International Journal of Research and Review
Vol. 10; Issue: 8; August 2023
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Inflammation Markers (CRP, LDH, D-Dimer, Ferritin) as a Predictor of Death in COVID-19 Patients with Type 2 DM at H. Adam Malik Hospital

Cempaka Dewi NST[1], Dian Anindita Lubis[2], M. Aron Pase[2]

[1]Department of Internal Medicine, [2]Division of Endocrine, Department Internal Medicine, Faculty of Medicine, University of North Sumatera, Medan, Indonesia

Corresponding Author: Cempaka Dewi NST

DOI: https://doi.org/10.52403/ijrr.20230802

ABSTRACT

Introduction: Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Infectious diseases, including Coronavirus disease 2019 (COVID-19) are usually found more frequently and/or seriously in people with diabetes mellitus, and increase mortality. Hematological parameters, such as CRP, LDH, D-dimer, ferritin can help predicting death in COVID-19 patients with type 2 diabetes mellitus.
Aim: To determine the relationship of inflammatory markers (CRP, LDH, D-dimer, ferritin) with the incidence of death in COVID-19 patients with type 2 DM at H.Adam Malik General Hospital.
Method: This research was an observational analytic study using medical record data of patients at the central installation at H.Adam Malik Hospital from 2020-2021 period. The sample was total sampling. The distribution test was carried out with the Shapiro Wilk test. Bivariate analysis was carried out to determine the relationship between inflammatory markers (CRP, LDH, D-dimer, ferritin) and the incidence of death in COVID-19 patients with type 2 DM using the chi square test if the data were normally distributed, or Fisher's exact test if the data were not normally distributed and data were calculated using multivariate analysis. The desired deviation (α) is 0.05, statistically significant if $p<0.05$.
Results: 239 subjects were included in the study, majority were men with comorbid coronary heart disease and majority of patients survived. Ferritin, CRP and LDH levels in patients with confirmed COVID-19 with type 2 DM were not associated with death with p values of 0.503, 0.401 and 0.671, respectively. D-dimer levels and the degree of severity of COVID-19 in type 2 DM patients had a significant relationship to death ($p=0.001$).
Conclusion: D-dimer levels in patients with confirmed COVID-19 with type 2 DM were associated with death.

Keywords: diabetes mellitus, COVID-19, LDH, ferritin, D-dimer, CRP

INTRODUCTION

Diabetes mellitus is a syndrome characterized by hyperglycemia caused by abnormality insulin secretion, insulin action, or both. Chronic hyperglycemia in diabetes mellitus caused dysfunction, and various organs failure, especially eyes, kidneys, nerves, heart, and blood vessels [1]. *Coronavirus disease* 2019 (COVID-19) infection was found more often and was more serious in people with diabetes mellitus, and increased morbidity significantly [2]. Severe COVID-19 infection related tightly with death caused by hyperinflammation induced by COVID-19 infection in the innate and adaptive immunity system and cytokine storm known as cytokine release syndrome (CRS) [3,4]. Laboratory was one of the parameters for risk stratification and predicting outcomes of COVID-19. History of diabetes mellitus,

cardiovascular events and their risks (hypertension, dyslipidemia, smoking) worsened the clinical outcome of COVID-19. Studies have reported that inflammatory parameters were related tightly with COVID-19 severity and mortality [5]. Haematological parameters could help predicting mortality in COVID- 19 patients with type 2 DM. This study was done to see the relationship of inflammation markers (CRP, LDH, D-dimer, ferritin) against death in COVID-19 patients with type 2 DM at H. Adam Malik General Hospital.

MATERIALS & METHODS

This study was observational analytic with retrospective on secondary medical record data to determine relationship between inflammation markers (CRP, LDH, D-dimer, ferritin) with the incident of death in COVID-19 patients with type 2 DM at H.Adam Malik General Hospital, Medan, North Sumatra.

This study was done using medical record data of inpatient at installation H. Adam Malik General Hospital Medan, North Sumatra after agreement Commission ethics Study USU FK Health Sector. The study was done for 3 months This study used *total sampling.*

Inclusion criteria were age ≥ 18 years; confirmed COVID-19; type 2 DM based on HbA1c ≥ 6.5, and /or fasting blood glucose > 125 mg/dL, blood glucose after 2 hour ≥ 200 mg/dL, ad random blood glucose ≥ 200mg/dL; type 2 DM patients or history consumption antidiabetic drug; type 2 DM with various comorbidities. Exclusion criteria were anemia; hyperglycemia stress and inflammation markers (CRP, LDH, D-Dimer, ferritin) were not completed.

