



Review Article

COVID ANXIETY AND IMMUNE SYSTEM

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ABSTRACT

In the era of global transmission, when all the luxurious concept stands meaningless people are forced to believe the concept of 'individualistic approach in disease management'. This pandemic COVID 19 has been an eye opener which showed the world that there doesn't exist any magic pill. The one and only protector we have is our immune system. Many people are prone to ill health due to their irregular dietary habit (*Āharaja*), activities (*Vihāraja*) change in climate, on the other hand, some people remain healthy in spite of violating healthy rules and do not get affected by any disease. This is because of the variation in their immune power. Ayurveda described *Vyādhikshamatva* in more detail and magnificent way which can be considered equivalent to modern concepts of immunity. The term *Vyādhikshamatva* is made up of two words; *Vyādhi* (disease) and *kshamatva* (suppress or overcome). Ayurveda describes numerous health practices as *Dinacarya*, *Ritucarya*, *Rasāyana*, *Sadvritta*, *Acāra rasāyana*, *Yoga* and meditation to help mind and body to thrive. Homeostasis of *Ojas*, *Agni*, *Srotas*, *Doṣa* and *Duṣya* along with and associated is the pleasant state of sensory organs and mind, soul essential for good health. The government interventions during COVID-19 like *Punarjani*, *Sukhayushyam*, *Swasthyam*, *Niramaya*, *Ayur raksha* clinics which aims at strengthening the preventive mechanism gives Ayurveda a new ray of hope to globalize its importance.

INTRODUCTION

In this COVID era many were concerned about health and health care facilities of their family members working abroad, others were concerned about self-getting afflicted with COVID 19 and the treatment expenses, and another set of people i.e., health care worker-who were very anxious regarding less number of Personal Protective Equipment, virus exposure, patients perishing despite heroic efforts to save them and difficult medical decision regarding which patient should receive limited resources. In a nut shell, every single person had gone through or still going through such thoughts and worries and these has got much impact our immune system.

12,000 years of human history, pandemics have killed an estimated 300 million to 500 million people, with the bubonic plague decimating an estimated 60% of the European population during the middle Ages. COVID 19 has caused more than 2 million reported deaths in less than a year. Aside from the death toll, the pandemic has triggered significant emotional, physical, and economic problems around the world. This pandemic has halted 93% of mental health service across the world resulting in relapse or increasing of reported cases. Many countries adopted telemedicine or teletherapy to overcome the disruptions in-person healthcare services. Of all the mental health queries recorded in India, 60 % were aged in btw 21-30, 25% belongs to the age group 31-40, 5% from 41-60 and 10% from those aged 60 and above^[1].

Stressors associated with this pandemic can be grouped as traumatic stressors and general stressors. Traumatic stressors include severe illness, hospitalisation, witnessing death of loved one, extreme exposure to COVID 19 details and general stressors include quarantine, social isolation, employment/income loss, making difficult medical decisions etc^[2].

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Along with this stressors bereavement, isolation, loss of income, fear are triggering mental health conditions or exacerbating existing ones and many people may be facing increased levels of alcohol and drug use, insomnia, and anxiety. Major mental health issues associated with the COVID 19 pandemic are stress, anxiety, depressive symptoms, insomnia, PTSD, panic attacks, anger, alterations in sleep, energy level, concentration and self-esteem^[3].

According to center for disease control and prevention survey, the prevalence of mental health issues, substance use and suicidal ideation during the COVID 19 pandemic were as follows^[4].

