Original paper

Prevalence of Cardiac Abnormalities in Post Covid-19 Adult Survivors Seen At Moi Teaching and Referral Hospital, Eldoret, Kenya

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Abstract

Background: Cardiovascular complications significantly contributed to the burden of Covid-19 morbidity and mortality during the 3-year pandemic that started in late 2019. Emerging evidence at the time showed that infection led to diverse cardiovascular complications associated with severe disease and increased morbidity and mortality. Covid-19 infection also resulted in the deterioration of pre-existing Cardiovascular Disease (CVD). Data from High-Income Countries (HIC) demonstrated that myocarditis, pulmonary thrombo-embolism with attendant right heart dysfunction, and acute coronary events were largely responsible for the complications but the long-term CV sequel remains unknown in populations residing in sub-Saharan Africa.

Objective: To describe the acquired cardiac, non-valvular, and rhythm abnormalities amongst patients and staff at Moi Teaching and Referral Hospital (MTRH) as well as students of Moi University School of Medicine (MUSOM) who had recovered from Covid-19 infection.

Methods: This was a cross-sectional study at MTRH with participants drawn from the in-patient wards, outpatient clinics, and staff and students of MTRH and MUSOM respectively. Participants aged 18 years and above who had previously been diagnosed with Covid-19 were consecutively recruited into the study. We excluded those with known cardiac disease prior to Covid-19 infection and those with severe chest deformities in whom imaging was technically difficult. Socio-demographic and clinical data were collected using a structured questionnaire. A standard 2-dimensional, Doppler (color and spectral) echocardiogram and 12 lead electrocardiogram were done. Blood samples were drawn for evaluation of LDL, glycated haemoglobin (HBA1c) and cardiac troponin.

Results: One hundred and seven participants were consecutively recruited between July 2022 and January 2023. Females comprised 53% of the population. Staff and students made up 45% of the study population. One hundred and four (97.2%) participants had normal Left Ventricular (LV) systolic function. There were no Regional Wall Motion Abnormalities (RWMA) reported. ECG changes which included T-wave inversions and Left Bundle Branch Block (LBBB) were reported in 3(2.8%) participants. Elevated (low density lipoprotein) LDL and overweight/obesity were the most prominent cardiovascular risk factors reported in 27% and 70% respectively.

Conclusion: Patients who recovered from Covid-19 infection at MTRH had a very low prevalence of cardiac disease but a high burden of cardiovascular risk factors.

Key words: Covid-19, Cardiac disease, Cardiovascular risk factors

Introduction

The Covid-19 pandemic ravaged the world between 2019 and 2022 causing over 766 million infections and 6.9 million deaths (1). Subsequently, studies demonstrated that infection led to diverse Cardiovascular Disease (CVD) complications, associated with severe disease and increased morbidity and mortality (2). Covid-19 infection also resulted in the deterioration of coexisting CVD through direct or indirect mechanisms. Moreover, the severity of Covid-19 correlates with cardiovascular manifestations. Accumulated evidence suggests that cardiovascular involvement is common, particularly in patients hospitalized with Covid-19 disease (3). Patients with cardiac risk factors and established CVD seem to have a heightened vulnerability to developing Covid-19 and tend to have more severe disease with worse clinical outcomes (4).

Several hypotheses have been postulated to explain the pathophysiology of cardiac disease in Covid-19 infection: they include Systemic

Inflammatory Response Syndrome (SIRS) with high levels of cytokine surge resulting in injury to multiple organs, including cardiac myocytes; direct myocardial injury, myocardial oxygen supply/demand mismatch, acute plaque rupture leading to Acute Coronary Syndromes (ACS) and catecholamine surge (5). Other mechanisms include adverse effects of medications e.g. corticosteroids, antiviral therapies and other immunological agents, and electrolyte imbalances, leading to arrhythmias (6).