Patients were selected if aged ≥ 18 years and were confirmed COVID-19 from history, physical examination and other examinations (RT-PCR swab, thorax CT scan). Demographic, clinical data, inflammation markers (CRP, LDH, ferritin, and D-dimer) and clinical outcome were taken from medical record.

STATISTICAL ANALYSIS

Data were analyzed in statistics using the SPSS computer program. Normality of data was tested with Shapiro Wilk or Kolmogorov-Smirnov. Chi-square test was used if data was normally distributed and Fisher exact if not distributed normally. The data was also tested using multivariate analysis. The magnitude of the desired deviation (α) was 0.05, significant if $p<0.05$.

RESULT

Demographics, clinical, inflammation markers characteristics

Based on medical record data of confirmed COVID-19 with type 2 DM patients who were hospitalized at the H. Adam Malik General Hospital Medan, there were 375 patients with 239 subjects fulfilling inclusion and exclusion criteria. Demographic, clinical and laboratory characteristics were presented in table 1.

Based on table 1, age median was 57 years old, the youngest was 26 years old and the oldest was 90 years old. Majority subject study was men, as many as 153 people (64%) and women as many as 86 people (36%). Based on COVID-19 patients with type 2 DM comorbidities, most subjects have coronary heart disease as many as 56 people (23.4%), chronic kidney disease as many as 3 people (1.3%), hypertension as many as 119 people (49.8%). Majority confirmed COVID-19 with type 2 DM patients lived, as many as 167 people (69.9%) and died as many as 72 people (30.1%).

Based on inflammation markers, the median CRP was 0.7 mg/dL, median LDH was 300 U/L, median ferritin was 670 ng/mL, median D-dimer was 473 ng/L. Median Hb was 13.8 and median HbA1C was 9.1.

Table 1. Characteristics baseline

Characteristics	**N = 239**
Age, (years)	
Median (minimum-maximum)	57 (26 - 90)
Gender, n (%)	
Men	153 (64)
Woman	86 (36)
Coronary heart disease, n (%)	
Yes	56 (23.4)
No	183 (76.6)
Chronic kidney disease, n (%)	
Yes	3 (1.3)
No	236 (98.7)
Hypertension, n (%)	
Yes	119 (49.8)
No	120 (50.2)
Outcome, n (%)	
Live	167 (69.9)
Die	72 (30.1)
Hb	
Median (minimum-maximum)	13.8 (10.3-18.50)
HbA1C	
Median (minimum-maximum)	9.10 (5.0-16.0)
CRP (mg/dL)	
Median (minimum-maximum)	0.7 (0.10-161)
LDH (U/L)	
Median (minimum-maximum)	300 (0.7-1696)
Ferritin (ng/mL)	
Median (minimum-maximum)	670 (27.53-3153.86)
D-dimer (ng/L)	
Median (minimum- maximum)	(0-100,000)

Table 2 Proportions comorbidities with death

	Life	Die	p value
Age Mean ± SD	56 ± 10	60 ± 1 1	
Median (minimum-maximum)	56 (26 - 90)	57 (31-89)	
Coronary heart disease	44 (18.4%)	12 (5%)	0.105*
Chronic kidney disease	2 (0.84%)	1 (0.42%)	0.903*
Hypertension	78 (32.64%)	41 (17.15%)	0.146*

**** Chi square test***

Based on table 2, mean age of patient with COVID-19 confirmed who lived was 56 years old and patient with COVID-19 confirmed who died was 60 years old. Based on comorbidities, 12 (5%) subjects who had coronary heart disease died, 1 (0.42%) subject with chronic kidney disease died, 41 (17.15%) subjects with hypertension died. Based on table 2, comorbidities didn't correlate with death significantly (p>0.05).

Relationship inflammation markers (Ferritin, CRP, LDH, D-Dimer) and COVID-19 severity with outcome

Based on Table 3, ferritin, CRP, LDH and D-dimer level in COVID-19 patients with type 2 DM who died was 781.4; 0.7; 409; and 1001.5 respectively. LDH and D-dimer level were correlated with *outcome* in COVID-19 patients with type 2 DM with p values were 0.001 and 0.01 respectively.

