

Article

Clinical Overview of *Ureum* Levels in Type II Diabetes Mellitus Patients Infected by COVID-19 Pandemic

Deswidya Sukrisna Hutauruk^{1,*} and Dame Cinta Hutagalung¹

¹ Department of Health Analyst, Faculty of Health, Universitas Efarina, Simalungun, Sumatera Utara Province, Indonesia; dame.hutagalung@gmail.com (D.C.H)

* Correspondence: sukrisna.hutauruk@gmail.com (D.S.H)

Citations: Hutauruk, D.S. & Hutagalung, D.C. (2022). Clinical Overview of Ureum Levels in Type II Diabetes Mellitus Patients Infected by COVID-19 Pandemic. *International Journal of Global Optimization and Its Application*, 1(3), 196-201.

Academic Editor: Liew Pay Jun.

Received: 5 May 2022

Accepted: 20 September 2022

Published: 30 September 2022

Abstract: Pneumonia caused by Coronavirus Disease (Covid-19) first appeared in Wuhan. Diabetes mellitus becomes one of the main risk factors for a person infected with the Covid-19 virus because it is susceptible to infection. Chronic complications in the form of diabetic nephropathy caused by diabetes can also increase the severity and mortality in diabetic patients infected with the Covid-19 virus. This study aims to determine the clinical overview of ureum levels in Covid-19-infected diabetes mellitus patients treated at Efarina Pangkalan Kerinci Hospital. This study was conducted from July to September 2021 at the Laboratory of Efarina Pangkalan Kerinci Hospital. This type of research is descriptive analytics. This examination uses a light intensity measurement method using an autoanalyzer with a sample of 30 samples taken at random. The results of the examination of ureum levels in Diabetic Mellitus patients infected with the Covid-19 pandemic at Efarina Pangkalan Kerinci Hospital obtained results that increased by 13 samples (43%) and normal ureum levels by as many as 17 samples (57%). For this reason, patients are advised to conduct regular health checks, eat healthy foods and comply with the 5M health protocol to prevent the transmission of the Covid-19 virus.

Keywords: COVID-19; Diabetes Mellitus; Ureum; patients.



Copyright: © 2022 by the author. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Since December 2019, pneumonia has been caused by a new type of coronavirus known as Novel Coronavirus 2019 (2019-nCoV) in Wuhan, Hubei Province, China. On December 31, 2019, China reported the outbreak to the World Health Organization (WHO). Shortly after that, the pathogen was identified as a new coronavirus called the new coronavirus. Coronavirus Disease (Covid-19) is a virus-like virus that causes severe acute respiratory syndrome (SARS-CoV-2) (Rasmussen & Thompson, 2020). The Covid-19 virus has infected more than 214,468,601 cases, with 4,470,969 confirmed deaths (World Health Organization, 2021). Data released by the Task Force on Accelerating the Handling of the Covid-19 virus in 2021, there were 4,043,736 confirmed cases with 130,182 deaths due to the Covid-19 virus in Indonesia. While data was obtained from Efarina Pangkalan Kerinci Hospital, there are 2,476 confirmed cases caused by the Covid-19 virus.

Wu & McGoogan (2020) found that diabetic patients had a mortality rate from the Covid-19 virus three times higher than the general non-diabetic population. These results suggest that accompanying diseases such as diabetes may increase the risk of infection and death in patients infected with the Covid-19 virus. Diabetes mellitus can cause complications both acute and chronic. One example of a chronic complication is diabetic nephropathy (Smeltzer, 2014). Diabetic nephropathy is a condition in which the kidneys experience a decrease in function and damage to the blood filter membrane caused by an increase in blood glucose levels.

Diabetic Mellitus with poor blood sugar control can cause damage to the glomerular endothelial capillaries resulting in glomerular filtration disorders (diabetic nephropathy) (Mustata et al., 2005) and associated with elevated levels of ureum blood (Molitoris et al., 2007). For this reason, patients infected with the Covid-19 virus who are treated at Efarina Pangkalan Kerinci Hospital need to be carried out several laboratory examinations, such as Ureum levels and blood glucose levels. It aims to determine if people with diabetes are one of the comorbid diseases to increase the risk of infection and mortality in patients infected with the Covid-19 virus.

Table 1. Normal Value of Ureum Levels.

