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Plasma Coenzyme Q10 and NT-proBNP Levels in COVID-19 Patients and Their Relation to Occurrence of Subtle Cardiac Abnormalities Detected by Echocardiography

Sandra Karas[1], Yasmine Elshiwy[1], Hany William Z. Hanna[1], Mahmoud Saad Nwar[2], Iman A. Mandour[1]

[1] Clinical and Chemical Pathology, Faculty of Medicine, Cairo University, Kasr Al Ainy, Cairo, Egypt
[2] Critical Care Medicine, Faculty of Medicine, Cairo University, Kasr Al Ainy, Cairo, Egypt

ABSTRACT: Background: COVID-19 outbreak led to a series of acute atypical respiratory diseases. The host immune response to the corona virus "SARS-CoV-2" is considered a key determinant of disease pathogenesis and the resulting clinical outcomes. Coenzyme Q10 (CoQ10) is known for its role as a potent antioxidant in affected organs specially the cardiovascular system. We sought to investigate the early occurrence of cardiac abnormalities that may arise in severe COVID-19 infections by testing blood levels of CoQ10, N-terminal pro-brain natriuretic peptide (NT-proBNP) and performing conventional transthoracic echocardiography.

Subjects and methods: Subjects were categorized into three groups. Group "1": 30 COVID-19 cases requiring intensive care unit (ICU) admission, group "2": 30 mild COVID-19 home-isolated cases and group "3": 30 healthy age and sex matched controls. All subjects were tested for CoQ10 and NT-proBNP blood levels as well as conventional transthoracic echocardiography.

Results: There was statistical significance between the three study groups regarding ejection fraction (EF), tricuspid annular plane systolic excursion (TAPSE) and NT-proBNP (p-value: <0.001, 0.001 and <0.001 respectively). CoQ10 level was not significantly different between the three study groups (p-value: 0.496). A cut-off of 960.9 µg/L NT-proBNP is desired to predict the likeliness of ICU admission in COVID-19 patients with sensitivity 73% and specificity 90%. There was a weak negative correlation between CoQ10 and interleukin-6 (r-value: -0.391 and p-value: 0.032).

Conclusion: Subtle cardiac abnormalities that may happen as a result of severe COVID-19 infection can be detected by measuring blood levels of NT-proBNP and performing an echocardiography as a screening tool to all ICU-admitted COVID-19 patients. However, it is not recommended to measure plasma levels of CoQ10 in COVID-19 patients.

INTRODUCTION

Cardiac injury associated with COVID-19 may arise from direct effects of SARS-CoV-2 on the heart or the immense host immune response mediated primarily by pro-inflammatory cytokines such as interleukin-6 and interleukin-10. Generally, viral infections are one of the most common causes of acute myocardial injury that may end up with heart failure. Growing evidence indicates that COVID-19 infection can precipitate acute coronary and cerebrovascular events (Aghagoli et al., 2020).

Considering the well-established role of CoQ10 in reducing oxidative stress across affected organ systems, especially the cardiovascular system, it may be used as a predictive marker of those susceptible to severe COVID-19 disease with cardiac complications (Polymeropoulos, 2020).

An increase in the level of NT-proBNP is indicative of impairment of cardiac function and recognized as a valuable biomarker for evaluating disease prognosis and identification of patients with a higher probability of mortality (Wang et al., 2021).

Echocardiography is a highly valuable tool in the process of diagnosis and follow up of myocardial involvement caused by COVID-19 (Chen et al., 2020). Generally, patients with pneumonia may exhibit early alterations in right ventricular structure and function. These changes can be easily and quantitatively identified by measuring TAPSE (Biteker et al., 2016).

Left ventricular dysfunction has also been reported in many cases of COVID-19 related myocarditis. The non-invasive evaluation of left ventricular function by measuring EF by echocardiography could be a simple parameter to refine the short-term prognosis of COVID-19 patients (Soulat-Dufour et al., 2020).

SUBJECTS AND METHODS

Population of study

A case-control study was conducted in the period from February 2022 to March 2024 on 30 severe cases of COVID-19 infection requiring intensive care unit (ICU) admission "group 1", 30 mild COVID-19 home-isolated cases "group 2" and 30 healthy age and sex matched controls "group 3". All participants were recruited from Kasr Al-Ainy, Cairo University Hospitals.

Inclusion and exclusion criteria

Positive COVID-19 reverse transcriptase - polymerase chain reaction (RT-PCR) patients were included. Patients with different causes of pneumonia were excluded, as well as patients with known history of cardiac dysfunction, including ischemic heart disease, heart failure and significant valvular diseases.