Table 3 Relationship rate marker inflammation (Ferritin, CRP, LDH, D-Dimer) in COVID-19 patients with type 2 DM against outcome

	Outcomes		p*
	Life	Die	
Ferritin			
Median	648	781.4	0.713
CRP			
Median	0.7	0.7	0.908
LDH			
Median	290	409	0.001
D-dimer			
Median	389	1001.5	0.01

*** Linear regression test**

Table 4 Relationship inflammation markers (Ferritin, CRP, LDH, D-Dimer) and severity of COVID-19 with outcome

	Outcome		p
	Live	Die	
Ferritin			
Normal	14 (5.9%)	8 (3.3%)	0.503
High	153 (64%)	64 (26.8%)	
CRP			
Normal	107 (44.8%)	42 (17.6%)	0.401
High	60 (25.1%)	30 (12.6%)	
LDH			
Normal	42 (17.6%)	20 (8.4%)	0.671
High	125 (52.3%)	52 (21.8%)	
D-dimer			
Normal	102 (42.7%)	22 (9.2%)	0.001
High	65 (27.2%)	50 (20.9%)	
COVID-19 degree			
Moderate	75	4	0.001
Severe	77	46	
Critical	15	22	

**** Chi square test***

Based on table 4, high levels of ferritin, CRP, LDH, D-dimer were found in type 2 DM patients with COVID-19 who died, 26.8%, 12.6%, 21.8% and 20.9%, respectively. Ferritin, CRP and LDH levels were high in type 2 DM patients with COVID-19 who died but not significant with p values were 0.503, 0.401 and 0.671 respectively. D-dimer levels and COVID-19 severity in type 2 DM patients correlated with outcome significantly (p=0.001).

Table 5 Relationship inflammation markers (Ferritin, CRP, LDH, D-Dimer) in COVID-19 patients with type 2 DM with COVID-19 severity

	COVID-19 degree			p*
	Moderate	Severe	Critical	
Ferritin				
Median	536	812	1225	0.145
CRP				
Median	0.7	0.7	0.7	0.523
LDH				
Median	257	320	435	0.02
D-dimer				
Median	315	650	570	0.109

*** Linear regression**

Based on table 5, ferritin, LDH and D-dimer levels in COVID-19 patients with type 2 DM increased along with COVID-19 severity, however ferritin, CRP and D-dimer levels didn't correlate with COVID-19 severity significantly with p value > 0.05. LDH levels were correlated with COVID-19 severity significantly (p = 0.02).

DISCUSSION

Diabetes was one of the most frequent diseases found in people with COVID-19. The prevalence varied between 7 to 30%. CDC data from January to May 2020 showed COVID-19 hospitalizations were 6 times higher and 12 times mortality for people with COVID-19 and underlying medical conditions such as diabetes, heart disease, or chronic lung disease [6,7].

The median age of COVID-19 patients with type 2 DM was 57 years old, with the youngest was 26 years old and the oldest was 90 years old. Majority of the subjects was man, as many as 153 people (64%) and women as many as 86 people (36%).

This result was similar to research by Li *et al.* (2021) where the average age of COVID-19 patients was 46.7 years, 51.8% is men, 22.9% have critical disease, and 5.6% dead [8]. Factors that correlated significant and independent related with worsened clinical outcome in COVID-19 patients with type 2 diabetes was ischemic heart disease, old age and low level of platelet [9]. Pathophysiology high hospitalization, morbidity, and mortality percentage between man than woman was not known yet, but current study showed that sex hormone affected the infectivity of the virus. ACE-2 expression levels differed between adults and children. Previous studies showed that ACE-2 were found more in differentiated ciliated epithelium cells and more as ones got old. Aging was related with enhancement cytokine proinflammatory that regulate the function of neutrophils and correlated with ARDS severity [10].

Based on comorbidities, subject experienced coronary heart disease, as many as 56 people (23.4%), chronic kidney disease as many as 3 people (1.3%), and hypertension as many as 119 people (49.8%).

Singh *et al*. (2020) reported that prevalence hypertension, diabetes and cardiovascular was 21%, 11%, and 7% respectively [11]. Meta-analysis of 8 trials with 46.248 COVID-19 patients by Yang et *al*. (2020) reported the prevalence for hypertension,

diabetes, and cardiovascular, was 17%, 8%, and 5%, respectively. COVID-19 with hypertension, cardiovascular disease, and diabetes mellitus were more prone to critical disease and higher mortality [12]. The prognosis of deteriorating COVID-19 patients with type 2 DM was related with enzyme- facilitated viral *uptake* angiotensin receptor 2 (ACE2). This was also related with higher proinflammatory cytokine basal level in diabetic patients [13,14].

