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Interleukin-6 level in male COVID-19 patients in Iraq

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Abstract---Background: Since the exacerbation of the Coronal Virus 2019, caused by the SARS-COV-2 Virus in December 2019, affected more than 200 countries, region or region on 6 continents. Currently, the rates of infection for the male sex were higher than the female. The aim of this study was to assess the levels of Interleukin-6, the male-infected Iraqi patients with Covid-19. Methods: Clinical features, laboratory results and PCR actual time have been reviewed by 60 patients with a certain laboratory COVID-19 virus. They entered Al - Amal Hospital. Iraq between September and December 2021. Healthy participants who underwent routine physical examinations and non-patients with COVID-19 was the study as a control group. Homocysteine and IL6 levels have been identified and compared between the obese COVID-19 group and the control group. Results: The results showed that the levels of interleukin-6 were higher than the normal range for patients with COVID-19 compared to the control group, while the levels of interleukin-6 for the obese recorded the highest reading among the three groups. The lipid profile levels were high in the obese group of patients with COVID-19, while the non-obese patients with COVID-19 had a lower lipid profile compared to the healthy control group. The levels of interleukin increased with statistically significant ($P < 0.001$), and the results recorded a decrease in the level of appetite in patients with COVID-19 disease. Conclusions: There is a close correlation between the severity of COVID-19 disease and the levels of interleukin-6, as it is clear that the exacerbation of infections and the exacerbation of the increased secretion of inflammatory cytokines in obese patients, which causes a cytokine storm.

Keywords---COVID-19, SARS-CoV-2, Iraq, COVID-19 patients, obese patients.

Introduction

In the Chinese city of Wuhan, at the end of 2019, the disease of the Corona virus appeared, which showed a wide range of symptoms, the most important of which were fever, shortness of breath, diarrhea and headache. (Kwok et al., 2020) Over 500 million cases were identified in 188 countries and territories, with over 6.26 million deaths as of May 14, 2022. (CSSE, 2022). The SARS-CoV-2-induced COVID-19 has become one of the most urgent issues of our time as a result of the novel extreme severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreading throughout the world and the World Health Organization (WHO) declaring a pandemic on March 11, 2020. (Azkur et al., 2020).

Coronaviruses are non-sense positive RNA viruses that cause gastrointestinal and respiratory diseases in animals and humans. (J. Liu et al., 2020) The Nidovirales order's Coronavirinae subfamily of the Coronaviridae class of viruses, which are enclosed, single-stranded, positive-sense RNA viruses, is what is known as a coronavirus (CoV). (Y. C. Liu et al., 2020). Coronaviruses are encapsulated by favorable circumstances RNA viruses have spike-like projections on their surface and range in diameter from 60 nm to 134 nm, giving them a crown-like appearance. then the time coronavirus, behind the electron microscope (Singhal, 2020)

Humans and other mammals are frequently infected with coronaviruses, which are mammals and members of the Nidovirales order and the Coronaviridae family. (Huang et al., 2020). Homocysteine It is one of the alpha-amino acids, which contains sulfur in its composition, and it is not included in the formation of proteins, as it is an intermediate product as a result of the transformation of methionine (Met) into homocysteine (Hou & Zhao, 2021) The accumulation of homocysteine in the blood is a serious matter and pathological indication, Homocysteine is converted to methionine by methylation reactions, or it can be converted to cystathionine and then to cytosine by transferring the sulfur group, This reaction requires vitamin B12, folic acid, and the enzyme methylenetetrahydrofolate reductase (MTHFR). (Raghubeer & Matsha, 2021) Homocysteine appears as a risk factor for cardiovascular disease and stroke Periodically (Chrysant & Chrysant, 2018) Studies show that those with severe infection with Covid-19 had high levels of homocysteine in the blood (Carpenè et al., 2022) High levels of Hcy in the blood plasma (>15 µmol/L) is a medical condition Systemic hyperhomocysteinemia (Smith & Refsum, 2021) Hypohomocysteinemia (less than 6 µmol/L) occurs in 1-5.0% of Similar to the population, Hcy is also considered an abnormally low concentration of Hcy as a factor Risk to Health Despite the high prevalence of Hcy in dialysis patients A decrease in the blood plasma concentration of Hcy in this patient group is linked to higher hospitalization and mortality rates in terms of maintaining kidneys. (Koklesova et al., 2021)

