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NEW ONSET HYPERTENSION IN POST COVID-19 RECOVERED PATIENTS: A CASE SERIES FROM A TERTIARY CARE HOSPITAL IN EASTERN INDIA

Internal Medicine

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ABSTRACT

Coronavirus Disease -19 (Covid-19) is a global challenge due to its catastrophic impact on healthcare demographics worldwide. Post Covid Syndrome is a new clinical entity that has emerged as a concern in recent times. It is defined as the presence of some persistent symptoms like fatigue, cognitive impairment and sleep disturbances in patients even after four weeks of recovery from Covid-19. Recent medical literature has hinted on Post-Covid vascular complications and our study has supplemented it by reporting new-onset hypertension in a series of eight patients within four weeks of recovery from laboratory proven Covid-19. None of the patients had pre-existing hypertension, cardiac disease, renal abnormalities or any history of long term steroid intake. These patients presented to the fever clinic with initial symptoms of fever, sore throat, mild cough and fatigue. `They were managed conservatively at home but one of the patients required hospital admission due to hypoxia.All the patients recovered within ten days of presentation and weekly follow-up visits were scheduled for six weeks at Post-Covid Recovery clinic. At the clinic, some of them complained of persistent headaches, occasional palpitations or prolonged fatigue. Examination incidentally revealed consistently elevated blood pressure in all the eight patients, even those who did not have any post covid symptoms. They were advised on antihypertensive drug therapy and lifestyle modifications after six week of routine follow-up and home monitoring. It is proposed that the close binding of the virus with Angiotensin Converting Enzyme-2 (ACE2) can lead to decrease in the serum enzyme levels, which in turn inhibit the protective pathway of the Renin-Angiotensin-Aldosterone (RAAS) axis. It might lead to imprudent rise in Angiotensin-2 and thereby blood pressure. Hypertension and its concomitant effect on target organ damage is a well known risk factor for increased mortality and morbidity among hospitalized Covid-19 patients. The development of hypertension and other cardiovascular manifestations in the post covid-19 recovery phase warrants further research to understand the molecular mechanisms, early identification and timely intervention to reduce incidence of adverse cardiovascular events in such patient cohorts.

KEYWORDS

Post Covid Syndrome; Hypertension; RAAS Axis; Endothelial Dysfunction

Introduction:

Coronavirus Disease 2019 (Covid-19) is a highly infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus -2 (SARS-CoV2). According to reports the first case was identified back in December 2019 in Wuhan, Hubei Province, China[1] and finally the World Health Organization(WHO) declared it as a pandemic on 11th March 2020. It has had a catastrophic impact on the global demographics with 450 million infections and more than 6 million deaths [2]. Although the virus primarily impacts the respiratory tracts , the disease can demonstrate clusters of symptoms ranging from mild cough, headache, dyspnea to critical symptoms like multi-organ failure and shock. Multiple long-term consequences exist even after recovering from the illness that is termed **Post-covid syndrome** [3]. Although there is no available definition in medical literature because of its recent advent, general consensus has elucidated it as the presence of persistent symptoms and/or long-term complications even after four weeks of recovery from Covid-19 [4]. It encompasses a range of symptoms that includes fatigue (the most common symptom), dyspnea, sleep disturbances, cognitive impairment as well as some mental conditions like anxiety and depression [5]. There has been some evidence of involvement of blood vessels in the acute phase of Covid-19 that leads to certain complications like micro-angiopathy, coagulation abnormalities, endothelial dysfunction and vessel inflammation [6]. However, in comparison, few studies are available on the vascular complications of patients recovering from Covid-19. Our study aims to bridge this gap by highlighting the diagnosis of new-onset hypertension in a series of eight patients within four weeks of recovery from Covid-19.Early diagnosis of hypertension and subsequent intervention measures will lead to decreased morbidity and mortality arising out of hypertension and its impact on target end organ damage.

