A Study of Endothelial Dysfunction Amongst Medical Professionals and Para Medical Staff in Pre- and Post-COVID-19 Pandemicity

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Introduction

Though endothelial dysfunction is often a long-standing chronic process, in acute infection endothelial cell injury may result in premature multiorgan system manifestations leading to severe morbidities[1]. This mechanism is the unifying underlying pathological process responsible for widespread long-term complications of SARS-CoV2 infection. Early recognition of endothelial dysfunction using non-invasive means like "Angio-defender" for assessing flow mediated dilatation (FMD) of brachial artery is desirable in younger age group – for recognising and treating modifiable risk factors of endothelial dysfunction. This denotes advanced vascular age as compared to their chronological age. For the purpose, we intended to record endothelial dysfunction status and vascular age among medical professionals of MGM medical college (a tertiary care hospital) who have served with heavy duties in COVID-19 pandemic.

Aim

To study endothelial dysfunction and vascular age status of medical resident doctors and paramedical personnel at MGM medical college and hospital, Chhatrapati Sambhaji Nagar, Maharashtra, India who were exposed to COVID-19 wards/OPD/ICU, using Angio-defender.

Objectives

To record and analyse various modifiable and non-modifiable risk factors observed in younger age group with higher vascular age vs biological age and compare the data with non-exposed medical/paramedical subjects.

Research design

Study area: Department of Medicine, MGM Medical College, Chhatrapati Sambhaji Nagar, Maharashtra, India.

Study period: 8 months.

Study design: Comparative analytical study.

Sample size: The study was done in two phases.

A. Phase I: 205 non-exposed medical/paramedical personnel (2018 - 2019).

B. Phase II: 200 medical/paramedical personnel exposed to COVID-19 pandemic while working in COVID OPD/wards/ICU.

Institutional ethics committee approval: Obtained.

Material and Methods

Medical personnel of age > 18 yrs who had engaged with COVID-19 patients' medical care in the hospital and who were ready to participate were included. Subjects irrespective of hypertension, dyslipidaemia, diabetes, obesity status were included for detailed records.

Endothelial dysfunction was considered when there was a change in flow mediated dilatation of artery using angio-defender. The vascular age was determined by using angio-defender device (Everist) which is CE certified and has been proven to be equivalent to the gold standard-BAUS imaging. The system comprises of inputs such as FMD, smoking habit, hypertension, HbA1C, total cholesterol and serum HDL levels for calculating the vascular age. The device used hyperaemia induced flow mediated vasodilatation for calculating FMD. Measurement of dilation of brachial artery was recorded at rest and after cut-off deflation after supra systolic compression (30 mm above systolic blood pressure for 5 mins) of either arm. Maximum flow velocity was measured in all subjects at rest and later within 15 sec of the cuff deflation. Vasodilation was assessed and calculated as percentage change in the arterial diameter compared to baseline value. Impaired FMD was defined as a value less than 10%, severe dysfunction was considered when value was less than 6% and moderate when values were between 6 - 10%. FMD value < 6% was considered a good predictor of presence of coronary artery disease.

For the purpose of this project, hypertension was defined as systolic pressure >140 mm Hg and diastolic pressure > 90 mm Hg for persons on anti-hypertensive medications. ADA criteria were used for defining type II diabetes

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mellitus. Cases of diabetes treated or on treatment having fasting blood glucose levels >126 mg% or HbA1C >6.4% were included. WHO criteria for Asian population were considered for defining body mass index {normal (18.5 - 23 kg/m²), overweight (23 - 27.5 kg/m²) and obese (>27.5 kg/m²)}. Dyslipidaemia was considered when total cholesterol value exceeded >200 mg/dL and HDL < 40 mg/dL. Smoking records were taken when the person smoked at least 5 cigarettes per day in the last month.

Results

The study result comprised analysis on pre-COVID phase and post-COVID phase in different age groups analysed for endothelial dysfunction using 'Angio-defender', calculating percentage change in arterial diameter compared to baseline. Results were statistically analysed and recorded.

Table I: Endothelial dysfunction in different age groups.