Disturbances in the folate-dependent remethylation of Hcy to Met are linked to high Hcy. The main water-soluble vitamin B9, folic acid, functions as a coenzyme in the synthesis process. DNA and cellular renewal (Román et al., 2019). Studies have shown that there is a close correlation between high levels of homocysteine and coronary artery disease and risks, and that homocysteine has a relationship

with obesity and weight gain, where the relationship is positive, that it was found to be high in obese people. (Wang et al., 2021)

Materials and Methods

Ninety Iraqi patients infected with COVID-19 participated in this study. Only 60 patients fulfilled all biochemical analysis tests. Their ages ranged from 45-65 years and the mean BMI of the patients was 29.95 ± 3.06 . Random blood glucose and HbA1c were 130.12 ± 20.14 mg/dL and $6.08 \pm 0.8\%$, respectively. These patients were registered as COVID-19 in Al-Amal Hospital in Najaf city-Iraq and "Al-Hakim General" Hospital in Najaf-Iraq during the period from January to April. The patient was diagnosed by clinical symptoms, PCR, and biochemical tests. The current study excluded female patients, patients suffering from high blood pressure, infections and endocarditis, heart diseases as well as patients from non-Arab ethnic groups, and patients with thyroid disease.

Thirty people were chosen as a control group. Their age was similar to that of the patients and their mean BMI was 22.94 ± 3.15 . The averages for random blood glucose and HbA1c were 101.9 ± 11.18 mg/dL, and $5.03 \pm 0.63\%$, respectively. People with anemia or with obvious systemic disease were excluded. The World Health Organization has classified body mass index (BMI). Weight and height were measured according to World Health Organization guidelines. The WHO guidelines calculated BMI as weight/height² (kg/m²). Obese individuals were defined as having a BMI of more than 30 kg/m², while the BMI of normal individuals was 18–25.

Five milliliters of venous blood samples were drawn using a disposable needle and plastic syringe from each control patient. The blood is divided into two anticoagulant tubes and gel tubes. The blood was left in the gel tube at room temperature for 15 min for coagulation, 3000 Xg centrifuged for 5 min, and then the serum was separated and transferred to new disposable tubes. Student's T-test was used to assess differences in scale variables between diagnostic categories and contingency table analysis (χ test) was used to verify the association between nominal variables. Correlations between variables were calculated using Pearson's product moment and Spearman's rank order correlation coefficients. All tests were two-tailed and a p-value of 0.05 was used for statistical significance. All statistical analyzes were performed using IBM SPSS windows version 25, 2017.

Results and Discussion

The mean age of COVID-19 patients was 58.3 ± 11.5 years male and did not differ statistically from COVID-19 or healthy subjects in age or gender. We found that interleukin ng/ml levels were higher in COVID-19 patients than the healthy group ($P < 0.001$).

Parameters	Mean±STD Patients	Mean±STD Controls	P-Value
IL-6, pg/mL	9.54±3.20	1.71 ± 0.21	<0.001*
Ghrelin pg/mL	44.32 ±3.44	51.32± 5.5	0.001*

D.dimer ng/mL	1224.6±211.63	278.53±84.96	<0.001*
Ferretin ng/mL	829.33±192.81	105.5±43.73	0.005*
Homocysteine ng/ml	655.2±24.6	922.2±15.5	<0.001*