METHODOLOGY:

A retrospective case series of 8 patients who presented to the Fever Clinic of Medical College and Hospital Kolkata, (a tertiary care hospital with a dedicated COVID wing and Post Covid Followup facilities),with complaints of fever, sore throat, fatigue during the period of December 2021 to January 2022 was done. The patients were detected COVID 19 Positive by RT PCR tests at the fever clinic. Regular follow-up visits were scheduled for six weeks post-recovery from Covid-19 at the Post Covid Recovery Clinic of Medical College and Hospital, Kolkata. Patient data was retrieved from Fever Clinic Case sheet, & Post Covid Recovery Clinic Records.Informed consent was obtained from the patients prior to publication of the patient data. No loss to follow-up was noted amongst the study subjects. Data has been anonymised and tabulated using Microsoft Word/Excel 2010 software.

Case Presentation:

Out of the eight patients observed, three were women;five were young adults (age< 40 years) and three were middle-aged adults (40-60 years).All patients were residents of Kolkata or its suburbs. None of the patients had any pre-existing hypertension, cardiac or renal abnormalities or any other medical conditions requiring regular steroid intake. Pre-existing comorbidity was present in some patients: **(Patient 5)** was diabetic with good glycemic control on oral hypoglycemic agents. His baseline serum fasting blood glucose, urea, creatinine, triglycerides & HbA1c done three weeks before presentation were 92mg/dl, 18 mg/dl, 0.7mg/dl and 98 mg/dl, 6.3 respectively. **Patient 3** had hypothyroidism on Levothyroxine (50) and a 54-year-old male had post-traumatic osteoarthritis **(Patient 4)** of the right knee. The co-morbid patients were on medication for their respective ailments and had no complications due to the existing illness at the time of presentation.**Patients 2 and 7** occasionally consumed alcohol and all patients were non-smokers.

The demographic characteristics, clinical signs, and laboratory

findings of all eight patients are summarized (in Table 1) below. The baseline blood pressures were normal (<130/80mmHg) for all individuals on presentation. Blood pressure measurements in the Post Covid Recovery Clinic were measured as per the JNC 8 Guidelines[7]. The baseline blood sugar, TSH, LFT, and serum electrolytes were found within the reference range for all patients. However, some other blood investigations like serum urea, creatinine, C-reactive protein, D-dimer, and ferritin were ordered on the fifth day of illness. The above mentioned blood tests were performed at the Central Laboratory of the hospital. All patients recovered within ten days of onset of symptoms but they continued to experience fatigue, joint pain,palpitations and headache, they were kept on weekly follow-up care for six weeks post-recovery and their blood pressure levels along with other parameters were monitored.