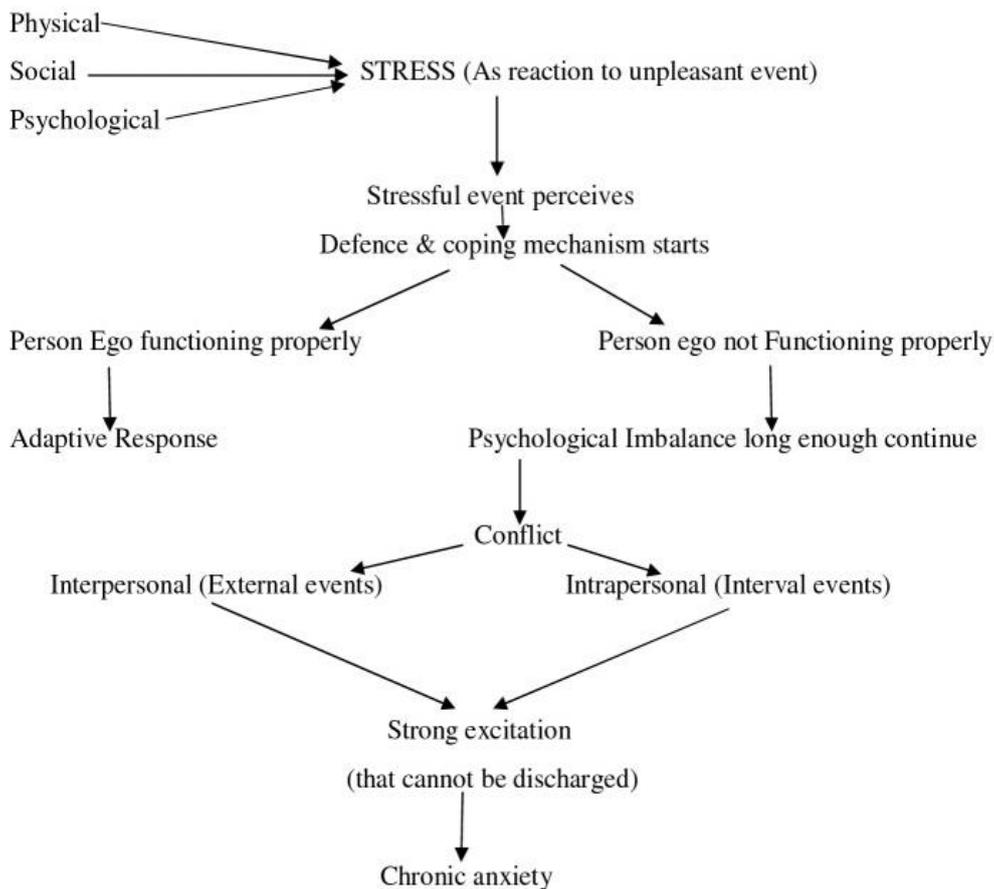
- Anxiety or Depression: 30.9 %

- Trauma and stress related disorders: 26.3%
- Substance use: 13.3 %
- Suicidal ideation: 10.7 %

Anxiety

Anxiety is the commonest psychiatric symptom in clinical practice and anxiety disorders are one of the commonest psychiatric disorders in general population and is a 'normal' phenomenon, which is characterized by a state of apprehension or unease arising out of anticipation of danger^[5]. Anxiety accounts 30% of all psychiatric disorders and it is the 6th leading cause of DALYs ^[6]. During the pandemic the global prevalence rate of anxiety is 31.9%^[7].

Aetiopathogenesis of Anxiety



Etiology and Psychopathology of Anxiety

This can be explained on the basis of following four factors.

1. Genetic factors
2. Psychological factors
3. Socio-economic factors
4. Neurobiological factors

1. Genetic Factors

About 15-20% of first-degree relatives of the patients with anxiety disorder exhibit anxiety disorders themselves. The concordance rate in the monozygotic twins of patients with panic disorders is as high as 80% (4 times more than in dizygotic twins).^[8]

2. Psychological Factors

The two major schools of thought about psychological factors leading to the development of generalized anxiety disorder are the cognitive behavioural school and the psychoanalytical school. According to cognitive behavioural school, anxiety patients respond incorrectly and inaccurately towards the perceived dangers because of their selective attention to negative details in the environment and the psychoanalytical school opines that anxiety raised as a result of unresolved unconscious conflicts^[9].

3. Socio-economic Factors

Economic crisis, low income, job loss, social distancing, lock down etc will increase the anxiety [2].

4. Neurobiological Factors

This includes Noradrenergic nervous system, Hypothalamic pituitary adrenal axis, Amygdala and the bed nucleus of the stria terminalis, Septo-hippocampal system, and other neurotransmitter System. Noradrenergic pathways have long been associated with fear and arousal and play an important role in the body's response to threat^[10]. HPA Axis and its end product cortisol involved in reaction to stress. Circulating cortisol exert inhibitory feedback on pituitary gland and on hippocampus. Reduction in the normal regulatory control of cortisol secretion can lead to persistent anxiety^[11]. Amygdala is thought to be responsible for detection of potential threat and Mobilization of a range of defensive responses^[12]. Septo-hippocampal system Responsible for mediating the emotion of anxiety as well as the major effect of anxiolytic drugs^[13]. Neurotransmitters play an important role in anxiety pathology. Serotonin is linked to both anxiety and depression^[14]. Hyper secretion of thyroid hormone causes severe anxiety and panic attacks^[15]. Higher levels of GABA possess mood boosting qualities and low levels of GABA has excitatory properties, that put one on edge^[16]. Epinephrine results many of the symptoms of anxiety^[17]. Improving dopamine level, will reduce social anxiety and other anxiety disorders^[18].