METHODS

All participants underwent comprehensive history taking, laboratory measurement of CoQ10 and NT-proBNP blood levels and conventional transthoracic echocardiography performance. ICU-admitted patients were routinely tested for blood levels of ferritin, C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, procalcitonin and interleukin-6 upon admission.

Serum level of CoQ10 was measured by "ELISA" technique using a commercial kit from Bioassay Technology Laboratory, England.

Serum NT-proBNP level was assayed using electrochemiluminescence immunoassay technique performed on COBAS e601 (Roche, Switzerland).

Conventional transthoracic echocardiography for assessment of EF and TAPSE was performed to all study population. All echocardiographic studies were performed by an experienced cardiologist using the Philips Affiniti 50C (Philips Ultrasound Inc, United States of America) machine with transducer model S4-2 (4-2MHz).

Routine investigations of ICU-admitted patients were retrieved from their files in the ICU.

Statistical analysis

Statistics was done using IBM© SPSS© Statistics version 24 (IBM© Corp. Armonk, NY) and MedCalc© version 20.218 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023).

P-values <0.05 are statistically significant.

Correlations relating numerical variables are examined using Spearman's rank correlation. The correlation coefficient (r-value) is interpreted as follows: < 0.2 is very weak, 0.2-0.39 is weak, 0.4-0.59 is moderate, 0.6-0.79 is strong, ≥ 0.8 is very strong.

Receiver-operating characteristic (ROC) curve analysis is used to examine the discriminative value of NT-proBNP. The area under the curve (AUC) is interpreted as follows: < 0.6 is fail, 0.6-0.69 is poor, 0.7-0.79 is fair, 0.8-0.89 is good and ≥ 0.9 is excellent.

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RESULTS

Table (1): Comparison of the three study groups

Variable	ICU-admitted COVID-19 patients Group "1" (N=30)	Home-isolated COVID-19 patients Group "2" (N=30)	Controls Group "3" (N=30)	P-value
Male sex (N (%))	N=13 (43.3%)[a]	N=13 (43.3%)[a]	N=10 (33.3%)[a]	0.659†
Age (years)	58.5 (42 - 70)[b]	45 (32 - 63)[b]	45.5 (30 - 56)[b]	0.090‡
EF (%)	60 (55 - 63)[c]	66 (64 - 68)[d]	66 (64.0 - 68.0)[d]	**<0.001‡**
TAPSE (cm)	2.0 (1.8 - 2.4)[e]	2.4 (2.1 - 2.5)[e,f]	2.5 (2.3 - 2.7)[f]	**0.001‡**
NT-proBNP (µg/L)	1890.5 (644.2 - 15765.0)[g]	55.4 (18.9 - 327.6)[h]	33.5 (10.3 - 115.4)[h]	**<0.001‡**
Coenzyme Q10 (µg/L)	16.3 (14.8 - 17.5)[i]	15.6 (10.0 - 23.7)[i]	14.45 (10.8 - 18.5)[i]	0.496

Results are presented as median (interquartile range); †. Pearson chi-squared test. ‡. Kruskal Wallis test; P-value <0.05 is considered statistically significant; Values carrying the same symbol are not statistically significant; EF of group "1" vs. group "2": p-value:<0.0001; EF of group "1" vs. group "3": p-value:<0.0001; TAPSE of group "1" vs. group "3": p-value:<0.001; NT-proBNP of group "1" vs. group "2": p-value:<0.0001; NT-proBNP of group "1" vs. group "3": p-value:<0.0001; EF: ejection fraction, TAPSE: tricuspid annular plane systolic excursion; NT-proBNP: N-terminal pro brain natriuretic peptide.

The current study showed no statistical significance between group "1", group "2" and group "3" regarding sex, age and CoQ10 level (p-value: 0.659, 0.090 and 0.496 respectively). There was statistical significance between the three studied groups regarding EF, TAPSE and NT-proBNP (p-value: <0.001, 0.001 and <0.001 respectively).

EF was significantly lower in group "1" than group "2" and group "3" (p-value: <0.0001).

TAPSE was significantly lower in group "1" than group "3" (p-value: <0.001).

NT-proBNP was significantly higher in group "1" than group "2" and group "3" (p-value: <0.0001).

