مجلة الدراسات التربوية والعلمية - كلية التربية - الجامعة العراقية
العدد الخامس والعشرون - المجلد الخامس - علوم الحياة - آذار 2025 م
doi.org/10.52866/esj.2025.05.25.20

Investigating Vitamin C level on COVID-19 Infection Progression and Biomarker Correlations

Mariyam Sabri Ibrahim[1] , Layla Mahmood Saeed[2] , luma Hakim Ali[3]
a-college of midicine auniversity of mustansiriyah ,b Ministry of Education, Karkh3 , Baghdad ,Iraq., c Ministry of education –Babil ,Iraq
mralazzawi@uomustansiriyah.edu.iq.1
Luma.h@bab.epedu.gov.iq3, laila.saeed2202p@ihcoedu.uobaghdad.edu.iq 2

Abstract:

The present study amid to estimate the role of vitamin C (VtC) in COVID-19 infection cases and its relation with some COVID-19 parameters including D-dimer, CT scans, C-reactive protein (CRP) and the infection severity level (simple, moderate and severe infection). Findings showed a significant elevation in CRP and D-dimer (p = 0.000, 0.003). No significant changes were observed in age and BMI (P=0.074, 0.899), VtC level showed non-significant changes between groups (p=0.235), non-significant differences were observed in all parameters in case groups with regard to sex, in contrast, within the control group differences between male and female in D-dimer level, the findings showed significant elevation in all parameters (p 0.00- 0.021), except VtC that non-significant changes among infection level (p=0.923), Correlation coefficient between VtC and study parameters were estimated in study groups, non-significant associations were found in the present study, change was observed in the association between BMI and VtC in the case group that sowed inverse association while in control the correlation was positive, conclusion; the present study didn't find changes in VtC level in COVID-19 patients, and no association with infection level, further investigations are needed to validate these findings.

Keywords: Vitamin C, COVID-19, infection level, D-dimer, CRP.

دراسة مستوى فيتامين C في تطور عدوى كوفيد - 19 وارتباطات العلامات الحيوية

مريم صبري ابراهيم[1] ، ليلى محمود سعيد [2] ، لمى حاكم علي [3]
1-كلية الطب -الجامعة المستنصرية 2- وزارة التربية /الكرخ الثالثة - بغداد -العراق
3- وزارة التربية تربية بابل- العراق

مستخلص:

تهدف الدراسة الحالية إلى تقدير دور فيتامين C (VtC) في حالات الإصابة بكوفيد-19 وعلاقته ببعض معلمات كوفيد-19 بما في ذلك D-dimer، والأشعة المقطعيةCT ، والبروتين التفاعلي (CRP) ومستوى شدة الإصابة (عدوى بسيطة ومتوسطة وشديدة). وأظهرت النتائج ارتفاعا كبيرا في CRP و0.000(D-dimer، p.(0.003= .لم تلاحظ أي تغييرات كبيرة في العمر ومؤشر كتلة الجسم =0.074 P، 0.899، لم تظهر مستوى VtC فروقا معنوية بين المجموعات =0.235 P، ولوحظت فروق غير مهمة في جميع المعلمات في مجموعات الحالة فيما يتعلق بالجنس، وعلى النقيض من ذلك، ضمن فروق المجموعة الضابطة بين الذكور والإناث في مستوى D-dimer، أظهرت النتائج ارتفاعا كبيرا في جميع المعايير =P 0.00- 0.021، باستثناء VtC ، أن التغييرات غير الهامة بين مستوى الإصابة =P 0.923، تم تقدير معامل الارتباط بين VtC ومعلمات الدراسة في مجموعات الدراسة، وتم العثور على ارتباطات غير مهمة في الدراسة الحالية، ولوحظ التغيير في الارتباط بين مؤشر كتلة الجسم وVtC في مجموعة الحالة التي زرعت الارتباط العكسي بينما كانت السيطرة على الارتباط إيجابية، الاستنتاج؛ لم تجد الدراسة الحالية تغييرات في مستوى VtC لدى مرضى كوفيد-19، ولا يوجد ارتباط بمستوى العدوى، هناك حاجة إلى مزيد من التحقيقات للتحقق من صحة هذه النتائج.

