Journal of Complementary and Alternative Medical Research

14(1): 53-60, 2021; Article no.JOCAMR.68648
ISSN: 2456-6276

Comparative Study on Iris Manifestations between COVID-19 Severe Cases and Non-COVID Individuals

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Authors' contributions

This work was carried out in collaboration among all authors. Authors YRA and AM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MHV, CAK and SV managed the analyses of the study. Authors YRA and NM managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JOCAMR/2021/v14i130238
Editor(s):
(1) Dr. Sahdeo Prasad, Texas Tech University Health Sciences Center, USA.
(2) Dr. Francisco Cruz-Sosa, Metropolitan Autonomous University, México.
Reviewers:
(1) Christulas Jyoti, Minerva College and School of Nursing, India.
(2) Kalpana Ojha, University of Rajasthan, India.
(3) Iram Manzoor, Akhtar Saeed Medical and Dental College, Pakistan.
Complete Peer review History: http://www.sdiarticle4.com/review-history/68648

Original Research Article

Received 28 March 2021
Accepted 13 May 2021
Published 15 May 2021

ABSTRACT

Aims: To compare the iris manifestations between COVID-19 positive (severe) cases and their age and gender matched non-COVID-19 individuals.
Study Design and Setting: A comparative cross sectional survey performed in Government Omandurar Medical College, Chennai
Methodology: This study was performed to compare the iris manifestations between COVID-19 positive (severe) cases (*n* = 119) and their age and gender matched non-COVID-19 individuals (*n* = 119). Iris manifestations (both right and left eyes) of all the subjects (both study and control groups) were observed at only one point in time, and was compared between the groups.
Statistical Analysis: Descriptive statistics (Frequency distribution and percentage) were performed using Microsoft excel 2010. Within-group analysis was performed using Wilcoxon Signed Ranks Test, while the between-groups (study and control) analysis was performed using

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Chi-square test with the use of statistical package for the social sciences, version 16. P value < 0.05 was considered as significant.

Results: The research findings in right iris showed a significant difference at p<0.05 in Inner Pupillary Border (IPB), Autonomic Nerve Wreath (ANW), Scurf Rim (SCR), Inflammatory Sign (IS) and Lung Lesion (LL), while no significant difference at p<0.05 in Pupil Size (PS), Absorption Ring (AR), Iris Constitution (IC) and Stress Ring (STR) between the study and control groups. Likewise, the results of the left iris showed a significant difference at p<0.05 in IPB, ANW, SCR, LL and STR, while no significant change at p<0.05 in PS, IC, AR and IS between the study and control groups.

Conclusion: The paper aid comparison of the iris manifestations between COVID-19 positive and their age and gender matched non-COVID-19 individuals. The findings are of broad use to the scientific and medical communities searching for safe, cost-effective diagnostic approach. The present study is important in furthering our understanding of the importance of looking into the iris for diagnostic purpose.

Keywords: Corona virus disease 19 (COVID-19); iridology; digital image processing; naturopathy.

1. INTRODUCTION

Corona viruses are positive-sense ribonucleic acid (RNA) viruses with a diameter of 60 nm to 140 nm with spike-like projections on their surface that provide it with a crown-like appearance in the electron microscope [1]. Corona virus disease 19 (COVID-19) has developed in Wuhan, China and spread throughout the world, which is a highly transmittable and pathogenic viral infection caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) [2]. The clinical symptoms of COVID-19 range from asymptomatic condition to acute respiratory failure and multiple organ dysfunction. In the elderly and those with underlying co-morbidities, adverse effects and fatalities are more likely (50%–75% of fatal cases), while the mortality rate ranged from 4 to 11 percent in hospitalised adult patients. Thus, 25-30 percent of the patients affected with COVID-19 required intensive care treatment [3].

According to Naturopathy, the disease is a result of the build-up of toxic matter within the body that has settled in the inherently weak regions and is often aggravated by mechanical pressure. Human iris is world-renowned for its unique feature and dynamic nature as the perfect biometric system solution. The diagnostic work on iris is called iridology. The core iridology theory is that the iris develops in layers representing the four phases of tissue activity, namely acute alterations, subacute changes, chronic changes, and degenerative adjustments. Iridology is an innovative, safe, feasible, cost-effective and non-invasive methods used for the diagnosis and prognosis of body's abnormalities. Any disease that occur due to inheritance or environmental factors [4] can be easily ruled out on looking at the iris by various iris manifestations such as size of the iris, rings around iris, open and closed lesions.