Excess thought and worries will cause excess stress which triggers the fight or flight response, which stimulates sympathetic nervous system, and results in hyper secretion of cortisol. Cortisol normally boosts blood sugar levels and triglycerides, so if it is not used for physical activities there will be serious physical consequences. If excessive worrying and high anxiety go untreated, patient may end up in depression and even suicidal thoughts. Since stress is the major cause of anxiety, role of different kind of stressors on immune system enumerated as follows;

Consistent stressors like death of loved one, divorce, chronic illness etc results in the decreasing of functioning of Suppressor, Helper and Cytotoxic T cells^[19]. Naturalistic stressors like academic examination, natural disaster etc results in the reduction in number and percentages of cytotoxic T cells, natural killer cell and helper T cells^[20]. Chronic stressors reduce natural killer cell cytotoxicity, results in suppression of lymphocyte proliferative responses and humoral immunity. Diminished immune responses in chronically stressed individual results in the heightened incidence of infectious and neoplastic diseases^[21]. So in order to correct this, psychological support should be routinely implemented not only to

consider psychological resilience but also to enhance psychoneuroimmunity against COVID-19.

Ayurvedic Perspective

Ayurveda states that both health and ill health arises first in mind which is considered as the controller of the senses and the body. Ayurveda with its holistic approach takes mind as an integral part of life. Definition of *Svastha* emphasizes equal importance to the mental state along with physical state. While explaining the definition of *Āyu*, Acarya Charaka gave due importance to *Satva* and *Ātma* along with other components *Śarīra* and *Indriya*. So it is understood that both the *Śārīrika* and *Mānsika vyādhi* are given equal importance^[22] i.e., some of the *Śārīrika doṣa* causes *Mānasika roga* like *Unmāda* and *Mānasika bhāva* causes *Śārīrika roga* eg, *Śoka* causes *Hridroga*, i.e., *Sokaja hridroga*. Anxiety has both physiological tremors, head ache, Tachycardia etc and psychological symptoms (poor concentration, hyper arousal, derealization, depersonalisation etc).^[23] If the anxiety is left untreated in its first stage, mild symptoms like head ache, palpitation, stomach upset will turn into major symptoms like panic attacks, depersonalization, derealization etc, i.e., a milder form of *Vāta-pitta duṣṭi* with the involvement of *Raja* and *Tama* causes *Manobuddhyādi vibhrama* in later stage. If the patient is not taking the medication even in this stage, he or she will be end up in serious mental health diseases like phobic anxiety disorder, obsessive compulsive disorder, post traumatic stress disorder i.e., *Unmadādi manovikāra*. So to cure as well as to prevent these kind of *Vyādhi* we have to boost our immune system. *Vyādhikṣamatva*, *bala*, and *Ojas* are the terms coined for the concept immunity in Ayurveda.

- **Vyādhikṣamatva:** *Vyadhikshamatva* is illustrated as the power of resistance capable enough to check the progress occurrence or recurrence of disease. It is the union of two words *Vyādhi balavirodhitva* (biological defensive power of the body to fight against the ongoing afflicted diseases) and *Vyādhi utpādaka pratibandhakatva*^[24] (the prevention of further development of diseases).
- **Bala:** *Bala* imparts firm integrity to the muscles, improves the voice and complexion, and helps the person to perform his natural functions^[25]. Three types of *bala* are described in Ayurveda classics as *Sahaja bala*, *Kālaja bala* and *Yuktikṛta bala*^[26]. *Sahaja bala* is the physical and mental strength present naturally by birth. So in this scenario *Sahaja bala* possess an important role, because not every person is afflicted with COVID 19, even though they have same circumstances. Similarly those with high immunity though they may have COVID, symptoms seems to be mild. *Kālaja bala* is the strength based on the division of seasons and age of the person. According to age, the person has naturally less

strength in childhood and old age. So additional measures should be taken for boosting their immunity. *Yuktikrta bala* is based on lifestyle management. AYUSH ministry advised a set of medications, dietary regimen, and *Vyāyama* for enhancing immunity during this period.