Majority COVID-19 confirmed with type 2 DM patients lived, as many as 167 people (69.9%) and died as many as 72 people (30.1%). Baron *et al.* (2020) showed that COVID-19 with type 2 DM had increased risk of death 2 times [15]. Studies registry Spanish from Spanish Society of Internal Medicine for COVID-19, which included 11,312 patients (18.9 % prior DM) hospitalized COVID-19 in 109 hospitals showed that patients who were not critical but hyperglycemia on admission, regardless from previously diabetes or not, suffered more complications and died and that risk increased along with hyperglycemia degree (blood glucose>180 mg/dL (>10 mmol/L), and glucose blood 140–180 mg/dL (7.8–10 mmol/L) [16]. The mechanisms were chronic inflammation, immunity response dysfunction and coagulation disorder in type 2 DM [17].

Based on inflammation markers, the median CRP was 0.7 mg/dL, median LDH was 300 U/L, median ferritin was 670 ng/mL, median D-dimer was 473 ng/L. The median Hb was 13.8 and median HbA1C is 9.1. Eissa *et al.* (2021) found increased Hb [12.6 vs 11.6 g/dl, p = 0.039], increased CRP (13.1 vs 6 mg/L, p = 0.003), increased ferritin (200 versus 43 ng/L, p = 0.008), and increased D-dimer significantly in COVID-19 patients compared with group control [0.33 vs 0.1 ng/ mL; p < 0.001] [18]. Bhandari *et al*. (2020) showed increased CRP (7.2 mg/L), LDH (881 U/L), ferritin (893 ng/mL), D-dimer (1.3 mcg/mL) significant (all p value < 0.05) in patients with severe COVID-19 [19]. Smati *et al*. (2022) showed that the median HbA1c was 7.7% (60.7 mmol/mol), higher than 7.1% (56.0 mmol/mol) which was observed in the French ENTRED study (representative national sample from diabetics in France) [20]. Mishra et al. (2020) showed that D-dimer levels were 1509 ± 2420 ng/mL (mean±SD) in diabetics and 515 ± 624 ng/mL (mean ± SD) in patients without diabetes with positive COVID-19 [21].

Severe inflammation was not only related with severity disease but also with *outcomes*. In study of 283 patients with COVID-19 RT-PCR confirmed, three inflammation markers, CRP (sensitivity 86.36%; specificity 88.89%), lactate dehydrogenase (LDH) (sensitivity 90.91%; specificity 80.56%), and ferritin (sensitivity 95.45%; specificity 86.57%) were proved to be useful in predicting death. Zeng *et al.* showed that series inflammation marker like procalcitonin, ferritin, LDH, high sensitivity CRP, and ratio high sensitivity ratio CRP to lymphocytes increased in critical COVID-19 patients. LDH was independent predictor for the severity COVID-19 disease [22].

Ferritin, CRP, LDH, D-dimer level were increased in type 2 DM patients with COVID-19 who died, 26.8 %, 12.6%, 21.8% and 20.9% respectively, but increased ferritin, CRP and LDH levels in type 2 DM patients with COVID-19 who died were not too significant with p values were 0.503, 0.401 and 0.671 respectively. D-dimer level and COVID-19 severity in type 2 DM patients correlated significant to *outcomes* (p=0.001).

Ferritin was the main mediator from immune dysregulation especially hyperferritinemia extreme, through direct immunosuppressive and proinflammatory, which contributed to the hurricane cytokine. Mechanism of ferritin in pathophysiology of COVID-19 was not yet fully known. However, current study showed that cytokines stimulate hepatic production of defense proteins, including CRP and ferritin as response to injury. Transcription and translation of ferritin were induced mainly by IL-1β, IL-6, and IFN-γ. Ferritin promoted release of proinflammatory

mediators, improved inflammation burden and inflammation circle devil. The fatal consequences of COVID-19 were usually accompanied with cytokines storm syndrome. Feld *et al.* (2020) show that deceased COVID-19 patients had average longer hospital length stay and higher ferritin level [23]. Diabetic patients showed increased ferritin levels and higher risk of severe complication due to COVID-19 [24,25]. Cheng *et al.* (2020) showed that COVID-19 patients with one or more underlying diseases including diabetes, thrombosis complication, and cancer had higher level of ferritin compared to those who did not ($P < 0.01$) [26].