Gender	Normal Values (mg/dl)
Men	8 – 45
Woman	8 – 40

2. Literature Review

The Covid-19 virus is zoonotic, so there is a possibility that the virus originated from animals and was transmitted to humans. Further development of data indicates human to human transmission, which is predicted through droplets and contact with viruses released in droplets (Zhou et al., 2020). Signs and symptoms of someone infected with the Covid-19 virus often occur fever $\geq 38^{\circ}\text{C}$, phlegm/dry cough, flu, shortness of breath, headache, anosmia/loss of smell, loss of taste, conjunctivitis, decreased oxygen saturation $\leq 95\%$. The pandemic caused by the Covid-19 virus has infected more than 1 million people from around the world. Data in Indonesia today also shows a growing trend. The Covid-19 virus can affect almost any age group. Still, current data show that older groups and people with a history of chronic (comorbid) disease are at risk for developing it more frequently and with worse illness complications. The history of chronic diseases in question includes hypertension, diabetes mellitus, cardiovascular disease, and chronic lung disease. Specifically, for those whose diabetes was the second most common comorbidity found, about 8% of cases after hypertension (Yang et al., 2020) and with a mortality rate three times that of sufferers in general (7.3% versus 2.3%) (Wu & McGoogan, 2020).

The primary pathophysiology of the Covid-19 virus in humans is a severe proinflammatory response or cytokine storm. It is stimulated by the virus when it enters the human body (Alkundi et al., 2020). The Covid-19 virus uses ace-2 acceptor (Angiotensin Converting Enzyme-2) as an entrance to human cells through bonding with s-glycoproteins found on the surface of the Covid-19 virus (Singh et al., 2020). Based on research by Singh et al. (2020), the entry of the virus into the cell triggers an inflammatory response through interferon-producing helper T cells that lead to cytokine storms. Research conducted on mice showed that in diabetic conditions, there was an increase in the expression on the ACE-2 receptor. The study was also supported by obtaining ACE-2 receptors in patients with type 1 and type 2 diabetes mellitus (Dualib et al., 2022). In addition, in diabetes mellitus, there is also an increase in furin protease membrane type 1, which plays a role in the entry of the Covid-19 virus into the cell and facilitates viral replication (Singh et al., 2020).

According to Ejaz et al. (2020), impaired T-cell function and increased levels of interleukin-6 (IL-6) also play an important role in increasing the severity of disease due to the Covid-19 virus in people with diabetes mellitus. As a result of the lengthening time of clearing the virus from the body of diabetic Mellitus patients, it can increase the severity of Covid-19 virus infection and even increase the risk of death. Such elongation can occur due to the cessation of activity of the enzyme Dipeptidyl Peptide IV (DPP4) by users of antidiabetic drugs (Abdi et al., 2020). A study conducted by Abdi et al. (2020) stated that a decrease in macrophage function also increased severity due to the Covid-19 virus in patients with diabetes mellitus. Chronic and inflammatory hyperglycemia causes abnormal and ineffective immune responses due to decreased mobilisation of polymorphonuclear leukocytes, chemotaxis, phagocyte activity, decreased cytokine excretion and inhibition of tumour necrosis alpha (TNF α) activity in T cells. This

pathophysiological mechanism can increase the risk of death in patients infected with the Covid-19 virus with a history of diabetes mellitus (Holman et al., 2020).

Hyperglycemia, or increased blood glucose levels, is the initial cause of diabetes. Glucose levels in the blood will increase when consuming carbohydrates in excess. When carbohydrates are digested, glucose is absorbed into the bloodstream. When blood glucose levels rise, the pancreas secretes the hormone insulin. Insulin allows the body's cells to absorb glucose in blood vessels to use it as energy reserves. The role of insulin is to work together with other hormones to maintain the stability of glucose levels in the blood. Diabetes mellitus occurs when the pancreas cannot produce insulin or the body becomes resistant to the effects of insulin (Kingham & Welham, 2009). Based on research conducted by Yasuda et al. (1984), that increased urea in the blood can signal a kidney problem. In patients with diabetes mellitus occurs because glucose in the blood cannot be converted into glycogen. In this event, it will cause microvascular complications in the kidneys. In the event of hyperglycemia, the kidneys cannot filter and absorb a certain amount of glucose in the blood. One indicator of kidney faal examination is to assess the Glomeruler Filtration Rate (GFR), if the GFR value decreases then ureum levels will increase.