The COVID-19 is an infectious illness that has caused a pandemic worldwide. As a novel type of disease with high infectivity and mortality, the pathophysiology of COVID-19 has not been fully studied. A number of studies have reported severe and complex effects of COVID-19 in several human organs and systems including respiratory, immune, digestive, circulatory, hepatic, renal, and hematological systems (Contini et al., 2020). Angiotensin-converting enzyme 2 (ACE2) is a receptor providing the main entry site for SARS-CoV to invade human cells, and this in turn facilitates direct damage of virus through the course of infection (Gheblawi et al., 2020) suggesting that the thyroid gland may be a potential target for direct attack of COVID-19. Our study showed that thyroid dysfunction tended to be associated with viral nucleic acid cleaning time, indicating virus infection and replication may account for the abnormal thyroid hormones. However, our study also showed that disease severity, which may influence the viral nucleic acid cleaning time, was associated with thyroid dysfunction, thus the true relationship of thyroid function and viral nucleic acid cleaning time need to be further studied.(Tharmarajah et al., 2021)

With an exponential increase in COVID-19 infection rate and mortality in an ongoing global pandemic, researchers, clinicians, and government agencies are focusing on repurposing drugs with known safety profiles (Zhang L, Liu Y (2020)). Previously known beneficial outcomes following high doses of vitamin C therapy in clinical studies have made this vitamin a frontline candidate for possible COVID-19 treatment. Also, there are very limited side effects and patients have high tolerability to ascorbic acid high doses (Padayatty SJ, et al. (2004)). Interleukin-6 is one of the immunomodulatory cytokines that is secreted in the case of inflammation and is pro-inflammatory and has a great similarity with proteins that makes it multifunctional The interleukin-6 R receptor is considered a pathophysiological cause of rheumatoid disease. (Potere et al., 2021). Interleukin-6 is considered one of the main causes of cytokine storm and causes inflammation when it is in very high concentrations, which stimulates self-attack on the body and causes organ failure and acute infections, which makes the task of inhibiting it one of the most important roles and methods of treatment for people with COVID-19(Tharmarajah et al., 2021)

References

- Azkur, A. K., Akdis, M., Azkur, D., Sokolowska, M., van de Veen, W., Brüggen, M. C., O'Mahony, L., Gao, Y., Nadeau, K., & Akdis, C. A. (2020). Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. In *Allergy: European Journal of Allergy and Clinical Immunology* (Vol. 75, Issue 7, pp. 1564–1581). Blackwell Publishing Ltd. <https://doi.org/10.1111/all.14364>
- Azkur, A. K., Akdis, M., Azkur, D., Sokolowska, M., van de Veen, W., Brüggen, M. C., O'Mahony, L., Gao, Y., Nadeau, K., & Akdis, C. A. (2020). Immune response to SARS-CoV-2 and mechanisms of immunopathological changes in COVID-19. In *Allergy: European Journal of Allergy and Clinical Immunology* (Vol. 75, Issue