CRP was inflammatory markers, synthesized in the liver, and it was protein as acute response to cytokine inflammation produced by monocytes or macrophages activated after infection. CRP level reflected the inflammation severity and its storm cytokine consequences related with poor COVID-19 outcome [18]. CRP was correlated with the incidence of VTE, AKI, critical disease, and death in COVID-19 [27]. In COVID-19, CRP levels ≥4 mg/L had been proven useful for triage suspect case compared to patient with positive PCR versus control negative result presenting to clinic as fever with respiratory symptom or high temperature (OR 4.75; 95% CI 3.28 to 6.88). Patient with CRP ≥40 mg/L, death was 28.6% compared with 10.4% patients with CRP <40 mg/L [28]. Smati *et al*. (2022) showed that older age, microvascular complications, treatment with insulin or a statin before admission, dyspnea on admission, as well as high levels of transaminases, leukocytes and CRP, and low platelets were associated with increased mortality [20]. Study by Abdi *et al*. (2020) showed patients had poorer ARDS prognosis, more severe symptoms, and higher mortality in COVID-19 patients with type 2 DM. Diabetic patients were treated with antibiotics, antivirals, and HCQ. Diabetes was risk factor and contributed to the severity and death in patient with COVID-19 [29].

LDH was enzyme found intracellularly in cell in almost all organs, which catalyzed interconversion pyruvate and lactate, with interconversion along with NADH and NAD+. Infection caused damage mediated cytokine network and LDH release. LDH was found in lung (isozyme 3) and the patient with severe COVID-19 released more LDH into the circulation. Preliminary data on COVID-19 patients showed significant difference in LDH levels between patient with and without critical disease. Increased LDH levels were found in >95% of those who died compared to <60% of people alive. Increased LDH levels were related with possibility ~6 fold increased of developing severe disease and increased ~16 times more likely death in patients with COVID-19 [30].

Study by Li *et al*. (2020) in 203 patients COVID-19 confirmed showed that serum LDH levels had sensitivity 58.7% and specificity 82.0%, based on *cutoff* 277.00 U/L, to predict severe COVID-19, and cut off LDH serum levels 359.50 U/L had sensitivity 93.8%, specificity 88.2% to predict COVID-19 deaths [31]. Han *et al*. (2020) showed that LDH was related positively with APACHE II and SOFA scores, as well as P/F ratio and CT score, LDH (AUC = 0.878) also had specificity maximum (96.9%), with cutoff 344.5 [32].

D-dimer level and COVID-19 severity in type 2 DM patients correlated significantly with outcomes (p=0.001). This result was similar to Miri *et al.* (2021) that D-dimer level were found higher respectively in COVID-19 patients with type 2 diabetes compared with non-diabetic patients (1745 vs 845, respectively, p = 0001) [33]. D-dimer level > 2885 ng/mL was predictor of mortality in COVID-19 patients with type 2 diabetes significantly with sensitivity 71.4% and specificity 70.7%. Increased D-dimer level and thrombocytopenia in patients with severe COVID-19 had also been reported, which showed hypercoagulability contributing to illness severity and death [30]. Mishra *et al*. (2020) showed that COVID-19 patients with diabetes had

higher D-dimer and COVID-19 infection in diabetes tend to cause hypercoagulation with bad prognosis [21].

Prothrombotic status can be induced by hyperglycemia through two different pathways: stress oxidative and non-enzymatic glycation. Acute hyperglycemia through stress oxidative increased thrombin formation, meanwhile non-enzymatic glycation reduced the antithrombin III and co- factor II heparin. Hyperglycemia can produce a pro-thrombotic status, because of imbalance between pro-coagulation, anti-coagulation and fibrinolysis [34].

CONCLUSION

Majority of the subjects in this study were man with comorbidities ranging from coronary heart disease, chronic kidney disease and hypertension. Majority confirmed COVID-19 patients with type 2 DM lived. Ferritin, CRP and LDH levels in patients confirmed COVID-19 with type 2 DM didn't correlate with outcomes. D-dimer levels and COVID-19 severity in type 2 DM patients correlated significant to outcome. LDH level was correlated with COVID-19 degree significantly, with p value = 0.02.

Declaration by Authors

Ethical Approval: Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

Acknowledgement: Authors admitted contributions of colleagues and institutions therefore authors like to show gratitude to supervisors and all parties who support and contributed in this research.