With longer periods of survival, long-term effects like the "long Covid syndrome" emerged, characterized by cardiopulmonary and neurologic symptoms, chronic fatigue, dyspnea, chest pain, and dysautonomia persisting beyond 12 weeks following infection (7). Due to the novelty of Covid-19, long-term implications on the cardiovascular system, have remained largely unknown, and as such more studies are required in this area.

We investigated the acquired cardiac, non-valvular, and rhythm abnormalities among patients and staff at Moi Teaching and Referral Hospital (MTRH) as well as Moi University School of Medicine (MUSOM) students who had recovered from Covid-19, and their pre-existing global cardiovascular risk profile.

Materials and methods

This was a cross-sectional study carried out among adult Covid-19 survivors at MTRH between July 2022 and January 2023. A sample size of 150 participants was calculated using Fischer's formula based on a prevalence of 11% from a prior study (8) assuming a 5% level of significance and a precision of 5%. Following a low recruitment rate with a low event rate, we amended the protocol after the first 5 months of recruitment to combine the first and second primary outcomes, into a single composite outcome and recalculated the sample size. The final sample size came down to 107 participants. In addition, we also expanded our study population to include MTRH staff and MUSOM students to be part of the study population.

Participants were consecutively recruited from out-patient clinics, in-patient wards and adults studying at MUSOM or working at MTRH aged 18 years and above with history of Covid-19. We excluded individuals known to have cardiac disease prior to Covid-19 infection and those with severe chest deformities that would make imaging difficult. Written informed consent was obtained from all participants.

Using a structured questionnaire and data collection form administered by the Principal Investigator (PI) or a trained Research Assistant (RA), a detailed cardiovascular history was taken and anthropometric parameters measured. For in-patients with a history of Covid-19 infection, recruitment was done while patients were admitted in the wards. For in-patients with a new diagnosis of Covid-19 during that admission, recruitment was done after discharge during scheduled follow-up clinics. For students and staff members, fliers with study details were distributed around MTRH and those who met the criteria contacted the RA or PI for recruitment.

Blood samples were taken for LDL and Troponin-T analysis (Cobas Immunochemistry analyzer E601, Serial number 28E7-01). HBA1c was analysed using the BIORAD D-10 haemoglobin testing system (Serial Number DJB062703) at the MTRH International Organization for Standardization (ISO) accredited laboratory facility by a certified laboratory technologist.

A 12 lead ECG (Phillips PagewriterTC-20, Serial number CN21404317) was then taken with the patient supine and tracing was interpreted by the PI and confirmed by a cardiologist interrogating for ischemic changes (ST wave deviation, T- wave inversions, Pathological Q-waves) and haemodynamically significant arrhythmias (Atrial fibrillation and flutter, ventricular tachycardias and bundle branch blocks).

Finally, a 2-D transthoracic echocardiogram (Phillips CX50, Serial SG42005064 version: 5.0.2) was done by the PI/certified echocardiographer based on the American Society of Echocardiography Guidelines on image acquisition and interpretation (9). The final diagnosis was confirmed by a cardiologist after reviewing archived images. Our outcome measures included LV systolic dysfunction (defined as a left ventricular ejection fraction of less than 49%), pulmonary hypertension (defined as a pulmonary artery systolic pressure of ≥40mmHg at rest), regional wall motion abnormalities (defined as regional abnormalities in contractile myocardial function) and right ventricular dysfunction (defined as Tricuspid Annular Plane Systolic Excursion (TAPSE) of less than 1.7 cm.

Validation of the data was done before being entered into the computer. Data was entered into Microsoft Excel and analyzed using STATA version 16. Descriptive analyses were done for the socio-demographic characteristics of the sample. Variables collected included: age, gender, vital signs, random blood sugar, weight, height, history of pre-existing comorbidities, disease severity at admission and symptom presentation at recruitment, current ECG (arrhythmias, Q-waves) and ECHO parameters (LV function, RWMA, pulmonary artery pressure, TAPSE). Continuous data were summarized by mean with standard deviation and median with interquartile range as appropriate while categorical data was summarized using frequencies and proportion.

