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Original Article

Sex Linked Differences in Blood Pressure Indices (Mean Arterial Pressure and Pulse Pressure) of COVID-19 Patients After Six Minute Walk Test

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Abstract

Objective: The study was aimed to assess the sex-linked differences in the Blood Pressure Indices (BPI) i.e., Mean Arterial Pressure (MAP) and Pulse Pressure (PP) of COVID patients after 6 Minute Walk Test (6MWT).
Study type, settings & duration: This observational study was conducted in the Institute of Basic Medical Sciences, Khyber Medical University, Peshawar from December 2021 to April 2022.
Methodology: There were 54 participants (21 Females and 33 Males). Participants with previous COVID-19 infection with a cut off of 3 months post COVID, were included in the study. The participant's Heart Rate and Blood Pressure were recorded both before and after performing 6MWT.
Results: Both pre and post stress comparison of mean difference between post COVID males and females, was significant for MAP (Post-Stress *p* =0.002 and Pre-Stress *p* =0.01) only. PP and HR did not show any significant differences between the males vs females in both pre and post stress phase. While, post COVID females had a higher HR than males in both pre and post phase. General Linear regression model was developed while controlling for age and to check the relation between MAP, PP and HR. R squared came out to be 0.648 while MAP was significant with a *p* value = 0.012.
Conclusion: This study found a significant difference in Mean Arterial Pressure (MAP) between male and female COVID-19 patients after a 6-minute walk test, suggesting sex-based variations in blood pressure response post-infection. Further research with larger samples is needed to explore the clinical implications of this finding.
Key words: COVID, gender, blood pressure, cardiac physiology.

Introduction

The COVID-19 pandemic swept across the world and affected millions of people leading to causing significant morbidity and mortality. It became quite clear as the pandemic progressed, that certain demographic groups are at higher risk of severe disease and death from COVID-19.[1,2] In this regard, one area of interest has been the differences in mean arterial pressure (MAP) between male and female COVID-19 patients due to the potential risk factors for cardiovascular complications.

MAP is the estimate of mean pressure in the arterial vasculature during one cardiac cycle.[3] It represents an important cardiovascular health indicator and is commonly used as a tool to gauge the progress of critically ill.[4,5] While, pulse pressure (PP) is the difference of systolic minus the diastolic BP i.e., the pressure exerted by the heart in the arterial tree per heartbeat. It has been found to be a

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Authors Contribution

SSR, LK, DSA & UZ conceptualized the project. SSR, LK, UZ & HA did the data collection. LK, NF, DSA & HA did the literature search. SSR, DSA & UZ performed the statistical analysis. Drafting, revision & writing of manuscript were done by SSR, UZ & HA.

potential predictor of adverse outcomes in COVID-19 patients. A few studies have evaluated the differences in MAP between male and female COVID-19 patients but the results have been mixed. Moreover, recent studies have suggested that there may be gender-based differences in pulse pressure among COVID-19 patients.[6,7]

Six-minute walk test (6MWT) is an exercise based, simple and affective test. It is very safe, is well established and assesses exercise capacity of an individual. The test is carried our by making the participant/patient walk in straight laps, on a flat surface and as fast as possible.[8]

At present, However, the evidence on the impact of, sex linked differences in blood pressure indices of COVID patients after six-minute walk test, remains poor, and no accurate study is available regarding sex linked differences of MAP and PP. In this research we aimed to assess the sex-linked differences in the BPI (MAP and PP) of covid patients after 6MWT.

Methodology

This observational study was carried out in the Institute of Basic Medical Sciences at Khyber Medical University from December 2021 to April 2022. A total of 54 (21 Females and 33 Males) post COVID participants (>3 months had passed after resolution of COVID infection) were selected using convenience sampling. Sample size estimation was carried out using G*Power. Statistical test adopted was: difference between two independent means, test family was Paired Sample T test. A priori analysis was performed by keeping power at 95% (1-β) and 5% margin of error. Effect size was taken as 0.93. Allocation ratio was taken as 0.65. Sample size for group 1 was derived as 21 and group 2 was 33. Total sample size came out to be 54. Participants with previous COVID-19 infection with a cut off of 3 months post COVID, were included in the study. Those without a PCR unconfirmed COVID or less than 90 days post COVID infection, were excluded from the study. A proforma was designed having a detailed research questionnaire and written consent form. The participant's demographic data, Heart Rate (HR) and Blood Pressure (BP) were recorded both before and after performing 6MWT. The participant was seated on the laboratory couch or seat to record their blood pressure and heart rate via the Omicron M5 blood pressure recording device. Participants were then asked to walk for six minutes in straight lines within the premises of the laboratory. Later, the recordings for HR and BP were noted again via the same apparatus used prior to 6MWT.