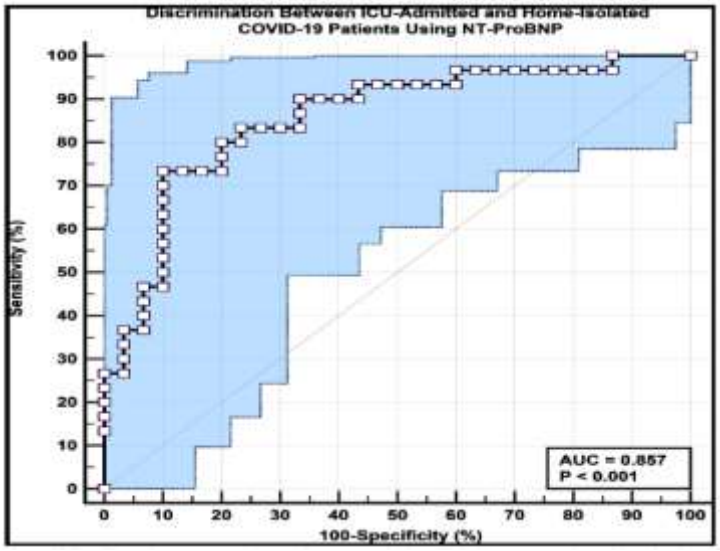


Figure (1): ROC curve for discrimination between group "1" and group "2" using NT-proBNP. Shaded area represents 95% confidence (95% CI) limits. NT-proBNP has good discriminative value (AUC = 0.86, p <0.0001). Best cutoff criterion is NT-proBNP >960.9 µg/L (sensitivity = 73%, specificity = 90%).

Natural Resources for Human Health
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NT-proBNP showed strong discriminative ability for prediction of ICU admission in COVID-19 patients (AUC: 0.86, p-value: < 0.0001) with anticipated cutoff of 960.9 µg/L (sensitivity: 73%, specificity: 90%).

In contrast, CoQ10 demonstrated poor discriminative value (AUC: 0.57, p-value: 0.312).

Table (2): Correlations among NT-proBNP, coenzyme Q10, EF and TAPSE

		NT-proBNP		Coenzyme Q10		EF		TAPSE	
Group	Variable	r	p	r	p	r	p	r	p
All subjects (groups "1", "2" and "3") (N=90)	NT-proBNP	-	-	0.072	0.498	**-0.658**	**<0.001**	**-0.539**	**<0.001**
	Coenzyme Q10	0.072	0.498	-	-	-0.063	0.553	-0.054	0.615
	EF	**-0.658**	**<0.001**	-0.063	0.553	-	-	**0.460**	**<0.001**
	TAPSE	**-0.539**	**<0.001**	-0.054	0.615	**0.460**	**<0.001**	-	-
COVID-19 (groups "1" and "2") (N=60)	NT-proBNP	-	-	0.023	0.862	**-0.674**	**<0.001**	**-0.460**	**<0.001**
	Coenzyme Q10	0.023	0.862	-	-	-0.012	0.925	-0.074	0.577
	EF	**-0.674**	**<0.001**	-0.012	0.925	-	-	**0.406**	**0.001**
	TAPSE	**-0.460**	**<0.001**	-0.074	0.577	**0.406**	**0.001**	-	-
ICU-admitted COVID-19 (group "1") (N=30)	NT-proBNP	-	-	-0.069	0.717	**-0.709**	**<0.001**	**-0.514**	**0.004**
	Coenzyme Q10	-0.069	0.717	-	-	-0.090	0.638	0.164	0.386
	EF	**-0.709**	**<0.001**	-0.090	0.638	-	-	**0.407**	**0.025**
	TAPSE	**-0.514**	**0.004**	0.164	0.386	**0.407**	**0.025**	-	-
Home-isolated COVID-19 (group "2") (N=30)	NT-proBNP	-	-	-0.011	0.952	-0.191	0.312	-0.108	0.570
	Coenzyme Q10	-0.011	0.952	-	-	0.061	0.748	-0.300	0.107
	EF	-0.191	0.312	0.061	0.748	-	-	-0.055	0.772
	TAPSE	-0.108	0.570	-0.300	0.107	-0.055	0.772	-	-
Control (group "3") (N=30)	NT-proBNP	-	-	0.117	0.538	**-0.493**	**0.006**	**-0.617**	**<0.001**
	Coenzyme Q10	0.117	0.538	-	-	-0.130	0.495	0.127	0.503
	EF	**-0.493**	**0.006**	-0.130	0.495	-	-	**0.568**	**0.001**
	TAPSE	**-0.617**	**<0.001**	0.127	0.503	**0.568**	**0.001**	-	-

r = Spearman's correlation coefficient (Spearman's rho), p = p-value; p-value<0.05 is considered statistically significant; r-value: <0.2 = very weak, 0.2-0.39 = weak, 0.4-0.59 = moderate, 0.6-0.79 = strong, and ≥0.8 = very strong correlation; NT-proBNP correlated negatively with EF in all 3 groups, 1st 2 groups, group "1" and group "3" (r-value: -0.658, -0.674, -0.709 and -0.493 respectively and p-value: <0.001, <0.001, <0.001 and 0.006 respectively).