Age groups (years)	Post-COVID – phase II Pre-COVID – phase I	Normal (>10%)	Moderate (6 - 10%)	Severe (< 6%)	Total	P-value
16 - 25	Post-COVID-19	19	29	16	64	
	Pre-COVID-19	3	26	11	40	
	Total	22	55	27	104	**0.02 (S)**
26 - 35	Post-COVID-19	28	48	14	90	
	Pre-COVID-19	5	117	16	138	
	Total	33	165	30	228	**0.00 (S)**
36 - 45	Post-COVID-19	10	17	5	32	
	Pre-COVID-19	3	10	2	15	
	Total	13	27	7	47	0.66 (NS)
>45	Post-COVID-19	0	8	6	14	
	Pre-COVID-19	0	8	4	12	
	Total	0	16	10	26	**0.00 (S)**

Endothelial dysfunction in 36 - 45 years age group, was non-significant and as the age advance to more than 45 years of age group, the endothelial dysfunction was significant. However, the younger age group of 16 - 25 – 26 - 35 years were also having statistically significant endothelial dysfunction. Severity of the disease was statistically significant with increasing age.

Table II shows that greater endothelial dysfunction was noted in subjects having risk factors (< 2). The values shown are statistically significant. 22 subjects had severe endothelial dysfunction in pre-COVID-19 stage and 7 subjects in post-COVID-19 phase. More number of subjects were affected in pre-COVID-19 phase, which could be attributable to modifiable and non-modifiable risk factors.

Table II: Showing relation between endothelial dysfunction and risk factor.

FMD (%)	Post-COVID – Phase II Pre-COVID – Phase I	< 2 Risk factors	≥2 Risk factors	Total	P-value
Normal (>10%)	Post-COVID-19	32	25	57	
	Pre-COVID-19	11	0	11	
	Total	43	25	68	**0.01 (S)**
Moderate (6 - 10%)	Post-COVID-19	89	13	102	
	Pre-COVID-19	89	72	161	
	Total	178	85	263	**0.00 (S)**
Severe (< 6%)	Post-COVID-19	34	7	41	
	Pre-COVID-19	11	22	33	
	Total	45	29	74	**0.00 (S)**

Table III: Showing relation with endothelial dysfunction and gender.

FMD (%)	Post-COVID – Phase II Pre-COVID – Phase I	Male	Female	Total	P-value
Normal (>10%)	Post-COVID-19	17	40	57	
	Pre-COVID-19	7	4	11	
	Total	24	44	68	**0.03 (S)**
Moderate (6 - 10%)	Post-COVID-19	41	61	102	
	Pre-COVID-19	86	75	161	
	Total	127	136	263	**0.04 (S)**
Severe (< 6%)	Post-COVID-19	26	15	41	
	Pre-COVID-19	17	16	33	
	Total	43	31	74	0.3 (NS)

Out of 68 persons having normal FMD value, 11 (16%) were in pre-COVID-19 period and remaining 57 (83.82%) were in post-COVID-19 period. Similar changes were noted for severe endothelial dysfunction (< 6%) in pre- and post-COVID-19 period (Table III).

Table IV: Showing relation between risk factors and gender.

Risk factors	Post-COVID – Phase II Pre-COVID – Phase I	Male	Female	Total	P-value
< 2	Post-COVID-19	76	108	184	
	Pre-COVID-19	66	45	111	
	Total	142	153	295	**0.00 (S)**
≥ 2	Post-COVID-19	8	8	16	
	Pre-COVID-19	44	50	94	
	Total	52	58	110	0.81 (NS)

Females had more affliction than males in post-COVID-19 phase with risk factors (< 2), for reasons of more female nursing staff employment for COVID-19 care in the hospital (Table IV).

Table V: Showing relation between age and risk factors.

Age group	Post-COVID – Phase II Pre COVID – phase I	< 2	≥2	Total	P-value
16 - 25	Post-COVID-19	61	3	64	
	Pre-COVID-19	24	16	40	
	Total	85	19	104	**0.00 (S)**
26 - 35	Post-COVID-19	77	13	90	
	Pre-COVID-19	76	62	138	
	Total	153	75	228	**0.00 (S)**
36 - 45	Post-COVID-19	26	6	32	
	Pre-COVID-19	7	8	15	
	Total	33	14	47	**0.02 (S)**
>45	Post-COVID-19	11	3	14	
	Pre-COVID-19	4	8	12	
	Total	15	11	26	**0.02 (S)**

Statistically significant findings were noted in the post- and pre-COVID-19 period was respect to age with both < 2 and ≥2 risk factors affection. ≥ 2 risk factors were seen in 94 subjects in pre-COVID-19 period and 25 subjects in post-COVID-19 period. < 2 risk factors were seen in 111 subjects in pre-COVID-19 and 175 subjects in post-COVID-19 (Table V).