الكلمات المفتاحية: فيتامين C، كوفيد-19، مستوى العدوى، CRP، D-dimer.

Introduction

Vitamin C is an vital vitamin that water-soluble with antioxidant properties that enhances immune response ,It is abundantly found in activity and enhance immune response, its found as a vital compound for organisms in fresh vegetables and fruit, and plays avital roles in maintaining the health of organisms The serum level of VtC decreased during an infection's acute phase (Earar et al., 2020; Carr et al., 2017).Du to its role in immune function, researchers observed that increasing VtC intake can enhance the immune response aganist COVID-19 infection, sometimes it has been utilized as an adjunct in COVID-19 treatment . Some studies observed that patients with sepsis and organ failure have small levels of VtC (Amaku et al., 2021; Amaku et al., 2021). Others observed that patients need 20-30 times the normal amount of VtC to restore serum level to normal (Paré et al., 2017; Baethge et al., 2019). In some cases, VtC quantity returned to low pre-infusion level, based on the pharmacokinetics researches (Earar et al., 2020). VtC has suggested as apotential therapeutic option for conditions associated with COVID-19 ,such as sepsis and acute respiratory distress syndrome (Shahbaz et al., 2022) indicates that COVID-19 infection is related to low antiviral cytokines, interferon levels (de Grooth et al., 2018), Inflammatory parameters are significantly elevated , in sever cases of COVID-19, and sometimes this may lead to a 'cytokine storm (Wiersinga et al., 2019).

The other functions of VtC have been documented as antioxidant and anti-inflammatory impacts which contributed in equilibrium maintain (Kashiouris et al., 2020). A study indicated that controlling VtC level perhaps depleted IL-6 concentration for up to more days after treatment (Zhang et al., 2020). The antioxidant effect of VtC was studied by numerous reports which provided direct and indirect role of VtC in oxidative stress (Liu et al., 2020; Nabzdyk CS, Bittner 2018). moreover, high concentration of oral VtC supplements may reduce the risk of viral infection and ameliorate features (Jamali et al., 2017; Cheng and Midd, 2020). The present study exam for the level of VtC in COVID-19 infection patients and investigate its rela-

tions with some covid-19 parameters, in addition to the severity of disease.

Methodology

Sample collection : This study involved 60 participants, equally divided into 30 COVID-19 patients and 30 healthy controls. A case –control study was suggested to investigate the study aim, blood samples were collected with data under sterilized conditions, samples were transferred to lab for VtC level measure using Spectrophotometric method according to Rajput and Gupta (2013), D-dimer levels were estimated by inchromx (REF CFPC-153), CRP by (148924004) procedures, CT scans were conducted under the guidance of specialist physicians

Inclusion and exclusion criteria: cases with COVID-19 in different infection levels with medications didn't use VtC in treatment. Exclusion criteria were smokers, other disease like hypertension, diabetes mellitus, cancer types and patients use VtC as a supplement were prohibited from study.

Data analysis: data was statistical analyzed using SPSS v26, results represent as mean±SD , t test of independent sample to compare between independent groups, ANOVA one way for comparing among subgroups, and correlation coefficient, significantly were estimated at (p value <0.05) .

Results

The findings of this research , which aimed to detect the role of VtC in COVID-19 infection cases and its relationship with some COVID-19 parameters including D-dimer, CT scan, CRP, and infection severity (simple, moderate, and severe), (Table 1) showed significant elevations in CRP and D-dimer levels ($p = 0.000$, $p = 0.003$, respectively). Non-significant changes were observed in age and BMI ($p = 0.074$, $p = 0.899$), and VtC concentration showed no significant differences between groups ($p = 0.235$)

Table (1) levels of parameters in case and control groups (independent t sample test , p<0.05).