- 7, pp. 1564–1581). Blackwell Publishing Ltd. <https://doi.org/10.1111/all.14364>
- Azkur, Ahmet Kursat, Mübeccel Akdis, Dilek Azkur, Milena Sokolowska, Willem van de Veen, Marie Charlotte Brügger, Liam O'Mahony, Yadong Gao, Kari Nadeau, and Cezmi A. Akdis. 2020. "Immune Response to SARS-CoV-2 and Mechanisms of Immunopathological Changes in COVID-19." *Allergy: European Journal of Allergy and Clinical Immunology*. Blackwell Publishing Ltd. <https://doi.org/10.1111/all.14364>.
- Azkur, Ahmet Kursat, Mübeccel Akdis, Dilek Azkur, Milena Sokolowska, Willem van de Veen, Marie Charlotte Brügger, Liam O'Mahony, Yadong Gao, Kari Nadeau, and Cezmi A. Akdis. 2020. "Immune Response to SARS-CoV-2 and Mechanisms of Immunopathological Changes in COVID-19." *Allergy: European Journal of Allergy and Clinical Immunology*. Blackwell Publishing Ltd. <https://doi.org/10.1111/all.14364>.
- Carpenè, G., Negrini, D., Henry, B. M., Montagnana, M., & Lippi, G. (2022). Homocysteine in coronavirus disease (COVID-19): a systematic literature review. *Diagnosis*, 0(0). <https://doi.org/10.1515/dx-2022-0042>
- Carpenè, G., Negrini, D., Henry, B. M., Montagnana, M., & Lippi, G. (2022). Homocysteine in coronavirus disease (COVID-19): a systematic literature review. *Diagnosis*, 0(0). <https://doi.org/10.1515/dx-2022-0042>
- Carpenè, Giovanni, Davide Negrini, Brandon M. Henry, Martina Montagnana, and Giuseppe Lippi. 2022. "Homocysteine in Coronavirus Disease (COVID-19): A Systematic Literature Review." *Diagnosis* 0 (0). <https://doi.org/10.1515/dx-2022-0042>.
- Carpenè, Giovanni, Davide Negrini, Brandon M. Henry, Martina Montagnana, and Giuseppe Lippi. 2022. "Homocysteine in Coronavirus Disease (COVID-19): A Systematic Literature Review." *Diagnosis* 0 (0). <https://doi.org/10.1515/dx-2022-0042>.
- Chrysant, S. G., & Chrysant, G. S. (2018). The current status of homocysteine as a risk factor for cardiovascular disease: a mini review. In *Expert Review of Cardiovascular Therapy* (Vol. 16, Issue 8, pp. 559–565). Taylor and Francis Ltd. <https://doi.org/10.1080/14779072.2018.1497974>
- Chrysant, S. G., & Chrysant, G. S. (2018). The current status of homocysteine as a risk factor for cardiovascular disease: a mini review. In *Expert Review of Cardiovascular Therapy* (Vol. 16, Issue 8, pp. 559–565). Taylor and Francis Ltd. <https://doi.org/10.1080/14779072.2018.1497974>
- Chrysant, Steven G., and George S. Chrysant. 2018. "The Current Status of Homocysteine as a Risk Factor for Cardiovascular Disease: A Mini Review." *Expert Review of Cardiovascular Therapy*. Taylor and Francis Ltd. <https://doi.org/10.1080/14779072.2018.1497974>.
- Chrysant, Steven G., and George S. Chrysant. 2018. "The Current Status of Homocysteine as a Risk Factor for Cardiovascular Disease: A Mini Review." *Expert Review of Cardiovascular Therapy*. Taylor and Francis Ltd. <https://doi.org/10.1080/14779072.2018.1497974>.
- Contini, C., Nuzzo, M. di, Barp, N., Bonazza, A., de Giorgio, R., Tognon, M., & Rubino, S. (2020). The novel zoonotic COVID-19 pandemic: An expected global health concern. *Journal of Infection in Developing Countries*, 14(3), 254–264. <https://doi.org/10.3855/jidc.12671>
- Contini, C., Nuzzo, M. di, Barp, N., Bonazza, A., de Giorgio, R., Tognon, M., & Rubino, S. (2020). The novel zoonotic COVID-19 pandemic: An expected global