In modern medical science, digital image processing (DIP) has become a valuable tool for recording, storing, analysing and processing medical imaging. Initially not really that empowering to treat diseases like kidney, cardiac disorders, morphological diabetes, fractal and cluster study, cancer diagnosis, hearing loss, and appendectomy because of technology deficiency, according to Ramirez and Montelongo [5]. The procedures of iridology and DIP approaches can be reported to help clinical diagnosis more methodologically. In the past 20 years non-invasive diagnosis of the DIP has been performed, including adrenal glands, the heart and aorta, solar plexus, kidney, pancreas, etc. [5]

A study integrating iris detection algorithms and iridology to assess a patient's health status has been published [5]. Lodin and Demea (2009) developed the general method of health diagnosis [6]. Ramlee and Ranjit developed a cholesterol detection system using a specific iris sign called sodium ring [7]. The value of the nutritional state of children was predicted by Ayda et al. [8], by recognizing iris signs. Lai and Chiu [9] have developed an iris-based clinical check-up program to assess the status of the organ defects. Shen et al. [10] described iris lesions to find out chronic disorders including bronchitis, brain dysfunction, erectile dysfunction. Wibawa and Purnomo [11] suggested to diagnose diabetes mellitus by the presence of broken tissues in the iris at pancreas's position, etc.

However, to the best of our knowledge, there is no known study reported the iris manifestations of the patients with COVID-19 infection. Thus, this study was performed to compare the iris manifestations between COVID-19 positive (severe) cases and their age and gender matched non-COVID-19 individuals.

2. MATERIALS AND METHODS

2.1 Study Design

A comparative cross sectional survey was performed in 238 participants of which, the study group involved 119 patients with COVID-19 positive and the control group involved 119 age and gender matched individuals without COVID-19. Iris manifestations (both right and left eyes) of all the subjects (both study and control groups) were observed at a point of time, and was compared between the groups.

2.2 Participants

A total of 238 participants (119 patients with COVID-19 positive in the study group and 119 age and gender matched individuals without COVID-19 in the control group) aged 53.74 ±11.21 years were recruited for the study. The study group participants were recruited from intensive care unit, Government Omandurar Medical College, Chennai (between 26 June 2020 and 2 July 2020), while the control group participants were recruited from out-patient department, Government Yoga and Naturopathy Medical College and Hospital, Arumbakkam, Chennai, based on the following inclusion and exclusion criteria: For the study group, male and female participants aged between 35 and 80 years with COVID-19 positive (severe condition) and admitted in intensive care unit and were willing to participant in the study were included, while people on COVID-19 quarantine, asymptomatic/mild/moderate COVID-19 positive cases, history of eye-related health problems and recent eye surgery were excluded. For the control group, male and female participants aged between 35 and 80 years with no history of COVID-19 infection were included, while people on COVID-19 quarantine, with any kind of active infections, history of eye-related health problems and recent eye surgery were excluded.

2.3 Assessments

The iris images (both right and left eyes') of all the subjects (both study and control groups) were captured using Iridology Camera [2014 CE FCC NEW 5.0 MP USB IRISCOPE IRIS ANALYSER with Pro Iris Software-GH11003, Germany] at only one point in time by an expert who have more than 10 years of experience in the field of iridology. In the present study, selected iris signs [Pupil Size (PS), Iris Constitution (IC), Autonomic Nerve Wreath (ANW), Inner Pupillary Border (IPB), Absorption Ring (AR), Scurf Rim (SCR), Inflammation Sign (IS), Lung Lesion (LL) and Stress Ring (STR)] were observed in both the groups by two independent experts and compared them in between the groups manually.

2.4 Data Analysis

Descriptive statistics (Frequency distribution and percentage) were performed using Microsoft excel 2010. Within-group (Right and left iris images of the same subjects) analysis was performed using Wilcoxon Signed Ranks Test, while the between-groups (study and control) analysis was performed using Chi-square test with the use of statistical package for the social sciences, version 16. P value < 0.05 was considered as significant.

