cited studies on immune mechanisms and *prakruti* concluded a reduced or compromised immune response in *vata prakruti* individuals

### Proposed personalized protocol for high to low risk primary contact



**Fig. 3.** Legend: Schematic diagram representing proposed Ayurvedic personalized prophylactic protocol in high to low risk primary contact with a positive case. Proper *panchakarma* therapy highlighting *virechana*, for preventing the inflammation driven tissue destructive phase of SARS CoV2 induced immune response is highlighted. This is followed by specific *bastis* for initiating immunomodulation as a prophylactic measure.

### Pilot prophylactic community level protocol implementation in COVID-19 – DOTS Model



**Fig. 4.** Legend: Schematic diagram representing the proposed Ayurvedic community level prophylactic protocol – a hypothetical DOTS model. Following the DOTS model of therapeutic intervention famous for TB surveillance and treatment, a community level *Ayurvedic* prophylactic protocol in COVID-19 is proposed.

making them more prone to infections [7,8]. Connecting the above statements, we hypothesize that although *vata prakruti* individuals may be more prone to infections of varied origin including the current viral outbreak, they may not enter into severe or deteriorating stages of tissue damage caused by the immune response. In summary, there is a comparatively lesser chance that the inflammation driven destructive phase of immune response be triggered in an infected COVID-19 case who is of *vata* predominant *prakruti*. Notably, respiratory functions are highly influenced by *vata dosha* [16]. Thus, a pro-environment should be created in such individuals to have a better immune homeostasis and healthier states.

*Basti* therapy refers to therapeutic enema which is specifically indicated in *vata* disorders or *vata dosha* aggravated states. The medicaments in *basti* are expected to reach the proximal colon [29]. The gut is the abode of diverse microbiome. The gut microbiota consist of complex organisms that significantly influence host immune homeostasis [30]. The gut microbiome displays *prakruti* specific differentiation in microbial colonies [31]. Therefore, it is not surprising that there are precise types of *basti* indicated in specific diseased conditions. For instance, *Tikta Ksheera Basti* is indicated in *Asthi majjagata vata* [6]. *Asthimajja gata vata* (disorders of bone and bone marrow origin) is a syndrome with features of *balakshaya* or altered host homeostasis [6]. The role of bone marrow in host immune mechanism is fundamental. Surprisingly, an aforesaid type of *vishama jwara*, namely the *chaturthaka jwara* (which resembles features of COVID-19 significantly) manifests as a result of *doshas* at the level of bony tissue and bone marrow (*asthi* and *majja dhathu*). A study has reported ankylosing spondylitis as a type of *asthi-majjagata vata*, wherein host immune homeostasis is altered and one of the treatment modalities adopted was *Basti* [32]. *Erandamooladi yapana basti* explained in the context of healthy longevity is commonly administered in *vata kapha* disorders [6]. Moreover, the hypothetical link between *vata dosha* and immunomodulation suggest the utilization of *basti* in immunocompromised *vata* predominant *prakruti* individuals or as a matter of fact, any individual in the resolving phase of immune responses, in order to bring back immune homeostasis. Also, there are scientific leads stating efficacy of *virechana* and *basti* in essential hypertension, obesity, hyperlipidemia and diabetes mellitus, making these procedures suitable in field trials [33].

Hence, we propose person-centered prophylactic *basti* therapy (with all precautionary measures like personal protective equipments for administering personnel, with standard COVID care facilities) in *vata* predominant *prakruti* individuals either diagnosed with COVID-19 affliction or those who are quarantined for a high to low risk primary contact with a positive case. Also, we suggest *basti* treatment in individuals of any *prakruti* while in resolving phases of immune response triggered by COVID-19 infection, to initiate a quicker immunomodulation for bringing about immune homeostasis.

*Rasayana* therapy (rejuvenative means), is always indicated after *shodhana* (bio-purificatory measures). Of the many benefits of *rasayana* therapy, immunomodulating and tissue homeostatic effects of *rasayana* holds good in this context. There are tested *Ayurvedic* single herbs exhibiting immunoadjuvant, immunosuppressant or immunostimulant activities targeting innate and adaptive immune responses [34]. There are scientific leads emerging which propose the use of single herbs such as *Ashwagandha* in immune homeostasis especially in COVID-19 cases [4]. Articles are lately being published highlighting several tissue specific host homeostasis and immune regulators (*naimittika rasayanas*) and single herbs with respect to the COVID-19 symptoms [35] There are many polyherbal formulations that are real time-tested *rasayanas*.