- health concern. *Journal of Infection in Developing Countries*, 14(3), 254–264. <https://doi.org/10.3855/jidc.12671>
- Gheblawi, M., Wang, K., Viveiros, A., Nguyen, Q., Zhong, J. C., Turner, A. J., Raizada, M. K., Grant, M. B., & Oudit, G. Y. (2020). Angiotensin-Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System: Celebrating the 20th Anniversary of the Discovery of ACE2. In *Circulation Research* (pp. 1456–1474). Lippincott Williams and Wilkins. <https://doi.org/10.1161/CIRCRESAHA.120.317015>
- Gheblawi, M., Wang, K., Viveiros, A., Nguyen, Q., Zhong, J. C., Turner, A. J., Raizada, M. K., Grant, M. B., & Oudit, G. Y. (2020). Angiotensin-Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System: Celebrating the 20th Anniversary of the Discovery of ACE2. In *Circulation Research* (pp. 1456–1474). Lippincott Williams and Wilkins. <https://doi.org/10.1161/CIRCRESAHA.120.317015>
- Hou, H., & Zhao, H. (2021). Epigenetic factors in atherosclerosis: DNA methylation, folic acid metabolism, and intestinal microbiota. In *Clinica Chimica Acta* (Vol. 512, pp. 7–11). Elsevier B.V. <https://doi.org/10.1016/j.cca.2020.11.013>
- Hou, H., & Zhao, H. (2021). Epigenetic factors in atherosclerosis: DNA methylation, folic acid metabolism, and intestinal microbiota. In *Clinica Chimica Acta* (Vol. 512, pp. 7–11). Elsevier B.V. <https://doi.org/10.1016/j.cca.2020.11.013>
- Hou, Huimin, and Huiying Zhao. 2021. “Epigenetic Factors in Atherosclerosis: DNA Methylation, Folic Acid Metabolism, and Intestinal Microbiota.” *Clinica Chimica Acta*. Elsevier B.V. <https://doi.org/10.1016/j.cca.2020.11.013>.
- Hou, Huimin, and Huiying Zhao. 2021. “Epigenetic Factors in Atherosclerosis: DNA Methylation, Folic Acid Metabolism, and Intestinal Microbiota.” *Clinica Chimica Acta*. Elsevier B.V. <https://doi.org/10.1016/j.cca.2020.11.013>.
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., ... Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395(10223), 497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., ... Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395(10223), 497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- Huang, Chaolin, Yeming Wang, Xingwang Li, Lili Ren, Jianping Zhao, Yi Hu, Li Zhang, et al. 2020. “Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China.” *The Lancet* 395 (10223): 497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
- Huang, Chaolin, Yeming Wang, Xingwang Li, Lili Ren, Jianping Zhao, Yi Hu, Li Zhang, et al. 2020. “Clinical Features of Patients Infected with 2019 Novel Coronavirus in Wuhan, China.” *The Lancet* 395 (10223): 497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
- Koklesova, L., Mazurakova, A., Samec, M., Biringer, K., Samuel, S. M., Büsselberg, D., Kubatka, P., & Golubnitschaja, O. (2021). Homocysteine metabolism as the target for predictive medical approach, disease prevention, prognosis, and treatments tailored to the person. In *EPMA Journal* (Vol. 12,