Ethical approval for the study was obtained from MTRH/Moi University ethical research committee (Research approval number 004136) and the study was carried out according to the principles of Helsinki.

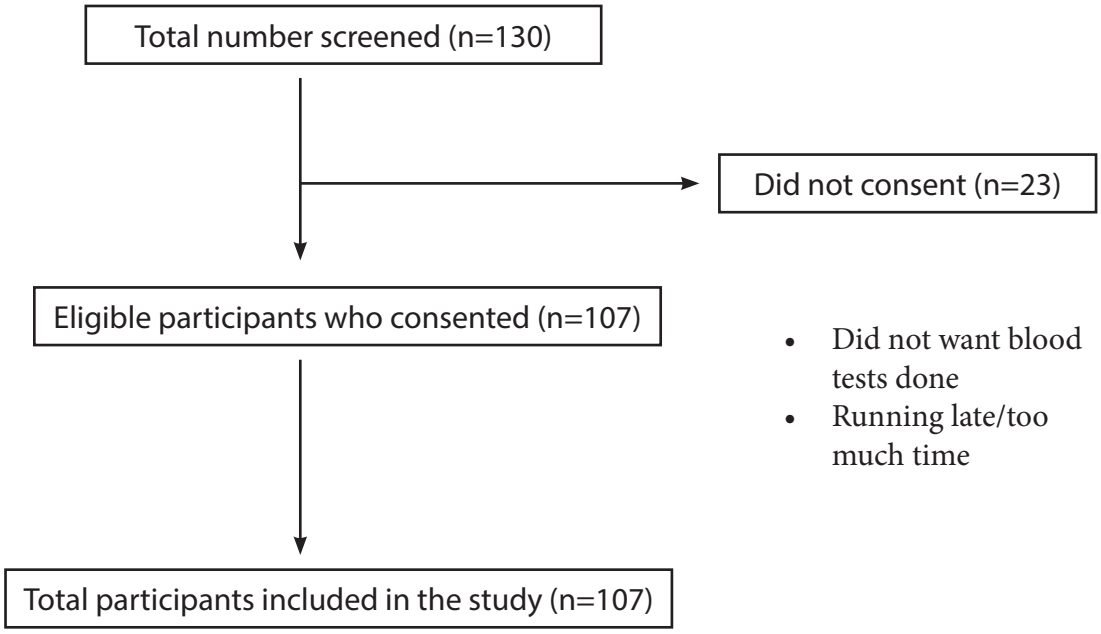
Results

A total of 130 participants who met the eligibility criteria were screened, out of whom 107 consented and were enrolled in the study (Figure 1).

There was an almost equal female to male distribution with 57 (53.3%) female participants recruited. Over 70% of study participants were under the age of 50 years. Forty-five per cent were medical personnel.

The mean duration from Covid-19 diagnosis was 17 months (range 4-32 months). The majority of the participants had mild Covid-19 disease at diagnosis, based on the level of care they required as per the WHO disease progression score (10) (Table 1).

Figure 1: Flow of study participants



Hypertension was reported in 40 (37.4%) of the participants, of whom 37 were on treatment. Abnormal HBA1c, defined as >6.5%, was reported in 23 (21.5%) participants out of these, 13 participants were on treatment for diabetes. Dyslipidemia was reported in 27% of participants having elevated LDL with only

Table 1: Baseline characteristics

Female gender – n (%)	57 (53.3%)
Age range in years (%)	10 (9.3%)
19-29	49 (45.8%)
30-39	19 (17.8%)
40-49	29 (27.1%)
>50	
Mean duration from Covid diagnosis in months (Range)	17 (4-32)
Medical profession – n (%)	49 (49.5%)
Covid vaccination – n (%)	84 (78.5%)
Presenting symptoms at enrollment – n (%)	
Dyspnea	4(6.5%)
Palpitations	6(5.6%)
Chest pain	24 (22.4%)
Tachycardia	8(7.5%)
Disease severity at diagnosis – n (%)	
Mild	99 (92.5%)
Moderate	7 (6.6%)
Severe	1 (0.9%)

one participant on treatment. Overweight and obesity were reported in 70% of the participants and 7 (6.5%) had a history of previous or current smoking (Table 2).