Table 1. Table detailing the clinical features, lab reports and blood pressure readings of all patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Demographics								
Age Gender	36/M	24/M	38/F	54/M	58/M	39/M	31/F	42/F
BMI (in kg/m^2)	22.5	27.4	23.1	22.7	24.8	24	23.2	22.8
Comorbidity	None	None	Hypothyroidism	Osteoarthritis	Type 2 Diabetes Mellitus	None	None	None
Presenting Symptoms								
Time Gap between onset of symptoms to presentation at the clinic (in days)	1	2	1	1	2	3	3	1
Fever with chills	+	+	+	+	+	+	+	+
Sore throat	+	+	+	+	+	-	-	+
Cough	+	_	+	+	±	+	-	+
Respiratory Distress	_	_	±	+	_	-	-	-
Loss of taste/smell	+	+	-	±	+	_	+	+
Abdominal Pain and Diarrhoea	_	_	_	_	±	_	-	_
Severity of COVID 19 Disease at admission & Home/Hospital admission	Mild Home	Mild Quarantine Center	Mild Home	Moderate IPD	Mild Home	Mild Home	Mild Home	Mild Home
Clinical Signs on Examination								
Blood Pressure (in mmHg)	116/82	122/84	108/74	128/84	128/80	116/74	134/74	128/78
Oxygen saturation (at Room air in %)	98	97	95	92	98	97	97	96
Pulse Rate (beats per minute)	110	102	98	116	98	94	98	100
Temperature(in °F)	101	100.6	99.8	102.4	100.8	100	100.6	101.4
Pedal/facial/sacral edema	-	-	-	-	±	_	_	_
6min Walk Test	NORMAL	NORMAL	NORMAL	6min- 91% /120per min	NORMAL	NORMAL	NORMAL	NORMAL
Systemic examination findings	WNL	WNL	WNL	B/L wheeze,with mild bi basal Mid-end inspiratory fine rales	WNL	WNL	WNL	WNL
Investigations								
Sr.Urea (Ref:7-22mg/dl)	14	21	18	9	`11	16	13	16
Sr.Creatinine (Ref:0.6-1.2 mg/dl)	0.9	1.1	0.7	0.9	1.0	0.8	0.9	0.9
Sr.C-Reactive Protein (CRP)(Ref:<5mg/L)	9.6	6.1	18.2	38.6	12	10	4.8	12
D-dimer(Ref:<0.5µg/ml)	0.2	0.2	0.6	2.6	0.8	0.1	0.2	0.2
Sr.Ferritin(24-336µg/L)	91	62.4	118.8	316.8	82.2	58	112	176
2D Echocardiography (on 4th week of presentation)	(EF) 62%, with normal LV wall thickness, no RWMA	Normal LV function (EF = 64%) normal LV wall thickness with no RWMA	Ejection Fraction(EF) 66%, with normal LV wall thickness, no RWMA	Ejection Fraction(EF) 60%, with normal LV wall thickness, no RWMA	Ejection Fraction(EF) 62%, with normal LV wall thickness, no RWMA	Ejection Fraction(EF) 61%, with normal LV wall thickness, no RWMA	Ejection Fraction(EF) 62%, with normal LV wall thickness, no RWMA	Ejection Fraction(EF) 65%, with normal LV wall thickness, no RWMA
Weekly Follow-up after recovery from Covid-19 (BP readings in mmHg along with Pulse rate)								
Week 1	128/86 94	134/86 96	142/90 92	144/88 98	148/94 92	130/94 98	144/92 110	154/100 112
Week 2	140/88 90	140/92 92	144/92 94	146/82 90	152/96 92	138/90 98	140/96 100	148/100 104
Week 3	146/92 88	148/90 84	144/96 88	160/90 76	152/92 74	150/94 102	144/90 100	150/92 106
Week 4	148/90 86	152/90 82	154/90 92	162/94 78	156/92 74	158/96 104	156/98 108	152/94 102
Week 6 (after initial lifestyle measures)	148/92 88	154/90 84	150/88 80	158/94 72	160/94 80	150/94 96	150/90 90	150/94 102

During the course of COVID 19 illness, The patients were managed conservatively with antipyretics, mucolytics, cough-expectorants and vitamin supplements as per the prevalent MOHFW, Govt of India Guidelines[8]. **Patient 4** depicted signs of lower respiratory tract infection with persistent fever and was admitted in the Indoor COVID ward and was put on oral antibiotics and MDI Budesonide for 7days. His CT Thorax at the time of admission was normal.The patient during subsequent followup visits had complaints of intermittent dry cough which was relieved with symptomatic management within Week 2 of Recovery. Chest Xray and Pulmonary Function Test performed on 4th week of recovery showed no abnormality. Sputum tested for AFB was negative. **Patients 2 and 5** complained of sleep disturbances and headache on follow-up visits following recovery from Covid-19. Due to the nature of persistent symptoms along with finding of borderline elevated blood pressure, close follow-up visits were scheduled for them. **Patient 1 and 3** came on regular follow-up visits post recovery but incidentally they were found to be in pre-hypertensive stage. They were advised at home BP measurement & charting on alternate days, with due explanation of requisite protocols. The BP reading was constantly elevated on the charts. **Patient 6,** had no comorbidity and was in home isolation for Mild Covid 19 disease, however on subsequent follow up visits to the hospital, his primary complaint was a dull aching headache which had developed towards the end of his recovery period , & it would persist after waking up the next day. On thorough physical examination his Blood pressure was found to be raised,and upon subsequent BP tracking too. He had no difficulty in vision/photophobia/autonomic symptoms and his CNS , CVS systemic examinations were found to be normal. In **Patient 7,** initially the blood pressure was slightly above the optimal level , whereas the follow up visits at the post covid clinic was due to complaints of occasional palpitations with a feeling of chest heaviness. Her ECG revealed Sinus Tachycardia, whereas her cardiac injury biomarkers were negative. BP tracking revealed persistently high levels, which warranted initiation of therapy & lifestyle modifications. Similarly **Patient 8,** had palpitations and disturbed sleep with high BP at follow up visits, that required initiation of anti-hypertensive drugs (ARB + Beta Blocker), however her cardiac injury markers, 2D Echocardiography reports were normal.