3. RESULTS

Comparison between the right iris and left iris of the study group:

The results showed a significantly higher LL in the right iris (73.11%) compared to that of left iris (47.90%) and a significantly higher STR in the left iris (83.19%) than that of right iris (46.22%).

Comparison between the right iris and left iris of the control group:

The results showed a significantly higher LL in the right iris (32.77%) compared to that of left iris (26.05%), while no significant changes were observed in rest of the variables (Table 1).

Comparison between the study and control groups:

Results of the right iris showed a significant difference in IPB ($p<0.001$), ANW ($p<0.003$), SCR ($p<0.001$), IS ($p<0.023$) and LL ($p<0.001$), while no significant difference in PS ($p<0.051$), AR ($p<1.000$), IC ($p<0.218$) and STR ($p<0.295$) between the study and control groups. Likewise, the results of the left iris showed a significant difference in IPB ($p<0.001$), ANW ($p<0.006$),

Table 1. Presentation of iris signs in the study group (n=119) and the control group (n=119)

Parameters	Right Iris [Frequency (%)]			Left Iris [Frequency (%)]		
	Study Group	Control Group	P value	Study Group	Control Group	P value
Pupil size						
• **Miosis**	33 (22.73)	22 (18.49)	0.051	32 (26.89)	24 (20.17)	0.397
• **Mydriasis**	2 (1.68)	8 (6.72)		3 (2.52)	5 (4.20)	
• **Normal**	84 (70.59)	89 (74.79)		84 (70.59)	90 (75.63)	
Iris constitution						
• **Biliary**	68 (57.14)	68 (57.14)	1.000	66 (55.46)	68 (57.14)	0.896
• **Hematogenic**	51 (42.86)	51 (42.86)		53 (44.54)	51 (42.86)	
Inner pupillary border						
• **Visible**	99 (83.19)	51 (42.86)	<0.001*	98 (82.35)	52 (43.70)	<0.001*
• **Not visible**	20 (16.81)	68 (57.14)		21 (17.65)	67 (56.30)	
Absorption ring						
• **Present**	45 (37.82)	36 (30.25)	0.218	43 (36.13)	34 (28.57)	0.212
• **Absent**	74 (62.18)	83 (69.75)		76 (63.87)	85 (71.43)	
Autonomic nerve wreath						
• **Constricted**	63 (52.94)	53 (44.54)	0.003*	66 (55.46)	53 (44.54)	0.006*
• **Dilated**	3 (2.52)	18 (15.13)		4 (3.36)	18 (15.13)	
• **Normal**	53 (44.54)	48 (40.34)		49 (41.18)	48 (40.34)	
Scurf rim						
• **Present**	96 (80.67)	50 (42.02)	<0.001*	99 (83.19)	48 (40.34)	<0.001*
• **Absent**	23 (19.33)	69 (57.98)		20 (16.81)	71 (59.66)	
Inflammatory sign						
• **Present**	83 (69.75)	98 (82.35)	0.023*	82 (68.91)	95 (79.83)	0.054
• **Absent**	36 (30.25)	21 (17.65)		37 (31.09)	24 (20.17)	
Lung lesion						
• **Present**	87 (73.11)†	39 (32.77) †	<0.001*	57 (47.90) †	31 (26.05) †	<0.001*
• **Absent**	32 (26.89)	80 (67.83)		62 (52.10)	88 (73.95)	
Stress ring						
• **Present**	55 (46.22) †	47 (39.50)	0.295	99 (83.19) †	47 (39.50)	<0.001*
• **Absent**	64 (53.78)	72 (60.50)		20 (16.81)	72 (60.50)	

*Note: Values are in frequency (percentage). † = p value <0.05 within group (Right eye Vs. left eye of the same group) analysis (Wilcoxon Signed Ranks Test). * = P value <0.05 between group (Study Vs. Control) analysis (Chi-Square test)*

SCR (p<0.001), LL (p<0.001) and STR (p<0.001), while no significant change in PS (p<0.397), IC (p<0.896), AR (p<0.212) and IS (p<0.054) between the study and control groups.