Parameters	COVID-19 cases	Control group	P value
Age	39.43±16.76	33.62±11.319	0.074
BMI	26.04±5.14	25.79±5.39	0.899
CT scan	25.58±23.10	-	-
Duration	8.25±10.56	-	-
CRP	37.01±41.61	2.68±1.807	0.000*
D-dimer	1410.93±2615.59	142.51±59.374	0.003*
VtC	0.87±0.078	0.89±0.043	0.235

The mean differences of study parameters according to sex demonstrated in table (2) of case and control group, non-significant differences were observed in all parameters in case groups regards with sex, in contrast, in control group, significant differences between male and female in the D-dimer level (p=0.018).

Table (2) the mean differences of study parameters according to sex (male and female), (independent sample t test)

Parameters	COVID-19 case group			Control group		
	man	women	p	man	women	p
Age	43.00±18.677	39.38±16.83183	0.563	31.67±8.885	45.00±27.495	0.054
BMI	27.67±5.215	26.016±5.3436	0.377	25.823±6.02948	28.483±1.78478	0.458
CT scan	36.266±29.910	19.88±16.813	0.056	-	-	-
Duration	13.00±15.679	6.05±3.4551	0.077	-	-	-
CRP	43.50±49.6361	39.06±40.106	0.778	2.5168±1.6764	2.780±2.0320	0.800
D-dimer	2021.50±3314.00	1258.22±2341.09	0.445	133.877±48.464	217.000±116.43	0.018*
VtC	0.8779±0.07973	0.868±0.08906	0.764	0.8890±0.049	0.8867±0.0305	0.938

There were three stages of infection by COVID-19 including simple, moderate and severe, the findings showed significant differences in all parameters (p 0.00- 0.021), except VtC that non-significant changed among infection level (p=0.923), the significant elevation was observed in age, BMI, CT-scan, duration, CRP and D-dimer (table 3).

Table (3) the mean differences of study parameters according to COVID-19 infection levels (ANOVA on way)

Parameters	Simple	moderate	Sever	P value
Age	38.31±13.00112	31.66±15.06968	56.25±15.94410	0.001
BMI	24.26±2.82577	24.53±4.14275	32.43±5.78346	0.001
CT scan	9.25±2.84019	20.33±4.32049	68.12±10.32940	0.001
Duration	4.87±1.54380	6.06±4.71270	19.12±19.61368	0.008
CRP	13.61±12.93964	28.77±18.94602	99.26±49.97064	0.000
D-dimer	452.34±534.25385	1095.05±2485.53004	3920.39±3828.8755	0.021
VtC	0.88±0.05406	0.88±0.08980	0.85±0.10706	0.923

Correlations coefficient between VtC and study parameters were estimated in study groups, non-significant associations were found in the present study, change was observed in the association between BMI and VtC in case group that sowed inverse association while in control the correlation was positive (table 4).

Table (4) the correlations coefficients between VtC and study parameters in study groups.

Parameters	Control group		Case group	
	r	p	r	p
Age	0.217	0.360	0.082	0.674
BMI	0.182	0.441	-0.162	0.401
CT scan	-	-	-0.169	0.380
Duration	-	-	0.022	0.909
CRP	-0.002	0.994	-0.098	0.611
D-dimer	0.048	0.839	0.107	0.579

Discussion

The current study showed that no significant impact between VtC and COVID-19 infection level. The connection between VtC level and COVID-19 infection has been well studied in other populations (Huang et al., 2022; Hui et al., 2022). Studies found in severe coronavirus cases, there is an association between hospitalization in the ICU

and insufficient level of VtC, thus the an effective impact of VtC in blocking and treating COVID-19 infection was documented, Moreover, researchers found that medicated with VtC to sepsis cases lead to reduce tissue damage, inflammatory indicators, and organ failure progress (Rowe et al., 2022).