3. Materials and Methods

This study is designed using descriptive analytics by describing ureum levels in patients with diabetes mellitus infected with the Covid-19 virus treated at Efarina Pangkalan Kerinci Hospital. The study was conducted at the Laboratory of Efarina Pangkalan Kerinci Hospital from July to September 2021. This ureum level examination uses a light intensity measurement method using the Mindray BS-230 autoanalyzer tool with a sample of 30 samples taken at random. The type of data used is secondary data, which is data obtained indirectly from the recapitulation of medical record data of type II diabetes mellitus patients infected with the Covid-19 virus at Efarina Pangkalan Kerinci Hospital.

3.1. Working Procedures

3.1.1 Sampling

- Prepared tools needed such as: sput 3 ml, tourniquit, yellow lid vacuum tube, alcohol swab 70%, plaster, handsoon.
- Hand washed before acting and hands coons are used to reduce nosocomial infections.
- Ascertain the identity of the patient in accordance with the patient who will be taking blood. Then ascertained again the name, and date of birth of the patient and medical record number in accordance with the examination form to clarify.
- The patient is instructed to clench his hands. Then installed tourniquit 5 cm above the elbow folds.
- Determined location of blood collection. Selected part of the cubital or chepalicmediana vein, then selected a large and visible vein for easy retrieval. The position of the patient's arm should be straight, do not bend the elbow.
- The location of the stabbing is sterilised using a 70% alcohol swab and allowed to dry out.
- Venous blood collection is done using a 3 ml sput, venous puncture at an angle of 30-45 degrees. It is certain that the needle enters the vein by pulling a little sput pump, if there is no blood entering then it is searched again without removing the needle. If it has entered, the sput pump is pulled and then sucked as much blood as needed. Then the tourniquit is released and then the patient is asked to remove his fist.
- Release /unplug the sput and immediately place the alcohol swab 70% on top of the injection marks while slightly pressed. After the blood stops coming out, then plastered the puncture marks.
- Inserted blood that has been taken into the vacuum tube yellow lid and labeled the patient.

3.1.2 Sample preparation

- Blood drawn that has been labeled before.
- Then the blood is dyscentral at a speed of 3000 rpm for 10-15 minutes until serum is obtained.

3.1.3 How it works

- Checked the condition of tool status, wholeness of reagent, cuvet segment
- Mindray BS-230 autoanalyzer is turned on.
- Checked and ascertained the status of the device in a standby state. If the status of the tool is not yet in a standby state, then the Utility clicked and then selected the Wake Upicon, then waited approximately 5 minutes until the standby tool

- Then clicked the Program icon, then selected ureum, creatinine and blood sugar examination parameters.
- After selecting the examination parameters, then clicking the Demog icon, the patient's identity filling format will appear. Then equipped with patient data as stated on the examination request form. It then clicked Save twice.
- Then next click the Result icon, then see what position the sample lays in the tool.
- After that, put 500 ul of the patient's serum into the microtube, then inserted into the BS-230 mindray tool in order of position.
- Click the play icon on the tool, then wait for the results according to the time listed on the tool.

4. Results

The results of the study obtained from the results of examination of ureum levels were an increase of 13 samples from 30 samples and normal as many as 17 samples. Percentage of blood glucose is calculated using the Percentage = (The number of blood glucose samples increases / the total number of samples) × 100% = (30 / 30) × 100% = 100%. Figure 1 displays the percentage of blood glucose examination results in diabetes mellitus patients infected with COVID-19 at Efarina Pangkalan Kerinci Hospital.

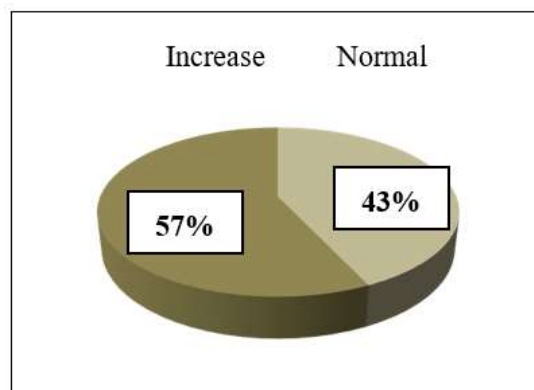


Figure 1. Result of blood glucose examination for diabetes mellitus patients infected by COVID-19 pandemic.