- **Ojas:** *Ojas* is the essence of *Saptadhātu* and it is the seat for strength^[27]. Psychological factors which are responsible for *Ojākṣhaya* are *Kopa*, *Dhyāna*, *Cinta*, *Soka*, *Bhaya* etc and results in *Bhaya* (fretful), *Durbala* (debilitated), *abhīkṣhna Dhyāna* (worries much again), *Vyathitendriya* (feels discomfort in the sense organs), *Durmana* (bad mention) etc^[28]. All these mental health issues are predominantly seen with COVID 19.
- **Satva:** *Satva* has genetic endowment as it is inherited at the time of conception and this part of the individual gets nurtured in the womb especially by the influence of '*Satvavaiśeṣyakara bhāva*' and also by the influence of 'one's own experiences' during infancy, childhood and adolescence and based on their characteristics they are classified into about 16 types (*Kāyabheda* or Personality traits). Though these classifications help to understand the mental disposition better, Acarya Caraka has utilized the concept of *Satva bala* in determining the predisposition to develop mental illness. *Satva bala* (mental strength) is graded into three^[28], *Pravara* (superior), *Madhyama* (medium) and *Avara* (inferior). An emotion like *Udvega* is a common response in part of life but persons having superior mental strength *Pravara satva* (superior mental strength) can resist the ill effect of such emotional disturbances very easily. On the other hand, when the person having *Alpa satva* (inferior mental strength) and when he is under stress, it initiates the disease process by resulting in imbalance of *Manodoṣa*. At this stage the person exhibits an exaggerated response to emotional disturbance, leading to clinical manifestation. Those with *Madhyama satva* (medium strength) can afford to take hardships, if consoled to do so.

Cittodvega

The aetiology and symptoms of anxiety is mostly similar to the *Mānasika bhāva* or *Vikāra 'Cittodvega'*. The term *Cittodvega* comprises of two words- *Citta* and *Udvega*. *Citta* means mind and *Udvega* means agitation/distressed. Thus, a state of distressed or agitated mind is known as *Cittodvega*. A reference to *Chittodvega* is found in *Caraka Samhita Vimāna sthāna* where *Ācārya Caraka* explains about physical and psychic *Doshas*. *Chittodvega* has been used by *Caraka* more classically under *Manodoṣa vikāra* along with emotional disturbances like *Kāma* (lust), *Krodha* (anger), *Lobha* (greed), *Moha* (infatuation), *Īrśya* (envy), *Māna* (arrogance), *Śoka* (grief) and *Cinta* (worry)^[29]. Even though the word *Cittodvega* is not explained by *Ācārya Śūsruta*, *Dalhana*, the commentator of *Susruta Samhita* has mentioned *Cittodvega* as synonymous with the term *Śoka* (Grief)^[30]. He has explained similar words like *Cittaviparya*, *Cittavibhrama* in which anxiety is found. *Ācārya Vāgbata* has referred the term *Cittopaplava* to denote anxiety^[31]. *Lakṣhana* of *Vāta-pitta vriddhi*, *Kapha kṣhaya*, *Dhātu duṣhti*, *ojākṣ Haya* are seen in *Cittodevga*. Even though *Cittodvega* is not a major psychiatric illness, this can hamper the social, occupational, personal functioning of an afflicted individual.

Management

Management of anxiety is based on its presentations, severity and presence of other associated diseases, i.e., *Doṣa* which are involved in this pathogenesis and extent of their *Duṣhti*. If anxiety is mild to moderate, one can adopt *Śamana cikitsa*, i.e., different formulations like *kaṣaya*, *Cūrṇa*, *Gulika* can be given. In moderate to severe anxiety, along with internal medication, external treatment modalities can also undertake like *Dhāra*, *Picu* etc. In very severe anxiety, *Śodhana* therapy is advised. Most of the drugs which are taken for the management, possess not only anxiolytic effect but also neuroprotective and immunomodulatory action e.g., - *Aśvagandha*, *Gulūci*, *Śankhupuṣpi*, *Bala* etc.