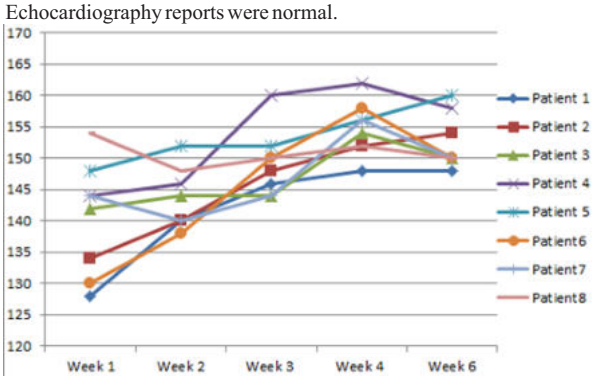

Figure 1. Graphical representation of Systolic Blood pressure (SBP) readings over six-week period

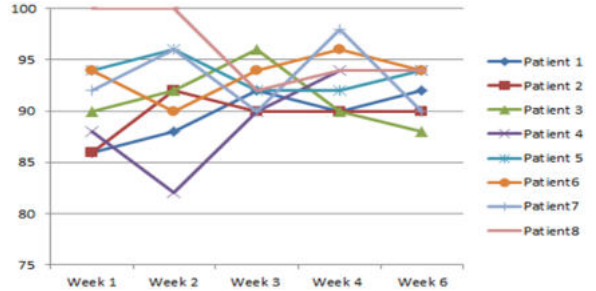

Figure 2. Graphical representation of Diastolic Blood pressure (DBP) readings over six-week period

The blood pressure reading of the patients is plotted in graphical format as follows in Figure 1 and Figure 2. It was seen that the blood pressure (BP) remained constantly elevated (>140/90mmHg) over the period of time and thereafter. The patients were encouraged to monitor and chart their Blood pressure at home. Initially after four weeks of constant monitoring and lifestyle interventions like exercise, DASH diet, low sodium intake etc, the BP continued to remain high. Thus, it depicted that all the patients had Stage 2 hypertension and immediate antihypertensive with regular follow-up visits were considered as management for the patients[9].

DISCUSSION:

There have been several studies that have recognized Post-Covid syndrome as a clinical entity. They have mostly reported incidences of fatigue, depression, myalgia, and olfactory or gustatory problems[10]. There is not much discussion on hypertension as a sequel of Covid-19. In a study conducted by Akpek, M et.al, there is evidence of new-onset hypertension within three to six weeks of recovery from Covid-19 [11]. In our observation we noted that the subjects did not have a history of hypertension , renal disease or known cardiovascular dysfunction, and the 2D echocardiographic studies performed showed no wall motion anomaly or Left ventricular hypertrophy, which serve as markers of long standing hypertension. Hence the development of hypertension could be deduced to be of recent onset amongst the study subjects. According to the European Society of Cardiology, new-onset hypertension is defined as values of Systolic Blood Pressure (SBP) ≥140mmHg and Diastolic Blood Pressure (DBP) ≥90mmHg in a hospital/clinic setting or SBP ≥135mmHg and DBP ≥85mmHg at home [12]. The pathophysiology behind this phenomenon is not yet fully understood. However, several theories have been proposed regarding this. SARS-CoV2 closely binds with the human ACE2(Angiotensin Converting Enzyme 2) receptor and thus can target the cells that express ACE2. It is formulated that ACE-2 acts as a protective enzyme to counteract the effect of the classical renin-angiotensin -aldosterone (RAAS) axis. ACE-2 degrades angiotensin-1 (ANG-1) and angiotensin-2 (ANG-2) into ANG-1-9 and ANG-1-7 respectively [13]. Thereby, it limits the amount of active ANG-2 available to bind to the ANG-1 receptor. The medical literature has various established evidence on the effects of levels of ANG-2 via the RAAS axis on cardiovascular conditions like hypertension and heart failure [14]. As ACE-2 acts as a receptor for binding of SARS-CoV2, an increase in infectivity may lead to excessive binding and depletion of ACE-2 enzymes. This can alter the balance between the classical RAAS axis and the protective axis(as shown in Figure 3). The decrease in ACE-2 can reduce the degradation of ANG-2 and the excessive ANG-2 levels might be responsible for cardiovascular complications like hypertension, heart failure, myocardial infarction, etc. Liu Y et al. in one of his studies also reported that the serum levels of ANG-2 in Covid-19 infected patients were in a linear correlation with the degree of viral load [15]. Some studies have shown that around 8-12% of patients having pre-existing hypertension who were infected with Covid-19 had direct myocardial injury and increased levels of cardiac enzymes like Troponin I, CK (Creatine Kinase) and CK-MB [16]. It also reported worsening of the disease and higher mortality in that population. As discussed earlier, the interaction of SARS-CoV2 with cardiac ACE-2, reports from a study by Park J. et. al. have demonstrated that RAAS inhibitors can be safely used in patients with Covid-19 [17]. RAAS inhibitors are known to decrease the inflammatory markers like Interleukin-6, CRP as well as the viral load and thereby shown to have mortality benefits. In a study conducted in Wuhan, China reports depicted that Covid-19 patients who had existing hypertension and not treated with any medications were found to have twice the mortality than those who underwent pharmacotherapy [HR =2.17 (1.03-4.54, P=0.04)] [18]. Thus, the rise in BP after recovery from Covid-19 is an area of concern in the practice of modern medicine that shall be studied in greater depth to determine the relationship and mechanism behind this phenomenon.

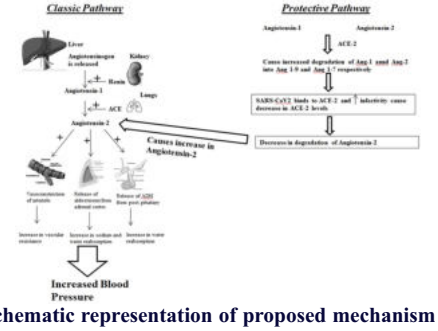

Fig. 3 Schematic representation of proposed mechanism of Post-Covid hypertension.

CONCLUSION:

Hypertension is the most common non-communicable risk factor worldwide and Covid-19 is a highly communicable disease that has

infected millions of individuals all over the world in recent times [19]. It can create havoc if they go into a cause-effect relationship. Even a mild infection with the disease can threaten an individual with the curse of hypertension, which might increase the morbidity and mortality because of its complications. Thus, regular follow-up visits shall be scheduled for a patient recovering from Covid-19 to monitor the blood pressure and manage it appropriately at the right point of time. We require further research into this field such that appropriate interventions and protocols can be devised for the delivery of quality healthcare in future.

Limitations of study:

The observation in 8 patients needs further validation by further studies among a larger set of post covid 19 recovery phase patients to understand a causal relationship between Covid 19 infection and hypertension. Molecular mechanisms involved need to be understood better which was beyond the scope of our study. To reduce Observer bias & incidence of White coat hypertension necessary precautions were taken, but such confounding factors were not possible to be eliminated.