4. DISCUSSION

The present study was performed to compare various iris manifestations such as PS, IC, IPB, AR, ANW , SCR, IS, LL, and STR sensitivity between patients with COVID-19 positive and their age and gender matched non-COVID-19 individuals. The findings of this study showed that the visibility of IPB, ANW, SCR, and LL (p<0.001) is higher both in the right and left irises, while IS was higher in the right iris and STR was higher in the left iris of the study group participants than that of the control group participants.

First, the iris sign PS plays a significant part in health of an individual. Pupil's abnormal contraction (miosis), abnormal relaxation (mydriasis) and flattening indicates the hyperactive digestive system, hypoactive digestive system and a disruption in the nerve supply to the organs respectively [4]. The findings of this study showed a difference (Slightly missed level of significance) (p<0.051) in PS on between-group comparison, which might signifies that patients with COVID-19 positive have constricted pupil than that of their non-COVID-19 control subjects.

Second, the evaluation of the IC (tissue integrity: both biliary and hematogenic) assesses the individual's ability to tolerate diseases and processes of impairment that lead to the disease [12]. The study showed no statistical significant difference but provides equal chance to both

biliary and hematogenic constitutions in study group.

Third, the IPB is the inner edge of the posterior epithelial layer curling through the iris towards the pupil. Literature suggests that IPB reflects the stomach area. The color of IPB is incredibly bright, when the stomach is over-acid, in contrast, and it is darker, when the stomach is in under-acid condition. Both the stomach and the sphincter muscle of pupil are innervated by the parasympathetic nervous system [10]. Pan et al. [13] reported that SARS-CoV-2 indirectly or specifically affects the digestive system by an inflammatory reaction. The chain reaction of inflammatory factors and viremia can affect the digestive system. Studies showed that up to 53.4% of patients find viral nucleic acid in stool samples. The study showed a higher visibility of darker colour IPB in the study group compared to the control group. It suggests that the presence of chronic under-acid condition of stomach in patients with COVID-19 compared to non-COVID-19 individuals.

Fourthly, AR (the nutritional area between the collarette and the inner pupil line) indicate the efficiency of gastrointestinal nutrient absorption ability which is not significant and the possible explanations will be discussed in further studies [12].

Fifthly, evaluation of the ANW (the area around one-third of the distance away from the pupil) is the most significant characteristic of the iris. In normal iris, the ANW and intestinal area should be symmetrically encircled around the pupil, but abnormalities are seen if this alignment is altered. A small narrowed sympathetic nerve wreath signifies spastic, over-irritation of the intestines which brings about spastic constipation [14]. The study showed higher visibility of constricted ANW in the study group compared to the control group which signifies the over-irritation of intestines of study group.

Sixthly, like lungs, skin plays a dual role of breathing and elimination. Skin has millions of pores streaming from a contrast current of gases and pollutants. Secrete moisture to regulate body temperature. When pores are closed, toxins accumulate under the skin and then return to the blood lymph. The skin also revolt with rashes while removing toxins. Extreme skin condition represents complex, persistent physiological imbalances. The skin region is on ciliary edge of iris, according to Naturopathy. When it is sluggish, inactive, or accumulated contaminants, it occurs in varying shadings of grey, brown, and black called Scurf rim. The black, the more acidic and inactive the skin [4]. According to Magro et al.COVID-19 may have small-vessel occlusion symptoms [15]. This may be petechiae or small bruises and brief livedoid eruptions. 8.8% of patients who tested positive for extreme acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have reported COVID-19 skin rash in several types and at various stages of illness [16]. The skin provides clues inside the body for many health problems. If the infection travels across populations, any new skin rashes should be paid careful attention. The SCR visibility was higher in the study group compared to that of the control group. This might suggest that COVID-19 severe cases might have had an underactive, sluggish skin than that of the individuals without COVID-19.