- Issue 4, pp. 477–505). Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s13167-021-00263-0>
- Koklesova, L., Mazurakova, A., Samec, M., Biringer, K., Samuel, S. M., Büsselberg, D., Kubatka, P., & Golubnitschaja, O. (2021). Homocysteine metabolism as the target for predictive medical approach, disease prevention, prognosis, and treatments tailored to the person. In *EPMA Journal* (Vol. 12, Issue 4, pp. 477–505). Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s13167-021-00263-0>
- Koklesova, Lenka, Alena Mazurakova, Marek Samec, Kamil Biringer, Samson Mathews Samuel, Dietrich Büsselberg, Peter Kubatka, and Olga Golubnitschaja. 2021. “Homocysteine Metabolism as the Target for Predictive Medical Approach, Disease Prevention, Prognosis, and Treatments Tailored to the Person.” *EPMA Journal*. Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s13167-021-00263-0>.
- Koklesova, Lenka, Alena Mazurakova, Marek Samec, Kamil Biringer, Samson Mathews Samuel, Dietrich Büsselberg, Peter Kubatka, and Olga Golubnitschaja. 2021. “Homocysteine Metabolism as the Target for Predictive Medical Approach, Disease Prevention, Prognosis, and Treatments Tailored to the Person.” *EPMA Journal*. Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s13167-021-00263-0>.
- Kwok, S., Adam, S., Ho, J. H., Iqbal, Z., Turkington, P., Razvi, S., le Roux, C. W., Soran, H., & Syed, A. A. (2020). Obesity: A critical risk factor in the COVID -19 pandemic . *Clinical Obesity*, 10(6). <https://doi.org/10.1111/cob.12403>
- Kwok, S., Adam, S., Ho, J. H., Iqbal, Z., Turkington, P., Razvi, S., le Roux, C. W., Soran, H., & Syed, A. A. (2020). Obesity: A critical risk factor in the COVID -19 pandemic . *Clinical Obesity*, 10(6). <https://doi.org/10.1111/cob.12403>
- Kwok, See, Safwaan Adam, Jan Hoong Ho, Zohaib Iqbal, Peter Turkington, Salman Razvi, Carel W. le Roux, Handrean Soran, and Akheel A. Syed. 2020. “ Obesity: A Critical Risk Factor in the COVID -19 Pandemic .” *Clinical Obesity* 10 (6). <https://doi.org/10.1111/cob.12403>.
- Kwok, See, Safwaan Adam, Jan Hoong Ho, Zohaib Iqbal, Peter Turkington, Salman Razvi, Carel W. le Roux, Handrean Soran, and Akheel A. Syed. 2020. “ Obesity: A Critical Risk Factor in the COVID -19 Pandemic .” *Clinical Obesity* 10 (6). <https://doi.org/10.1111/cob.12403>.
- Lee J.I., Burckart G.J. Nuclear factor kappa B: important transcription factor and therapeutic target. *J. Clin. Pharmacol.* 1998;38(11):981–993 .
- Lee J.I., Burckart G.J. Nuclear factor kappa B: important transcription factor and therapeutic target. *J. Clin. Pharmacol.* 1998;38(11):981–993 .
- Liu, J., Li, S., Liu, J., Liang, B., Wang, X., Wang, H., Li, W., Tong, Q., Yi, J., Zhao, L., Xiong, L., Guo, C., Tian, J., Luo, J., Yao, J., Pang, R., Shen, H., Peng, C., Liu, T., ... Zheng, X. (2020). Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine*, 55. <https://doi.org/10.1016/j.ebiom.2020.102763>
- Liu, J., Li, S., Liu, J., Liang, B., Wang, X., Wang, H., Li, W., Tong, Q., Yi, J., Zhao, L., Xiong, L., Guo, C., Tian, J., Luo, J., Yao, J., Pang, R., Shen, H., Peng, C., Liu, T., ... Zheng, X. (2020). Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine*, 55. <https://doi.org/10.1016/j.ebiom.2020.102763>
- Liu, Jing, Sumeng Li, Jia Liu, Boyun Liang, Xiaobei Wang, Hua Wang, Wei Li, et al. 2020. “Longitudinal Characteristics of Lymphocyte Responses and Cytokine