The present finding didn't find connection between VtC and severity of COVID-19 infection, the literature review suggested that although no direct report indicating that VtC is beneficial specially against COVID-19, the report aids of VtC in the ICU context proposed that it could be depended for cases. In early study, it is unlikely that a healthy individual can importantly by daily dose of VtC more than 0.5 g/day (Levine et al., 1996). However, for cases with a respiratory virus infection, a dose of (6–8) g/day VtC was volubility more impactful than (3–4) g/day (Hemilä, 2017).

On the other hand, VtC is a crucial, low cost nutrient. Based on the severe clinical infection of COVID-19, even equinoctial aids can be worthwhile. Meanwhile, the best safety value of VtC and the necessity of ICU medication for huge proportion of COVID-19 cases perhaps justify consideration of clinical using of VtC, even before the finding of large study are free (Spoelstra-de et al., 2018). VtC has been suggested for COVID-19 cases medication also by other reports (Feyaerts et al., 2020; Cerullo et al., 2020; Carr and, Rowe, 2020) .

No evidences agree with present finding, the non-changes in VtC level in patients may be because the nutrition style of patients that rich with vitamins and minerals, also, the oxidative stress may be balanced by antioxidant molecules like antioxidant enzymes, vitamins and minerals. Although of the medication approach didn't use VtC in the current study, the level of VtC didn't valuable changes with severity of infection, we need further analysis and testing other factors contributed in severity of infection.

Limitation of present study is the restricted sample size, difficult to obtain the patients approval and almost of patients were smoking thus it cannot be enrolled in the present study.

Conclusion : the present study didn't find changes in VtC level in COVID-19 cases, and no association with infection level, it needs further studies.

References

- Earar K, Arbune M, Dorobat CM, *et al*. Biochemical effects and therapeutic application of VtC (C6H8O6) on COVID-19 infection. Rev Chim. 2020;71:473–478. doi: 10.37358/RC.20.5.8159.

- Carr AC, Rosengrave PC, Bayer S, *et al*. Hypovitaminosis C and VtC deficiency in critically ill patients despite recommended enteral and parenteral intakes. Crit Care. 2017;21:1–10. doi: 10.1186/s13054-017-1891-y.

- *Amaku M, Covas DT, Coutinho FAB, et al. Modelling the impact of delaying vaccination against SARS-CoV-2 assuming unlimited vaccines supply. Theor Biol Med Model. 2021;18:14. doi: 10.1186/s12976-021-00143-0.*

- *Nishikimi M, Fukuyama R, Minoshima S, et al. Cloning and chromosomal mapping of the human nonfunctional gene for L-gulono-gamma-lactone oxidase, the enzyme for L-ascorbic acid biosynthesis missing in man. J Biol Chem. 1994;269:13685–13688. doi: 10.1016/S0021-9258(17)36884-9.*

- Paré G, Kitsiou S. Methods for literature reviews. In: Lau F, Kuziemsky C, editors. Handbook of eHealth evaluation: An evidence-based approach. 2017. Available from: https://www.ncbi.nlm.nih.gov/books/NBK481583/ [PubMed] [Google Scholar]

- Baethge C, Goldbeck-Wood S, Mertens S, *et al*. SANRA-a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev.* 2019;4:5. doi: 10.1186/s41073-019-0064-8.

- Shahbaz U, Fatima N, Basharat S, Bibi A, Yu X, Hussain MI, Nasrullah M. Role of VtC in preventing of COVID-19 infection, progression and severity. AIMS Microbiol. 2022 Mar 30;8(1):108-124. doi: 10.3934/microbiol.2022010. PMID: 35496992; PMCID: PMC8995185.

- de Grooth HJ, Manubulu-Choo WP, Zandvliet AS, et al. VtC pharmacokinetics in critically ill patients: a randomized trial of four IV regimens. Chest. 2018;153:1368–1377. doi: 10.1016/j.chest.2018.02.025.

- Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA. 2020;4:782–793. doi: 10.1001/jama.2020.12839.

- Kashiouris MG, L›Heureux M, Cable CA, et al. The emerging role of VtC as a treatment for sepsis. Nutrients. 2020;12:292. doi: 10.3390/nu12020292.

- *Zhang J, Rao X, Li Y, et al. High-dose VtC infusion for the treatment of critically ill COVID-19. Res Square. 2020;10 doi: 10.21203/rs.3.rs-52778/v1.*

- Liu Q, Gao Y, Ci X. Role of Nrf2 and its activators in respiratory diseases. Oxid Med Cell Longev. 2019;2019:7090534. doi: 10.1155/2019/7090534.

- Nabzdyk CS, Bittner EA. VtC in the critically ill-indications and controversies. World J Crit Care Med. 2018;7:52–61. doi: 10.5492/wjccm.v7.i5.52.

- Huang WY, Hong J, Ahn SI, Han BK, Kim YJ. Association of VtC Treatment with Clinical Outcomes for COVID-19 Patients: A Systematic Review and Meta-Analysis. Healthcare (Basel). 2022 Dec 5;10(12):2456. doi: 10.3390/healthcare10122456.

- Hui, L.L., Nelson, E.A.S., Lin, S.L. et al. The role of VtC in pneumonia and COVID-19 infection in adults with European ancestry: a Mendelian randomisation study. Eur J Clin Nutr **76**, 588–591 (2022). https://doi.org/10.1038/s41430-021-00993-4

- *Rowe S, Carr ACJN. Global VtC status and prevalence of deficiency: a cause for concern? Nutrients. 2020;12:2008. doi: 10.3390/nu12072008.* [

- Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, Dhariwal KR, et al. VtC pharmacokinetics in healthy volunteers: evidence for a recommended dietary allowance. Proc Natl Acad Sci USA. (1996) 93:3704–9. doi: 10.1073/pnas.93.8.3704.

- Hemilä H. VtC and infections. Nutrients. (2017) 9:339. doi: 10.3390/nu9040339

- Spoelstra-de Man AME, Elbers PWG, Oudemans-Van Straaten HM. VtC: should we supplement? Curr Opin Crit Care. (2018) 24:248–55. doi: 10.1097/MCC.0000000000000510

- Feyaerts AF, Luyten W. VtC as prophylaxis and adjunctive medical treatment for COVID-19? Nutrition. (2020) 79–80:110948. doi: 10.1016/j.nut.2020.110948

- Cerullo G, Negro M, Parimbelli M, Pecoraro M, Perna S, Liguori G, et al. The long history of VtC: from pre-

vention of the common cold to potential aid in the treatment of COVID-19. Front Immunol. (2020) 11:574029. doi: 10.3389/fimmu.2020.574029

- Carr AC, Rowe S. The emerging role of VtC in the prevention and treatment of COVID-19. Nutrients. (2020) 12:3286. doi: 10.3390/nu12113286.

- Cheng RZJMidd. Can early and high intravenous dose of VtC prevent and treat coronavirus disease 2019 (COVID-19)? Med Drug Discov. 2020;5:100028. doi: 10.1016/j.medidd.2020.100028.

- JamaliMoghadamSiahkali, S., Zarezade, B., Koolaji, S. *et al.* Safety and effectiveness of high-dose VtC in patients with COVID-19: a randomized open-label clinical trial. *Eur J Med Res* **26**, 20 (2021). https://doi.org/10.1186/s40001-021-00490-1

- Rajput, S., & Gupta, K. (2013). "Spectrophotometric determination of ascorbic acid in pharmaceutical formulations using 2,4-dinitrophenylhydrazine reagent. "*International Journal of Pharmaceutical Sciences and Research,* 4(8): 3014-3019.