The majority of participants 104 (97%) had normal left ventricular function with EF above 50%. Pulmonary hypertension was reported in 7 (6.5%) participants, with 99 (92.5%) of participants having normal RV function. No significant RWMA abnormalities were reported in the entire population (Table 3).

Table 2: Cardiovascular risk profile

Abnormal HbA1c	23 (21.5%)
Hypertension	40 (37.4%)
Dyslipidemia	29 (27.1%)
Overweight/Obesity	75 (70%)
Smoking	7 (6.5%)

ECG abnormalities were reported in three participants, with T-wave inversions and LBBB in 1.8% and 0.9% respectively. There were no pathological Q waves. Elevated troponin T was reported in 7 (6.5%) participants (Table 4).

Table 3: Echocardiographic features

Reduced LVEF	3(2.8%)
Pulmonary hypertension	7(6.5%)
Reduced TAPSE	8(7.5%)
RWMA	0

Table 4: ECG changes and biomarkers

Pathological Q-waves	0
ST segment deviation	0
T-wave inversion	2 (1.8%)
LBBB	1 (0.9%)
Elevated TnT	7 (6.5%)

Discussion

Numerous studies done in the past 3 years on the long-term effects of Covid-19 on the cardiovascular system have reported varying prevalence of cardiac disease following recovery. We found a low prevalence of left ventricular dysfunction in this study population with only 2.8% of participants showing reduced left ventricular function of less than 50%. This is consistent with a retrospective study done in a cardiology clinic at the Washington University School of Medicine in St. Louis, Missouri, USA (11). Similarly Garcia-Zamora *et al* (12) in a multicenter ECHO-based registry demonstrated reduced LVEF and RWMA at 3% and 1.1% respectively.

Most studies on post-Covid cardiac disease are based on Cardiac MRI (CMR). One study done on recently recovered patients (median duration, 71 days from diagnosis to CMR), demonstrated cardiac involvement in 78% and ongoing myocardial inflammation in 60% of participants (13). Our study being ECHO based may explain the lower prevalence of cardiac injury likely due to the lower sensitivity of echocardiography in demonstrating sub-clinical injury. We also attribute the low prevalence of LV dysfunction to the largely mild disease the participants suffered, as opposed to the high prevalence reported in participants with severe disease (3). Additionally, the mean duration of our study was much longer (mean of 17 months) and hence many participants had likely recovered from any injury that may have occurred over the acute phase.

Pulmonary hypertension and reduced TAPSE, signifying reduced RV systolic function were reported in 6.5% and 7.5% of participants respectively. Similarly, an ECHO-based study by Tudoran *et al* (14)

demonstrated pulmonary hypertension in 6.5% and right ventricular dysfunction in 10.3% on Right Ventricular Global Longitudinal Strain Pattern (RV-GLS). The higher prevalence of pulmonary hypertension and right ventricular dysfunction as compared to left ventricular dysfunction is likely due to the sequelae of lung disease as a result of fibrosis, inflammation and microthrombi formation during acute infection (8). A prospective, single-center, observational cohort study of individuals with possible subclinical cardiac involvement with no formal clinical indication for CMR imaging, showed a prevalence of 1.4% of right ventricular failure on ECHO at a median duration of 1 year following Covid-19 diagnosis (15). Daher *et al* (16) found no abnormalities in an echocardiogram performed 6 weeks after discharge in 33 patients.