It also correlated negatively with TAPSE in all 3 groups, 1st 2 groups, group "1" and group "3" (r- value: -0.539, -0.460, -0.514 and -0.617 respectively and p-value: <0.001, <0.001, 0.004 and <0.001 respectively).

CoQ10 showed no correlation with NT-proBNP, EF or TAPSE, but was negatively correlated with IL-6 in group "1" (r-value: -0.391 and p-value: 0.032).

DISCUSSION

In the current study, there was a statistical significance between the three studied groups regarding NT-proBNP level in blood (p value: <0.001). NT-proBNP levels were significantly higher in group "1" (ICU-admitted COVID-19 patients) than both group "2" (home-isolated COVID-19 patients) and group "3" (controls group) (p-value: <0.0001).

These results come in agreement with (Wang et al., 2021) and (Mojón-Álvarez et al., 2024) who stated that elevated NT-proBNP levels at hospital admission in patients with COVID-19 are associated with unfavorable short- and long-term clinical outcomes and significantly related to the severity of pneumonia.

Several mechanisms may contribute to increased NT-proBNP release in patients with pneumonia. Oxygen deprivation, as well as, activation of inflammatory response lead to oxidative stress of heart muscle ending in excessive release of NT-proBNP, in addition to, the occurrence of microvascular dysfunction caused by increased angiotensin-converting enzyme 2 expression in heart capillary pericytes (Usta Atmaca et al., 2023).

The current study showed that there was no statistical significance between the three studied groups regarding CoQ10 level (p-value: 0.496).

Consistent with the current study, (Kaya et al., 2024) stated that plasma CoQ10 level alone cannot be a factor predicting mortality and morbidity in COVID-19 patients. The study involved 96 COVID-19 patients and 62 COVID-19 negative controls.

In contrast, the studies done by (Pagano et al., 2021), (Sumbalová et al., 2022) and (Mantle et al., 2024) stated that endogenous CoQ10 level was reduced in patients with COVID-19.

In this study, the results of CoQ10 testing were as follow: In group "1", the values of CoQ10 ranged from 14.8 to 17.5µg/L with median value of 16.3µg/L. In group "2", the values of CoQ10 ranged from 10.0 to 23.7µg/L with median value of 15.6µg/L. In group "3", the values of CoQ10 ranged from 10.8 to 18.5µg/L with median value of 14.45µg/L.

In literature, the supposed reference range for plasma CoQ10, measured by HPLC, is 433 -1532µg/L according to (Mayo Clinic Laboratories, 2026) based on the study performed by (Miles et al., 2004) including 106 adults from United States of America.

Another study, performed by (Kaikkonen et al., 2002) in a Finnish population of 705 subjects, showed that the reference range of CoQ10 in plasma, assessed by HPLC, is 345 - 1485 µg/L for males and 371 - 1269 µg/L for females.

It is noted that the plasma levels of CoQ10, measured by ELISA, in the current study population were much lower than the published reference ranges in literature.

This finding agrees with the study done by (Abdelkader et al., 2022). The study was performed on 20 healthy Egyptians, where CoQ10 levels were assayed by ELISA. CoQ10 levels measured ranged from 12.5 to 29.5µg/L with mean value of 19.7µg/L.

This may be due to increased prevalence of secondary CoQ10 deficiency in general as proposed by (Mantle et al., 2022). In the aforementioned study, Mantle and colleagues have suggested that secondary CoQ10 deficiency may arise from multiple factors, including mutations in genes that are not directly involved in the CoQ10 biosynthetic pathway, oxidative stress that accompany chronic conditions as neurodegenerative disorders, diabetes, cancer and muscular diseases and the effects of pharmacological substances such as statins.

Another point of view, regarding low plasma CoQ10 levels in this study population, is that plasma samples must not be used to estimate CoQ10 levels as they are influenced by dietary intake and that it is better to measure CoQ10 levels in muscle tissue or mononuclear blood cells (Pallotti et al., 2022).

In the current study, there was a statistical significance between the three studied groups regarding echocardiography functions; EF (for assessment of left ventricular function) and TAPSE (for assessment of right ventricular function) (P-value: <0.001 and 0.001 respectively).