Discussion

Endothelial dysfunction has been recognised as a vital and critical component of COVID-19 disease. Since the vascular endothelial cells cover the entire circulatory system from heart to small capillaries, their study bears great prognostic significance as altered endothelial function presents with varied clinical complications and adverse outcomes. The importance of endothelial dysfunction has often been discussed in the setting of acute COVID-19 infection, with disparities observed in the extent of endothelial dysfunction/FMD lowering[2].

Endothelial dysfunction is a chronic process and may result in premature multiorgan system manifestations as 'long COVID-19 disorder'[2,3]. We have attempted to record endothelial dysfunction status and vascular age amongst medical/paramedical professionals of MGM medical college who have served arduous duties in the COVID-19 pandemic 2019 - 2021 (phase II study). The results were compared with phase I study wherein FMD values of medical professionals/paramedical personnel unexposed to this pandemic during 2018 - 2019 was carried-out. The present phase II study was carried-out with certain modifiable and non-modifiable risk factors like age, BMI, diabetes mellitus-

II and smoking, assessed using flow mediated vasodilation (FMD) of brachial artery, similar to study done in phase I. It was matched with age, gender and risk factors as cited.

The maximum number of subjects in the phase II study belonged to age 16 - 25 yrs. In apparently young (< 35 yrs), healthy individuals with abnormal values of endothelial dysfunction (< 10%) suggested subclinical/premature atherogenicity. In the phase II study with advancing age (>45 yrs), the severity of endothelial dysfunction was also noted to be higher. FMD values < 6% are considered valid predictors of the presence of coronary artery disease. However, discriminations are noted in the percentage of FMD and presence or absence of coronary artery disease (CAD) in study reported by Enderle *et al* in 1998[4]. Similar observations are found in the present study. A higher number of subjects (64/200), between 16 - 25 yrs, and despite receiving vaccination had FMD < 10% as compared to phase I study (40/200). The difference observed was statistically significant (Table I). A higher number of subjects with >10% FMD values could be attributed to good herd immunity in them and/or good development of immunity post-vaccination. Vaccination protection only provide a limited reference for immune status. Abnormalities of vascular disease, notably CAD, can possibly be modified over weeks to months with risk reduction therapy.

As regards association between endothelial dysfunction and risk factors, it was noted that in subjects having ≥ 2 risk factors, more subjects were affected in pre-COVID-19 than post-COVID-19. Reasons could be attributed to modifiable and non-modifiable risk factors (Table II and III). It was also observed in the post-COVID-19 phase II study that females had more affliction than males having risk factors < 2. The reasons to could be attributed more employment of female nursing staff in pandemic period (Table IV).

Higher affliction with < 2 risk factors was seen in post-COVID-19 period and may be attributed to presence of COVID-19 infection in either subclinical or symptomatic subjects. Further, ≥2 risk factors showed more number of subjects in pre-COVID-19 period as they had no exposure to COVID-19 pandemic. The probable reasons for less number of subjects in post-COVID-19 with ≥2 risk factors can be presumed to be strict confinement of these subjects at home who had minimal chances of street exposure during pandemic (Table V).

FMD serves as an important marker for premature atherogenesis. Age recognition of normal FMD values in post-COVID-19 phase in young when noted, may speak of lower vascular age to their chronological age. Such individuals are also advised supplementary vaccination with optimum time interval between doses to strengthen their

immune system. Though vaccination protection can only be assessed indirectly by detecting neutralising antibody level, has otherwise limited value. It is therefore, imperative, to have FMD assessment and the measures to intervene and prevent overt vascular disease by adopting timely risk reduction therapy.

Conclusion

COVID-19 infection continues to evolve since the beginning of the pandemic. The risk factors for endothelial dysfunction include history of CVD, history of COVID-19 in medical personnel and residents/paramedical staff who were on heavy duties in pandemic, could be regarded as risk factors for others and their own future endothelial dysfunction. Therefore, focus should be on assessment of endothelial function and identification of high-risk subjects through non-invasive endothelial function testing for finding their vascular age. Other biomarkers evaluation is also needed, viz., diabetes mellitus, hypertension, obesity, CVD, to recognise high-risk individuals. In our study, higher groups were significantly low having ≥2 risk factors.

Reasons attributable to this fact could be strict confinement and better care of modifiable risk factors at home. Use of angio-defender for FMD could prove as a useful tool in screening test for recognising early anticipated problems and long COVID derangements, especially in young age group.

References

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