Data was first organised in an excel sheet. Furthermore, formulas for obtaining MAP and PP were appplied to the data i.e., Mean Arterial Pressure (MAP) = Diastolic Blood Pressure (DBP) + 1/3 Pulse Pressure (PP) and Pulse Pressure (PP) = Systolic Blood Pressure (SBP) - Diastolic Blood Pressure (DBP). This data was then analysed on IBM SPSS Statistics for MacBook Pro, Version 26.0. (Armonk, NY: IBM Corp.). T test was applied to both pre and post stress variables to check for significance. Furthermore, matrix scatter plot was obtained and regression analysis was applied to the data. Data was presented as tables and figures.

The ethical approval was obtained from the Ethics Committee of Khyber Medical University Peshawar vide letter no. Dir/KMU-EB/CP/00098.

Results

A total of 54 participants including twenty-one females and thirty-three males were part of the study. The mean age of males was 25.12±5.18 years and females was 24.18±4.23 years. Height of males was 167.27±5.15 and females was 155.14±2.10 cm. Male participants had a mean weight of 69.94±9.12, while for females it was 59.19±4.18 Kgs. All these parameters were statistically significant i.e., p <0.05.

Both pre and post stress (6MWT) comparison of mean differences between post covid males and females, was significant for MAP (Post-Stress p =0.002 and Pre-Stress p =0.01) only (Table-1 & 2 and Figure). Sex linked differences in the pre and post stress significant BP Index (MAP) can be seen in Table-1 & 2.

PP and HR did not show any significant differences between the males vs females in both pre and post stress phase. There was gender-based differences in the MAP among the post COVID infection participants and the value of significant pre and post stress variables i.e., MAP was higher for males than the corresponding values for females. While, post COVID females had a higher HR than males in both pre and post phase.

Matrix Scatter Plot was obtained for MAP, PP and HR. In the post stress phase, MAP shows a positive correlation with HR and a negative correlation with PP**.** While in the pre stress phase, all the variables (MAP, PP and HR) show a positive correlation with each other.

General linear regression model

(Univariate Regression) was applied to the data set keeping gender as the dependant variable and MAP, PP, HR and Age as independent variables. R squared came out as 0.643 with age (p =0.023) and MAP (p =0.012) having significant p

values. In the second step, general linear model was developed while controlling for age and to check the relation between MAP, PP and HR. R squared came out to be 0.648 while MAP was significant with a *p* value =0.012.

Table 1: Comparison of blood pressure indices (MAP and PP) between post COVID males and females before performing 6 minute walk test.

	Group Statistics (Pre 6MWT)				
	Gender	*Mean± Std. Deviation*	*Mean Difference*	*Sig. (2-tailed)*	*95% CI of the Mean Difference*
Mean arterial pressure (MAP) DP + 1/3(PP) (mm Hg)	Male Female	97.87±8.99 90.87±10.03	-6.99	0.01	-12.52, -1.48
Pulse pressure (mm Hg)	Male Female	38.73±7.47 36.7±8.6	-2.03	0.38	-6.72, 2.65
Heart rate (beats/min)	Male Female	82.26±8.61 86.7±13.77	4.43	0.15	-1.66, 10.54

Table 2: Comparison of blood pressure indices (MAP and PP) between post COVID males and females after performing 6 minute walk test.

	Group Statistics (Post 6MWT)				
	Gender	*Mean± Std. Deviation*	*Mean Difference*	*Sig. (2-tailed)*	*95% CI of the Mean Difference*
Mean arterial pressure (MAP) DP + 1/3(PP) (mm Hg)	Male Female	102.69±13.52 91.77±10.61	-10.92	0.002	-18.01, -3.83
Pulse pressure (mm Hg)	Male Female	41.12±9.94 37.3±12.8	-3.81	0.227	-10.08, 2.44
Heart rate (beats/min)	Male Female	95.23±16.11 98.9±22.21	3.66	0.48	-6.84, 14.17