Only three (2.8%) participants in our study demonstrated significant ECG changes, with two participants having T-wave inversion and one with LBBB. Two of the participants with abnormal ECG findings had a history of severe Covid-19 disease with one being admitted to the Cardiac Care Unit (CCU) and undergoing thrombolysis for ST Segment Elevation Myocardial Infarction (STEMI-ACS) and the second one admitted to the ICU requiring ventilatory support. The high proportion of normal ECG findings (97.2%) are likely due to milder disease with minimal cardiac inflammation due to the younger age group of participants. However our ECG findings are in contrast to the Uganda post-Covid study that reported 18.9% abnormal ECGs with non-specific T-wave inversions being the most common abnormality (17). An ECG-based systemic review in young athletes similarly showed a very low prevalence of ECG changes in study participants (18), more consistent with the results in our study.

Only 6.5% of participants in this study had elevated troponin levels. Several studies have reported elevated cardiac biomarkers following Covid-19 infection, especially in the acute phase of infection (13). There is scanty data on elevated TnT levels beyond 6 months. One case-control study found that there was no difference in TnT levels between cases and controls at a median follow-up of 173 days (19), showing that these biomarker levels normalize with time. This would explain the low prevalence of elevated TnT in our study.

In terms of cardiovascular risk factors, overweight/obesity was the most common, with 70% of participants having a BMI ≥25kg/m^2. Systemic hypertension, abnormal HBA1c and dyslipidemia occurred in 37%, 21%, and 27% respectively with only 6.5% having current or past smoking history. Several studies done during the pandemic reported increased risk of Covid infection and worse clinical outcomes in overweight and obese patients (20,21). Therefore, it is likely that the high prevalence of overweight and obesity in our study population may have introduced a selection bias as these population was at a higher risk of contracting infection due to their high BMI. The high prevalence of elevated HBA1c, which is in contrast to currently available local data (22) as reported in the STEP wise Survey, is alarming and needs further interrogation with regular follow-up of this population and correlation with symptoms and fasting blood sugars. It is likely that due to the younger age of the participants, the duration of these CVD risk factors hasn't been long enough to manifest as coronary artery disease but there is potential for progression and hence need for follow-up. Studies in the acute phase of severe Covid-19 infection reported increased mortality in patients with prior CVD (4) demonstrating a mortality of 69.4% in patients with prior CVD and elevated troponins compared to 7.62% in patients without prior CVD and normal troponin levels.

Chest pain, dyspnea, palpitations and tachycardia, which are part of the long Covid syndrome, were reported in 22.4%, 3.7%, 5.6% and 7.5% respectively. This is lower compared to a study carried out in Uganda on ECG findings in long Covid (17) which reported chest pain, dyspnea and palpitations in 55%, 42% and 29.3% respectively.

The lower prevalence of persistent symptoms may be due to the fact that the majority of study participants suffered mild disease during acute Covid-19 infection with 92.5% recovering at home with a WHO severity score of 2 (10). A study carried out in the U.K. reported that at least a third of those who recovered from Covid would go on to develop long-term symptoms (23), which was consistent with our study findings. Furthermore, a meta-analysis by Chen *et al* (24) reported a global prevalence of 0.43 (95% CI: 0.39, 0.46) with fatigue being the most common symptom.

Our study has several limitations, firstly it was a single-center study. Secondly, the younger age and history of mild disease in our study participants, may not allow generalization of our findings to an older population, who suffered from more severe disease and with more CVD risk factors. Thirdly, this being an ECHO-based study, it may have missed more subtle features of residual cardiac disease as 2D- ECHO and resting ECG are relatively insensitive for screening of asymptomatic myocardial / coronary disease, unlike CMRI which has been used in comparative studies.

Conclusion

Adults who recovered from Covid-19 infection at MTRH had a very low prevalence of cardiac disease but with a high burden of cardiovascular risk factor profile. The heightened CVD risk factor profile is concerning for a relatively young and ambulatory patient population, hospital staff and medical students.

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