Figure 2 displays the result of blood glucose examination for diabetes mellitus patients infected by COVID-19 pandemic. This study found that patients' blood glucose is categorised as increasing as much as 17 patients or 57 percent. Also, 43 percent or 13 patients' blood glucose is normal due to COVID-19 pandemic. Percentage of Ureum Level is calculated by percentage = (number of ureum samples increased) / (total number of samples) = (13/30) × 100% = 43%. Percentage = (normal ureum sample count) / (total number of samples) = (17/30) × 100% = 57%

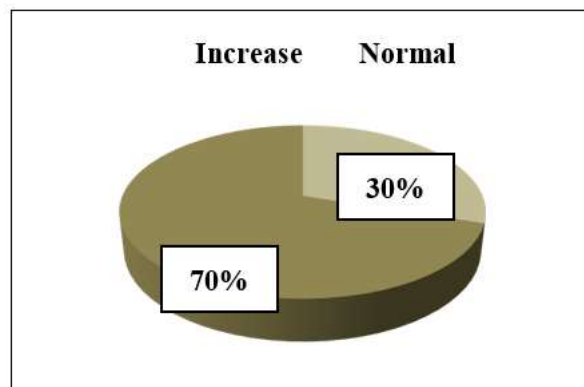


Figure 2. Result of Creatinine Examination for Diabetes Mellitus Patients Infected by COVID-19 Pandemic

Figure 2 displays the result of creatinine examination for diabetes mellitus patients infected by COVID-19 pandemic. This study indicated that most of Diabetes Mellitus patients increased due to infected by COVID-19 pandemic (21 patients or 70 percent). The remaining 30 percent or 9 patients categorised as normal.

Table 2. Result of Ureum Examination for Diabetes Mellitus patients infected with COVID-19 pandemic

No.	Ureum Rate	Sum	Percentage
1	Normal	17	57
2	Increase	13	43
Total		30	100

Table 2 displays the result of Ureum Examination for Diabetes Mellitus patients infected with COVID-19 pandemic. This study found that the Ureum rate of patients is categorised as normal as 17 patients or 57 percent. Also, 43 percent or 13 patients Ureum rate is increase due to COVID-19 pandemic.

5. Discussion

The study results of the examination of ureum levels in Diabetic Mellitus patients infected with the COVID-19 virus at Efarina Pangkalan Kerinci Hospital indicate that ureum levels increased by 13 samples (43%) and normal ureum levels resulting in 17 samples (57%). People with diabetes mellitus are susceptible to infection due to hyperglycemia. The severity of infection and mortality from the Covid-19 virus was higher in patients with a history of diabetes mellitus than in non-diabetic patients. Due to the impaired immune function of diabetics, it has become one of the factors triggering the ease of the Covid-19 virus infecting humans (Parveen et al., 2020). Factors that influence the examination ureum are (i) If the sample used undergoes hemolysis, the results of the ureum are likely false. (ii) Ureum results are also affected by dilution. (iii) A protein supply (low-protein diet) can affect urea nitrogen levels, thereby lowering the value of BUN (Blood Urea Nitrogen) and Creatinine, and urea nitrogen should be considered when assessing kidney function. If there is a significant increase or decrease, the results can be compared to the creatinine ratio before assessing kidney function (Chernecky & Berger, 2013).

An increase in the ureum in the blood can indicate a kidney problem. In patients with diabetes mellitus, increased ureum levels occur because glucose in the blood cannot be converted into glycogen. This event will cause microvascular complications in the kidneys, one of which is diabetic nephropathy. Hyperglycemia plays a role in the formation of atherosclerosis, so there is a narrowing of the lumen of blood vessels and a decrease in the speed of blood flow that leads to reduced blood supply to the kidneys. It can lead to impaired filtration processes in the glomerulus and decreased kidney function, characterised by increased levels of ureum in the blood (Yunisrah, 2019).

6. Conclusions

In conclusion, this study identified that Diabetic Mellitus infected with the Covid-19 virus treated at Efarina Pangkalan Kerinci Hospital, normal ureum levels were obtained in as many as 17 samples (57%) and ureum levels increased by 13 samples (43%).

Author Contributions: Conceptualisation, D.C.H. and D.S.H.; methodology, D.C.H.; software, D.S.H.; validation, D.C.H. and D.S.H.; formal analysis, D.C.H. and D.S.H.; investigation, D.C.H. and D.S.H.; resources, D.C.H.; data curation, D.S.H.; writing—original draft preparation, D.C.H. and D.S.H.; writing—review and editing, D.C.H. and D.S.H.; visualisation, D.C.H.; supervision, D.C.H.; project administration, D.S.H.; funding acquisition, D.C.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Not applicable.