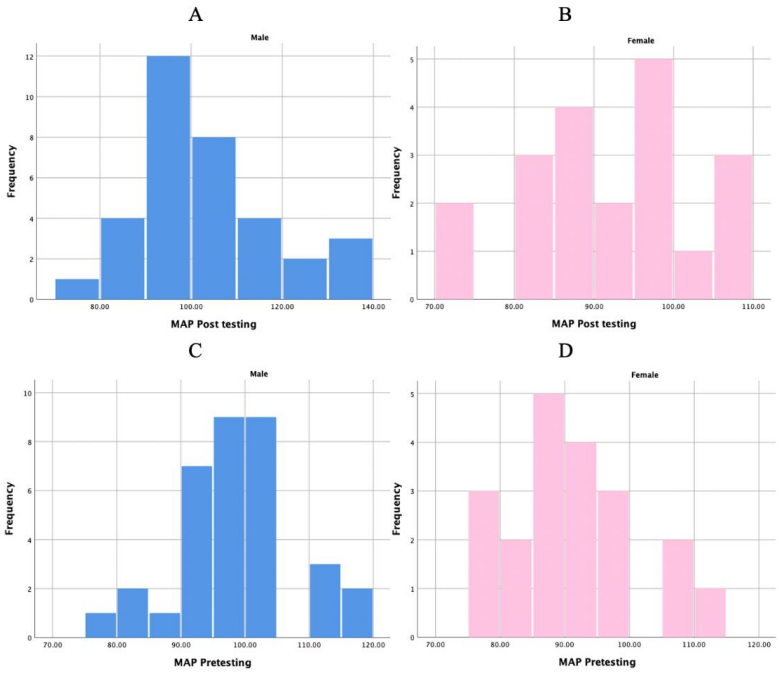

Figure: Significant mean arterial pressure. A. Post stress MAP of male participants B. Post stress MAP of female participants C. Pre stress MAP of male participants D. Pre stress MAP of female participants.

Discussion

To our knowledge, the current study is the first of its kind to comprehensively evaluate sex-related differences in BP indices following 6MWT. To date, there has been no reported evidence of a significant relation between COVID-19 and BP indices in our population. These significant parameters are of utmost importance given the sex-based design of the study. The gender-based differences in blood pressure indices have been studied in healthy populations but not in post COVID-19 population.[9] There have been evidence and recent published data on the gender differences in COVID-19 patients with arterial hypertension [10] or blood pressure readings during hospital stay [11] but no study reported relation between the gender based differences of MAP and PP with COVID-19.

Increased sympathetic tone also occurs during exercise, severe haemorrhage, and in times of psychological stress. The combination of these events increases both cardiac output and systemic vascular resistance, effectively increasing MAP. Hence, the measurement of MAP and PP both before and after the stress was taken into account in the study.[12]

The pathophysiology behind the gender-based differences in MAP isn't fully known. Several factors contribute to the difference. Severe cardiovascular complications, including myocarditis and thromboembolism have been reported with COVID-19 infection,[13,14] which could contribute to changes in mean arterial pressure. Additionally, sex differences in immune response and hormonal regulation may play a role in the differences observed.[15] The vasodilatory effect of oestrogen in females is also noteworthy while discussing gender differences in MAP.[16]

PP may also show gender based differences due to the several factors including higher estrogen levels in females contributing to arterial hardening and a raised PP in females. [17-19] The differences in MAP and PP between COVID-19 patients and healthy adults may have important clinical implications. Lower MAP and higher PP are associated with increased mortality in critically ill patients, and monitoring these values may be important in the management of COVID-19 patients.[12]

The results of studies on the participant have been inconsistent. Further research is needed to determine the underlying mechanisms and clinical implications of these differences. Given the importance of mean arterial pressure as a predictor of cardiovascular health,[4,5] it is an area of research that warrants continued investigation.

A few studies have checked BP values in the COVID patients [10,11] but not a single study had so far checked or reported the sex-linked differences in BP indices including MAP and PP after physiological stress. Thus, making our study unique, more meaningful and adding significant value to medical literature.

Our study, however, did have some limitations. Firstly, the grades of stress could have been defined and their effect on BPI studied. Secondly, a larger sample size with equal proportions of male and female participants would be better in studying gender differences. Thirdly, the study participants were mostly students, laboratory staff and faculty members. Hence, a sample with a more general and equal proportion of participants from a more diverse study population would be better in studying gender differences. Lastly, it was a single centre study, which is another potential limitation to consider.

This study found a significant difference in Mean Arterial Pressure (MAP) between male and female COVID-19 patients after a 6-minute walk test, suggesting sex-based variations in blood pressure response post-infection. Further research with larger samples is needed to explore the clinical implications of this finding.

Conflict of interest: None declared.

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