Seventhly, the IS, a sign with white markings in the iris that indicates acute inflammation [4]. SARS corona viruses have been shown to attack immune cells in addition to lung epithelium as the main injury site and hyper-reaction plays an important role in immune damage and pathogenesis of the virus [17]. Immune responses triggered by other viral infections such as influenza induce changes in the gut microbiota resulting in dysbiosis and increased permeability of the intestine, which can cause secondary infection [18]. High levels of circulating pro-inflammatory cytokines from viral infections can change gut microbiota and disrupt intestinal integrity. Due to the well-balanced bidirectional interaction between gut microbiota and immune system, a malfunction in the small intestine leads to altered gut microbiota and inflammation. Increased inflammation in the intestine leads to leaky gut for translocation of bacterial antigens and contaminants into systemic circulation, further aggravating the septic state of COVID-19 patients. An inflammatory response may then lead to multiple organ failure [19]. A review of critically ill patients hospitalised in an intensive care unit found multiple organ dysfunction associated with elevated intestinal permeability [20]. Decreased gut barrier integrity includes translocating bacteria and inflammatory agent to distant organs via intestinal lymphatics, leading to sepsis and multiple organ failure syndrome [21]. The findings in our study showed that the visibility of IS seem higher in the control group, which may speculate that associated co-morbid conditions of the elderly control group participants might be

an important underlying factor for the development of this occurrence.

Eighthly, numerous iris marks showed lung disease detail. Inherent weakness appears as open and closed lesions paired with white-black shades [10]. Human respiratory tract is the primary entry site for various microorganisms. Interestingly, gut and lung microbiota are linked by a complex bidirectional axis through lymphatic [22] and blood circulation, and alteration of one mucosal compartment will directly affect distant mucosal site. This could be the reason for higher frequency (percentage) of lung lesions in the study group compared to that of the control group. There is indeed a major variation in lung lesion visibility frequency (percentage) and STR when comparing within group outcomes. The frequency (percentage) of lung lesion in the right iris tends to be higher compared to that of left iris, which could be partly linked to anatomical differences in the left and right lungs. The right primary bronchus of the trachea is longer, narrower, and more upright than the left, touching the right lung root an inch higher than the left bronchus, [23] partially explaining why the right lung is more vulnerable to infection. This anatomical variation may explain why our finding showed the right iris was a better predictor of lung lesion involvement.

Ninthly, the results in our study showed the visibility of STR was higher in the left iris of the study group than the control group. If stressed, some people develop maladaptive symptoms, while others maintain normal behaviour. This adaptive response to stress is known to be controlled with the medial prefrontal cortex (mPFC). The left hemisphere's mPFC neurons control social behaviour stress effects. Under stressful conditions, the right mPFC plays a dominant role in stress acquisition, while the left-hand mPFC determine the expression of a social, chronic stress-influenced behaviour which may be reflected in the iris, as concentric circles known as STR [24].

Early signs of chronic illness can be recognized to treat the condition before an incurable condition develops. Literature suggests that the iris is a microcosmic screen that symbolically displays the microcosmic realities of constitutionally inherited strengths, weakness, disease pathways, toxic accumulations, inflammatory and exudative conditions [25]. The research findings correlates few iris signs such as PS, IPB, ANW, SCR, IS, LL and STR concurrently with the health status of covid-19 severe cases that can be used in the clinical setup.

5. CONCLUSION

This non-interventional observational study suggests that iris manifestations of patients with COVID-19 positive are significantly different from that of individuals without COVID-19. To establish the relationship and its clinical and public health potential, further research is required.

CONSENT AND ETHICAL APPROVAL

The study protocol was approved by the institutional ethics committee (RES/IEC-GYNMC/2020/81), and written informed consents were obtained from all the individuals who were participated in the study.

STRENGTHS OF THE STUDY

This study appears to be the first study to compare the iris manifestation of COVID-19 severe cases and non-COVID-19 participants. The findings will be of broad use to the scientific and medical communities searching for safe, cost-effective diagnostic approach. The present study is important in furthering our understanding of the importance of looking into the iris for diagnostic purpose.

LIMITATIONS OF THE STUDY

The study had relatively small sample size and the sample size was not calculated based on the previous studies and the study findings need to be interpreted cautiously. Thus, more research is required with larger sample size to develop a deeper understanding of the relationships between changes in the iris and specific disease conditions.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/68648