Table 1: Management of anxiety disorders

<i>Kaṣāya</i>	<i>Ghrita</i>	Single drugs or in combination	<i>Vataka/Ariṣṭa</i>
<ul style="list-style-type: none"> • <i>Brahmi drākṣādi kaṣāya</i> ^[32] • <i>Drākṣadi kaṣāya</i> ^[33] 	<ul style="list-style-type: none"> • <i>Kalyānaka ghrita</i> ^[34] • <i>Mahā kalyānaka ghrita</i> ^[35] • <i>Panchagavya ghrita</i> ^[36] 	<ul style="list-style-type: none"> • <i>Aśvagandha</i> ^[37] • <i>Gulūci</i> ^[38] • <i>Śankhupuṣpi</i> ^[39] • <i>Jadāmānsi</i> ^[40] • <i>Somalata</i> ^[41] • <i>Bala</i> ^[42] • <i>Yaṣṭi</i> ^[43] • <i>Brahmi</i> ^[44] 	<ul style="list-style-type: none"> • <i>Mānasamitra vataka</i> ^[45] • <i>Aśvagandha ariṣṭa</i> ^[46]

Śiroabhyanga	Śirolepa	Tala	Śirodhāra
<ul style="list-style-type: none"> • <i>Candanādi taila</i> [47] • <i>Śankhupuṣpi taila</i> [48] 	<ul style="list-style-type: none"> • <i>Samjna sthāpana gana</i> [49] • <i>Pancagandha cūrṇa</i> [50] • <i>Daśamūla cūrṇa</i> [51] • <i>Musta</i>[52]+ <i>Āmalaki</i>[53] <i>cūrṇa</i> 	<ul style="list-style-type: none"> • <i>Panchagandha cūrṇa</i> [50] • <i>Kachūrādi cūrṇa</i> [54] 	<ul style="list-style-type: none"> • <i>Kṣīradhāra</i> [55] • <i>Tailadhāra</i> [56] • <i>Takradhāra</i> [57] • <i>Jaladhāra</i> [58]

As Śodhana therapy, *Nasya* and *Virecana* are commonly advised in the mitigation of anxiety symptoms. *Nasya* with *Panchagavya grita*[59] and *Kṣīrabala taila* [60] are some examples. Similarly *Virecana* with *Avipatti cūrṇa*[61] is used to a very great extent.

Satvāvajaya Cikitsa

Ayurveda is a comprehensive science which gives ultimate importance to health and longevity as well as prevention, rather than treatment and cure of any diseases. These measures are to be strictly followed to bring the things under control, in the crisis of COVID pandemic. Such a pandemic as COVID 19 is having an inevitable impact in the mind of people throughout the world in various levels and various age groups also, rather than affecting the body. In any individual, if the quality of life is affected during this pandemic, needs a psychological assessment as well as right intervention. This requires the help of psycho supportive therapy which is denoted as *Satvāvajaya cikitsa* in *Ayurveda*[62]. According to Ācārya Caraka, *Satvāvajaya cikitsa* is nothing but withdrawal of mind from unwholesome objects[63] and for the balance of *Mānasika doṣa*, *Satvāvajaya cikitsa* can be administered. *Satvāvajaya cikitsa* is to be performed in psychologically affected subjects in a stepwise manner.[64]

Step I - Jnāna

- Knowledge of self is provided, i.e., creating awareness, of, how one has to perform or react in such an unfamiliar situation of pandemic.
- For this, if they suspecting any features of the COVID 19, inform the authorities at the earliest.
- Maintain a daily routine comprising of regular physical activities, healthy food habits, and healthy sleep pattern to maintain one's own health.
- Involve in stress relieving activities such as reading, breathing exercises or any other hobbies according to one's interest.

Step II - Vijnāna

- Awareness is created about the disease condition in a proper manner.
- So, one should Have proper theoretical knowledge about the occurrence of disease and its possible prevention
- Avoid believing myths and fake news

- Depend Government bulletins, scientific journals or WHO publications for actual data related to COVID 19.

Step III - Dhairya

- One has to develop patience to stick on to the rules for a better future.
- For this, one must possess the determination to obey rules such as lock down, social distancing and hygienic measures for the possible prevention
- Reinforce the coping skills

Step IV - Smṛiti

- One has to recollect the previous victories over such pandemics
- Give attention to those who had similar experiences with a positive ending
- Find opportunities to amplify hopeful stories and positive images of local people who have experienced COVID 19

Step V - Samādhi

- Step to have a stable state of mind, which is to be done as per the advice from the experts in this regard.
- For this, follow some simple stretching exercises and *Yogāsana*, regular *Prānāyāma* and other breathing exercises which calms the body as well as mind
- Chanting of *Mantra* may also be tried to improve concentration

These are the usual steps of *Satvāvajaya* to be adopted which are applicable in any psychological issues, including that of resulting from COVID as well.