## 6. Bridging predictive medicine with stage-wise COVID-19 management strategy

Based on the above discussion, we hereby propose a person-centered prophylactic-therapeutic strategy based on *prakruti*, intended for effective host immune responses in COVID-19 diagnosed cases (with mild to moderate symptoms) and in quarantined cases for high to low risk primary contact with a COVID-19 case (avoiding cases presenting with any sort of respiratory distress). We also propose a community level personalized Ayurvedic prophylactic protocol taking leads from the DOTS model [36].

### 6.1. Prophylactic – therapeutic internal medications in COVID-19 protocol

Instead of prescribing single herbs/herbal extracts in a particular diseased state manifested in the community, as in an outbreak, Ayurveda mostly recommends pharmacodynamically balanced polyherbal formulations as specific person-centered therapeutic strategy in illnesses. Clinically too, such advocacies are much more promising than a single herb or a herbal extract which is prescribed irrespective of individualistic physiological-pathological states. Polyherbal formulations are stable compounds and are therefore safer and more effective when compared to single herbs or herbal extracts especially when there is a tissue homeostatic crisis as in COVID-19 [37]. Evidence supports the efficacies of potent immunomodulatory, anti-inflammatory, antimicrobial, antioxidant (*rasayana* and *non-rasayana*) herbs that are present in commonly practiced polyherbal formulations and which are specifically indicated in particular diseased states or in comorbid conditions [38,39]. [Supplementary Table S1](#) contains the list of various formulations in different forms that may be incorporated as internal medications for the protocol in a blackbox frame, where the *vaidya* is free to logically select the medicament based on personalized day today status of health domains. The list contains medicaments which are indicated in basal metabolic errors (*ama dosha*), hyperinflammation, oedema, fever, respiratory ailments and which have immunomodulating/*rasayana* effects.

### 6.2. Proposed person-centered prophylactic-therapeutic protocol for enhancing host immune responses in COVID-19

[Figs. 2–4](#) represent the schematic diagram of the proposed protocols. In summary, different types of *virechana* (like *snigdha virechana*, *rooksha virechana*, etc) based on individualistic *prakruti* patterns along with specific internal medications have been highlighted as a prophylactic measure in different stages of COVID-19 manifestation or as a general prophylactic measure to manage the inflammation driven immune response phase of the disease. *Basti* and *rasayana* treatment along with specific internal medications are highlighted in the resolving phases of an exaggerated immune response for a quicker immunomodulation and subsequent immunohomeostasis.

#### 6.2.1. Outcome measure to assess changes in host immune responses while and after the intervention

Host immune responses are very much distinctive and thus personalized prophylactic or therapeutic measures are decisive to sustain in a highly contagious outbreak such as COVID-19. Time tested and real world experience based traditional knowledge should be experimented while such pandemics within a broad framework of personalized immune homeostasis which is adjusted day-to-day on the basis of symptomatic response and other quantitative or functional host immune response parameters. Through a hypothetical model, we tried to explore the odds of adopting



prakruti-based personalized medicine in prophylactic-therapeutic management aimed at improving host immune homeostasis. It is a matter of fact that adopting personalized treatment strategies in epidemics or pandemics is of course a controversial topic with respect to its feasibility. Yet, we believe manifestation of any illness in an individual (be it an epidemic manifestation) is significantly dependent on his/her physiology, as it's observed that not all individuals succumb to a cytokine storm or pneumonia or respiratory failure in case of COVID affliction. Thus, there are definite personalized factors that determine the fate of any illness, even in pandemics. The protocol is proposed with the objective of imparting better personalized host immune responses. Hence, the following may be assessed as an intervention and as an outcome measure to quantify the changes in host immune responses if any:

1. Host immune homeostasis and inflammatory levels after intervention [4,40,41]: Th1/Th2 cytokine balance/viral load by RTPCR/ multi colour flow cytometry/CBC with stain analysis/ TNF  $\alpha$ /IL-1/IL-6 for assessing the inflammatory status.
2. Host immune functional homeostasis after intervention: Incidence and severity of any infection/Differential blood count/ Total count/Erythrocyte Sedimentation Rate/C- Reactive Protein levels.

## 7. Conclusion

Our hypothetical model discusses the significance of *prakruti* assessment in predicting the chances of falling into deteriorating states of immune hyper-activation following a COVID infection. This model may be analyzed for testing in controlled integrative settings along with standard care in people who are at risk for primary contact with positive cases or who have mild to moderate symptoms of COVID attack. Community level implementation of Ayurvedic prophylactic measures is also hypothesized. We put forward a novel person- centered approach which may positively induce a better host immune homeostasis by reducing the chances of untoward events of aggravated immune responsiveness and subsequent inflammation driven tissue destruction which are candidate causes for COVID-19 related casualties.

## Conflict of interest

None.

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None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jaim.2020.08.004>.

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