- Profiles in the Peripheral Blood of SARS-CoV-2 Infected Patients.” *EBioMedicine* 55 (May). <https://doi.org/10.1016/j.ebiom.2020.102763>.
- Liu, Jing, Sumeng Li, Jia Liu, Boyun Liang, Xiaobei Wang, Hua Wang, Wei Li, et al. 2020. “Longitudinal Characteristics of Lymphocyte Responses and Cytokine Profiles in the Peripheral Blood of SARS-CoV-2 Infected Patients.” *EBioMedicine* 55 (May). <https://doi.org/10.1016/j.ebiom.2020.102763>.
- Liu, Y. C., Kuo, R. L., & Shih, S. R. (2020). COVID-19: The first documented coronavirus pandemic in history. In *Biomedical Journal* (Vol. 43, Issue 4, pp. 328–333). Elsevier B.V. <https://doi.org/10.1016/j.bj.2020.04.007>
- Liu, Y. C., Kuo, R. L., & Shih, S. R. (2020). COVID-19: The first documented coronavirus pandemic in history. In *Biomedical Journal* (Vol. 43, Issue 4, pp. 328–333). Elsevier B.V. <https://doi.org/10.1016/j.bj.2020.04.007>
- Liu, Yen Chin, Rei Lin Kuo, and Shin Ru Shih. 2020. “COVID-19: The First Documented Coronavirus Pandemic in History.” *Biomedical Journal*. Elsevier B.V. <https://doi.org/10.1016/j.bj.2020.04.007>.
- Liu, Yen Chin, Rei Lin Kuo, and Shin Ru Shih. 2020. “COVID-19: The First Documented Coronavirus Pandemic in History.” *Biomedical Journal*. Elsevier B.V. <https://doi.org/10.1016/j.bj.2020.04.007>.
- Padayatty SJ, Sun H, Wang Y, Riordan HD, Hewitt SM, Katz A, et al. (2004). Vitamin C pharmacokinetics: implications for oral and intravenous use. *Annals of Int Med*, 140:533-537
- Padayatty SJ, Sun H, Wang Y, Riordan HD, Hewitt SM, Katz A, et al. (2004). Vitamin C pharmacokinetics: implications for oral and intravenous use. *Annals of Int Med*, 140:533-537
- Raghubeer, S., & Matsha, T. E. (2021). Methylenetetrahydrofolate (Mthfr), the one-carbon cycle, and cardiovascular risks. *Nutrients*, 13(12). <https://doi.org/10.3390/nu13124562>
- Raghubeer, Shanel, and Tandi E. Matsha. 2021. “Methylenetetrahydrofolate (Mthfr), the One-Carbon Cycle, and Cardiovascular Risks.” *Nutrients* 13 (12). <https://doi.org/10.3390/nu13124562>.
- Román, G. C., Mancera-Páez, O., & Bernal, C. (2019). Epigenetic factors in late-onset alzheimer’s disease: MTHFR and CTH gene polymorphisms, metabolic transsulfuration and methylation pathways, and B vitamins. *International Journal of Molecular Sciences*, 20(2). <https://doi.org/10.3390/ijms20020319>
- Román, Gustavo C., Oscar Mancera-Páez, and Camilo Bernal. 2019. “Epigenetic Factors in Late-Onset Alzheimer’s Disease: MTHFR and CTH Gene Polymorphisms, Metabolic Transsulfuration and Methylation Pathways, and B Vitamins.” *International Journal of Molecular Sciences* 20 (2). <https://doi.org/10.3390/ijms20020319>.
- Singhal, T. (2020). A Review of Coronavirus Disease-2019 (COVID-19). In *Indian Journal of Pediatrics* (Vol. 87, Issue 4, pp. 281–286). Springer. <https://doi.org/10.1007/s12098-020-03263-6>
- Singhal, Tanu. 2020. “A Review of Coronavirus Disease-2019 (COVID-19).” *Indian Journal of Pediatrics*. Springer. <https://doi.org/10.1007/s12098-020-03263-6>.
- Smith, A. D., & Refsum, H. (2021). Homocysteine – from disease biomarker to disease prevention. In *Journal of Internal Medicine* (Vol. 290, Issue 4, pp. 826–854). John Wiley and Sons Inc. <https://doi.org/10.1111/joim.13279>

- Smith, A. D., and H. Refsum. 2021. "Homocysteine – from Disease Biomarker to Disease Prevention." *Journal of Internal Medicine*. John Wiley and Sons Inc. <https://doi.org/10.1111/joim.13279>.
- Tharmarajah, E., Buazon, A., Patel, V., Hannah, J. R., Adas, M., Allen, V. B., Bechman, K., Clarke, B. D., Nagra, D., Norton, S., Russell, M. D., Rutherford, A. I., Yates, M., & Galloway, J. B. (2021). IL-6 inhibition in the treatment of COVID-19: A meta-analysis and meta-regression. *Journal of Infection*, 82(5), 178–185. <https://doi.org/10.1016/j.jinf.2021.03.008>
- Wang, J., You, D., Wang, H., Yang, Y., Zhang, D., Lv, J., Luo, S., Liao, R., & Ma, L. (2021). Association between homocysteine and obesity: A meta-analysis. *Journal of Evidence-Based Medicine*, 14(3), 208–217. <https://doi.org/10.1111/jebm.12412>
- Wang, Jinxiang, Dingyun You, Huaping Wang, Yanhong Yang, Dan Zhang, Junyan Lv, Sufeng Luo, Rui Liao, and Lanqing Ma. 2021. "Association between Homocysteine and Obesity: A Meta-Analysis." *Journal of Evidence-Based Medicine* 14 (3): 208–17. <https://doi.org/10.1111/jebm.12412>.
- Zhang L, Liu Y (2020). Potential interventions for novel coronavirus in China: A systematic review. *J of Med Vir*, 92:479-490.