Acknowledgments: The author would like to thank Universitas Efarina, Indonesia for supporting this research and publication. We would also like to thank the reviewers for their constructive comments and suggestions.

Conflicts of Interest: The authors declare no conflict of interest.

References

- Abdi, A., Jalilian, M., Sarbarzeh, P. A., & Vlaisavljevic, Z. (2020). Diabetes and COVID-19: A systematic review on the current evidences. *Diabetes Research and Clinical Practice*, *166*, 108347.
- Alkundi, A., Mahmoud, I., Musa, A., Naveed, S., & Alshawwaf, M. (2020). Clinical characteristics and outcomes of COVID-19 hospitalised patients with diabetes in the United Kingdom: a retrospective single centre study. *Diabetes Research and Clinical Practice*, *165*, 108263.
- Dualib, P. M., Taddei, C. R., Fernandes, G., Carvalho, C. R. S., Sparvoli, L. G., Silva, I. T., Mattar, R., Ferreira, S. R. G., Dib, S. A., & Almeida-Pititto, B. de. (2022). Gut microbiota across normal gestation and gestational diabetes mellitus: A cohort analysis. *Metabolites*, *12*(9), 796.
- Ejaz, H., Alsrhani, A., Zafar, A., Javed, H., Junaid, K., Abdalla, A. E., Abosalif, K. O. A., Ahmed, Z., & Younas, S. (2020). COVID-19 and comorbidities: Deleterious impact on infected patients. *Journal of Infection and Public Health*, *13*(12), 1833–1839.
- Holman, N., Knighton, P., Kar, P., O’Keefe, J., Curley, M., Weaver, A., Barron, E., Bakhai, C., Khunti, K., & Wareham, N. J. (2020). Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *The Lancet Diabetes & Endocrinology*, *8*(10), 823–833.
- Kingham, E., & Welham, M. (2009). Distinct roles for isoforms of the catalytic subunit of class-IA PI3K in the regulation of behaviour of murine embryonic stem cells. *Journal of Cell Science*, *122*(13), 2311–2321.
- Molitoris, B. A., Levin, A., Warnock, D. G., Joannidis, M., Mehta, R. L., Kellum, J. A., Ronco, C., & Shah, S. (2007). Improving outcomes from acute kidney injury. In *Journal of the American Society of Nephrology* (Vol. 18, Issue 7, pp. 1992–1994). Am Soc Nephrol.
- Mustata, G. T., Rosca, M., Biemel, K. M., Reihl, O., Smith, M. A., Viswanathan, A., Strauch, C., Du, Y., Tang, J., & Kern, T. S. (2005). Paradoxical effects of green tea (*Camellia sinensis*) and antioxidant vitamins in diabetic rats: improved retinopathy and renal mitochondrial defects but deterioration of collagen matrix glycoxidation and cross-linking. *Diabetes*, *54*(2), 517–526.
- Rasmussen, S. A., & Thompson, L. A. (2020). Coronavirus disease 2019 and children: what pediatric health care clinicians need to know. *JAMA Pediatrics*, *174*(8), 743–744.
- Singh, A. K., Gupta, R., & Misra, A. (2020). Comorbidities in COVID-19: Outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *14*(4), 283–287.
- Smeltzer, S. C. (2014). *Smeltzer, SC (2014). Keperawatan medikal bedah (handbook for Brunner & Suddarth’s textbook of medicalsurgical nursing) edisi 12. Diterjemahkan oleh Devi Yulianti & Amelia Kimin. Jakarta: EGC. Jakarta: EGC Medical Book.*
- World Health Organization. (2021). *WHO Coronavirus (COVID-19) Dashboard*.
- Wu, Z., & McGoogan, J. M. (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama*, *323*(13), 1239–1242.
- Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., Ji, R., Wang, H., Wang, Y., & Zhou, Y. (2020). Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis*, *94*(1), 91–95.
- Yasuda, K., Miyagi, H., Hamada, Y., & Takata, Y. (1984). Determination of urea in whole blood using a urea electrode with an immobilised urease membrane. *Analyst*, *109*(1), 61–64.
- Zhou, P., Yang, X.-L., Wang, X.-G., Hu, B., Zhang, L., Zhang, W., Si, H.-R., Zhu, Y., Li, B., & Huang, C.-L. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, *579*(7798), 270–273.