Psychotherapy and counseling are somewhat similar to *Satvāvajaya cikitsa*. The anxiety disorder is treated with some form of counseling or psychotherapy, either singly or in combination. The range of available techniques for psychotherapy is wide and includes the following [65]:

1. Cognitive- behavioural therapy
2. Supportive therapy
3. Insight oriented therapy
4. Directive counseling
5. Non-directive counseling

Under these techniques counseling therapy has a significant role. During this pandemic situation people hesitate to have direct consultation with doctors, so that patients prefer for non-directive counseling which may enable social distancing also. In

this scenario tele- counseling methods have their significant role. Tele-Counseling is an ideal option in such situations which allows all modes of communication that provide information technology platforms, which includes voice message, text message and digital data exchange which helps for diagnosing, prescription writing and evaluation. Tele-counseling comes under non-directive counseling category and it is the technology assisted distance counseling which enables counselors and client to communicate at a distance when circumstances make this approach necessary or convenient^[66]. Recent meta-analysis of Research into tele mental health provided to children, young people and adults are found to be feasible, acceptable, and as effective as in-person services.

In this scenario, Ayurveda also developed a programme for moral and psychological support i.e. 'KOODE', an Initiative to curb psychological concerns among the public. KOODE was the first and foremost tele counseling programme from the field of Ayurveda. Main agenda of KOODE was

- To Assess the compliance with quarantine
- To provide mental health support
- To distribute emergency physical aids
- To arrange services of Ayurvedic specialties.
- To conduct orientation classes.

Because of the group effort taken by the team KOODE, District Medical Officer of Malappuram (district in Kerala) invited team members of KOODE into COVID 19 Surveillance team. KOODE was an Inspiration to formation of state Ayurveda COVID response cell in Kerala.

Pranayama and Meditation

Along with *Satvāvajaya cikitsa*, some forms of *Pranayama* and meditation also plays an important role in reduction of anxiety symptoms and their probable mode of action can be explained as, these techniques conditions the lung and respiratory tract, stimulates lymphatic system, thus removing toxins from the body and ensures the optimal functioning of organs. *Pranayama* and meditation practice on a regular basis can increase endorphins, dopamine, serotonin, and melatonin they are the feel-good chemicals within the body and decrease cortisol levels which cause stress. These provide natural support to immune system^[67].

- Hands in and out breathing
- Hands up and down breathing
- Sectional breathing
- Full yogic breathing
- Tiger breathing
- Dog breathing, these are some breathing techniques which can be advise for anxiety patients.

- Repeated Om chanting results in physiological alertness, and increased sensitivity to sensory transmission^[68].

Though all these treatments are mainly for the attainment of normalcy of *Śārīrika* and *Mānasika doṣa*, the best treatment to a disease is the avoidance of causative factors i.e., *Nidāna parivarjana*^[69]. For this purpose, one can adopt measures for psycho-immune enhancement.

Psycho-Immune Enhancement

Being *Trayopasthambha*, *Āhāra* and *Nidrā* plays a vital role in balance of *Śārīrika* as well as *Mānasika doṣa*. Relation between *Āhāra* and *Mana* is beautifully explained in *Cāṇḍokyopaniṣat 'Āhāra śuddhau satva śuddhi'*^[70]. Sleep and the circadian system are strong regulators of immunological processes. So proper and adequate sleep is inevitable for the goodness of body and mind^[71]. *Ācāra rasāyana* is a unique concept in Ayurveda that implies mental and personal hygiene. This brings about rejuvenation in the body and mind system without physically consuming any *Rasāyana*. Practice of *Ācāra rasāyana* will reduce the stress and anxiety and thus prevent the release of free radicals and improves the psychoneuro immunity^[72].

CONCLUSION

COVID 19, the global pandemic have severe impact on human beings, physical and mental stress being a major one. Stress is a common trigger for anxiety which weakens the immune system, leading to vulnerable infections and frequent illnesses. It is important to detect anxiety symptoms early to prevent occurrence of anxiety disorders. The term *Cittodvega* goes hand in hand with anxiety and is mainly caused by vitiation of *Mānasika doṣa* as well as *Śārīrika doṣa* and has a greater impact on our immune system. Therefore, treatment is mainly aimed to bring back these into normalcy. *Yuktivyapāśraya cikitsa* is recommended for correcting the vitiated *Doṣa*, attainment of *Dhātu sāmyata* and finally for *Ojovridhi*. *Satvāvajaya cikitsa* helps mind and body to thrive along with proper *Āhāra* and *Nidrā*, and practices such as *Yoga* and *Āchāra Rasāyana*.

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