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REFERENCES:

1. CDC. 2019 Novel Coronavirus, Wuhan, China. CDC. Available at https://www.cdc.gov/coronavirus/2019-ncov/about/index.html. January 26, 2020; Accessed: December 1, 2021.
2. WHO COVID-19 Dashboard. Geneva: World Health Organization, 2020. Available online: https://covid19.who.int/ (last cited: 03/15/2022, 4:22pm IST).
3. Patient-Led Research Collaborative Report: What Does COVID-19 Recovery Actually Look Like? An Analysis of the Prolonged COVID-19 Symptoms Survey by Patient-Led Research Team. [(accessed on 7 May 2021)]; Available online: https:// patientresearchcovid19.com/research/report-1/
4. Nalbandian, A., Sehgal, K., Gupta, A. et al. Post-acute COVID-19 syndrome. Nat Med 27, 601–615 (2021).
5. Arnold DT, Hamilton FW, Milne A, Morley AJ, Viner J, Attwood M, Noel A, Gunning S, Hatrick J, Hamilton S, Elvers KT, Hyams C, Bibby A, Moran E, Adamali HI, Dodd JW, Maskell NA, Barratt SL. Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort. Thorax. 2021 Apr;76(4):399-401
6. Roberts Kirsty A., Colley Liam, Agbaedeng Thomas A., Ellison-Hughes Georgina M., Ross Mark D. Vascular Manifestations of COVID-19 – Thromboembolism and Microvascular Dysfunction Frontiers in Cardiovascular Medicine Vol.7 2020.
7. James P. A., Oparil S., Carter B. L., Cushman W. C., Dennison-Himmelfarb C., Handler J. et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8) [published erratum appears in JAMA 2014;311(17):1809] JAMA. 2014;311 (5):507–20.
8. Availabe from : https://www.mohfw.gov.in/pdf/ Clinical Guidancefor Managementof Adult Covid19Patientsupdatedason17thJanuary2022.pdf
9. Smith, L., 2005. New AHA recommendations for blood pressure measurement. American Family Physician, 72(7), p.1391.
10. Androula Pavli, Maria Theodoridou, Helena C. Maltezou, Post-COVID Syndrome: Incidence, Clinical Spectrum, and Challenges for Primary Healthcare Professionals, Archives of Medical Research, Volume 52, Issue 6, 2021, Pages 575-581, ISSN 0188-4409
11. Akpek M. Does COVID-19 Cause Hypertension? Angiology. 2021 Dec 10:33197 211053903. doi: 10.1177/00033197211053903. Epub ahead of print. PMID: 34889662.
12. Williams, B, Mancia, G, Spiering, W, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018; 33: 3021–3104.
13. Santos RAS, Sampaio WO, Alzamora AC, Motta-Santos D, Alenina N, Bader M, Campagnole-Santos MJ. The ACE2/Angiotensin-(1-7)/MAS Axis of the Renin-Angiotensin System: Focus on Angiotensin-(1-7). Physiol Rev. 2018 Jan 1;98(1):505-553.
14. Patel, VB, Zhong, J-C, Grant, MB, Oudit, GY. Role of the ACE2/Angiotensin 1-7 axis of the renin-angiotensin system in heart failure. Circ Res 2016; 118: 1313–1326.
15. Liu, Y, Yang, Y, Zhang, C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci 2020; 3: 364–374.
16. The Task Force for the management of COVID-19 of the European Society of Cardiology T1 ESC guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 2—care pathways, treatment, and follow-up 2021 DO 10.1093/eurheartj/ehab697 Vol. 43: 11 SP 1059 11030195-668X
17. Park J, Lee S-H, You SC, Kim J, Yang K (2021) Effect of renin-angiotensin-aldosterone system inhibitors on Covid-19 patients in Korea. PLoS ONE 16(3): e0248058. https://doi.org/10.1371/journal.pone.0248058
18. Li J, Wang X, Chen J, Zhang H, Deng A. Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China. JAMA Cardiol. 2020;5(7):825–830. doi:10.1001/jamacardio.2020.1624
19. Gupta, R. and Xavier, D., 2018. Hypertension: The most important non communicable disease risk factor in India. Indian heart journal, 70(4), pp.565-57