EF was significantly lower in group "1" than both group "2" and group "3" (p-value: <0.0001).

In accordance with this study, (Hadidchi et al., 2025) stated that COVID-19 patients, especially those who were hospitalized, were associated with lower left ventricular EF.

TAPSE was significantly lower in group "1" than group "3" (p-value: <0.001).

In harmony with the current study, (Kunak & Kunak, 2026) stated that lower TAPSE was associated with mortality in patients with COVID-19.

However, the study performed by (Van den Heuvel et al., 2020) did not recommend routine echocardiographic evaluation of COVID-19 patients because cardiac complications occur less often in COVID-19 infection.

The current study showed the presence of statistically significant negative correlation between NT-proBNP and EF (r-value: -0.658 and p-value: <0. 001).

This finding is consistent with the study proposed by (Ziaie et al., 2022) which stated that left ventricular EF had a significant negative correlation with serum NT-proBNP level in COVID-19 patients.

The current study showed the presence of statistically significant negative correlation between NT-proBNP and TAPSE (r-value: -0.539 and p-value: <0.001).

This finding comes in agreement with the study proposed by (Grimaldi et al., 2023) which stated that TAPSE is significantly correlated with NT-proBNP concentrations.

In contrast, (Van den Heuvel et al., 2020) found no relation between elevated NT-proBNP and ventricular dysfunction.

In the current study, there was no statistically significant correlation between CoQ10 and NT-proBNP (r-value: 0.072 and p-value: 0.498).

This finding agrees with the study proposed by (Castro-Marrero et al., 2022) that stated that plasma levels of NT-proBNP were not significantly decreased after 8 weeks of CoQ10 administration.

On the other hand, the study done by (Bodea et al., 2025), stated that serum CoQ10 level was negatively related to NT-proBNP level.

Finally, the current study showed statistically significant negative correlation between CoQ10 and interleukin-6 (r-value: -0.391 and p-value: 0.032).

In agreement with our study, (Dabbaghi Varnousfaderani et al., 2023) stated that CoQ10 supplementation significantly reduce interleukin-6 concentrations.

Opposing to our study, (Zhai et al., 2017) stated that no effect of CoQ10 supplementation on interleukin-6 concentration.

CONCLUSION

The current study showed a clear noticeable relation between severity of COVID-19 infection (determined by the need for ICU admission) and occurrence of cardiac complications. Screening for subtle cardiac abnormalities by measuring blood levels of NT-ProBNP, together with conventional echocardiography, have been promising in the early detection of cardiac affection because of severe SARS-CoV-2 infection. Measuring plasma levels of CoQ10 did not yield any prognostic or diagnostic information in COVID-19 patients.

RECOMMENDATIONS

Routine assessment of cardiac condition, by measuring blood level of NT-proBNP and performing conventional echocardiography, is recommended in all ICU-admitted COVID-19 patients.

It is recommended to set a population-based reference interval for CoQ10 blood levels in Egyptians.

ABBREVIATIONS

COVID	**coronavirus disease**
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
CoQ10	coenzyme Q10
NT-proBNP	N-terminal pro-brain natriuretic peptide
ICU	intensive care unit
EF	ejection fraction
TAPSE	tricuspid annular plane systolic excursion
RT-PCR	reverse transcriptase - polymerase chain reaction
ELISA	enzyme-linked immunosorbent assay
CRP	C-reactive protein
LDH	lactate dehydrogenase
ROC	receiver-operating characteristic
AUC	area under curve

AUTHORS' CONTRIBUTIONS

Concept: S.K., H.W.Z.H., I.A.M.; design: H.W.Z.H., M.S.N.; supervision: H.W.Z.H., M.S.N., Y.E., I.A.M.; materials: H.W.Z.H., M.S.N., S.K.; data collection and/or processing: S.K.; analysis and/or interpretation: S.K., H.W.Z.H., Y.E., I.A.M.; literature review: S.K., M.S.N.; writing: S.K., H.W.Z.H., Y.E., M.S.N.; critical review: M.S.N., H.W.Z.H. ,Y.E., I.A.M., All authors read and approved the final manuscript.

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DATA AVAILABILITY

Not applicable.

DECLARATIONS

Ethics approval and consent to participate

The study protocol was conformed confidentially to the Declaration of Hel-sinki. The Research Ethics Committee (REC) of the Faculty of Medicine, Cairo University, reviewed and approved the study protocol (REC code #MD-129– 2022) in 8/2022. The purpose of the study was explained to each participant and they were reassured of confidentiality. An informed written consent was taken from them.

Competing interests

The authors declare no competing interests.

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