Source of Funding: None

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

REFERENCES

1. ADA. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2014; 37(1): S81-S90.
2. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab. 2012; 16(1): S27-S36.
3. Mostaghim A, Sinha P, Bielick C, Knudsen S, Beeram I, White LF, et al. Clinical outcomes and inflammatory marker levels in patients with Covid-19 and obesity at an inner-city safety net hospital. PLoS ONE. 2020; 15(12): e0243888.
4. Mahat RK, Panda S, Rathore V, Swain S, Yadav L, Sah SP. The dynamics of inflammatory markers in coronavirus disease-2019 (COVID-19) patients: A systematic review and meta-analysis. Clin Epidemiol Glob Health. 2021; 11: 100727.
5. Wolff D, Nee S, Hickey NS, Marschollek M. Risk factors for Covid-19 severity and fatality: a structured literature review. Infection. 2021; 49(1): 15–28.
6. CDC. Diabetes and COVID-19. Accessed at: 19 November 2022. Available at: https://www.cdc.gov/diabetes/library/reports/reportcard/diabetes-and-covid19.html
7. Lima-Martínez MM, Carrera Boada C, Madera-Silva MD, Marín W, Contreras M. COVID-19 and diabetes: A bidirectional relationship. COVID-19 y diabetes mellitus: una relación bidireccional. Clin Investig Arterioscler. 2021; 33(3): 151-157.
8. Li J, Huang DQ, Zou B, Yang H, Hui WZ, Rui F, et al. Epidemiology of COVID-19: A systematic review and meta-analysis of clinical characteristics, risk factors, and outcomes. J Med Virol. 2021; 93(3): 1449-1458.
9. Izzi-Engbeaya C, Distaso W, Amin A, Yang W, Idowu O, Kenkre JS, et al. 2021. Adverse outcomes in COVID-19 and diabetes: a retrospective cohort study from three London teaching hospitals. BMJ Open Diabetes Res Care. 2021; 9(1): e001858.
10. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clin Immunol. 2020; 215: 108427.
11. Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. Diabetes Metabol Syndrome Res Rev. 2020; 14(4): 283-287.
12. Yang, J., et al. 2020. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. International Journal of Infectious Diseases. 2020; 94: 91-95.
13. Azar WS, Njeim R, Fares AH, Azar NS, Azar ST, El Sayed M, Eid AA. COVID-19 and diabetes mellitus: how one pandemic worsens the other. Rev Endocr Metab Disord. 2020; 21(4): 451-463.
14. Bulut C, Kato Y. Epidemiology of COVID-

19. Turk J Med Sci. 2020; 21(50): 563-570.
15. Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: A whole-population study. Lancet Diabetes Endocrinol. 2020; 8(10): 813–822.
16. Carrasco-Sánchez FJ, López-Carmona MD, Martínez-Marcos FJ, Pérez-Belmonte LM, Hidalgo-Jiménez A, Buonaiuto V, et al. Admission hyperglycaemia as a predictor of mortality in patients hospitalized with COVID-19 regardless of diabetes status: Data from the Spanish SEMI-COVID-19 Registry. Ann. Med. 2021; 53(1): 103–116.
17. Bellido V, Pérez A. Inpatient Hyperglycemia Management and COVID-19. Diabetes Ther. 2021; 12(1): 121-132.
18. Eissa M, Shaarawy S, Abdellateif MS. The Role of Different Inflammatory Indices in the Diagnosis of COVID-19. Int J Gen Med. 2021; 8(14): 7843-7853.
19. Bhandari S, et al. 2020. Inflammatory Markers in COVID-19. Accessed at 20 November 2022, Available at: https://annals.edu.sg/pdf/49VolNo6Jun2020/V49N6p393.pdf
20. Smati S, Tramunt B, Wargny M, Gourdy P, Hadjadj S, Cariou B. COVID-19 and Diabetes Outcomes: Rationale for and Updates from the CORONADO Study. Curr Diab Rep. 2022; 22(2): 53-63.
21. Mishra Y, Pathak BK, Mohakuda SS, Tilak TVSVGK, Sen S, P H, et al. Relation of D-dimer levels of COVID-19 patients with diabetes mellitus. Diabetes Metab Syndr. 2020; 14(6): 1927-1930.
22. Wong RSY. Inflammation in COVID-19: from pathogenesis to treatment. Int J Clin Exp Pathol. 2021; 14(7): 831-844.
23. Feld J, Tremblay D, Thibaud S, Kessler A, Naymagon L. Ferritin levels in patients with COVID-19: A poor predictor of mortality and hemophagocytic lymphohistiocytosis. Int J Lab Hematol. 2020; 42(6): 773-779.
24. Vargas-Vargas M, Cortés-Rojo C. Ferritin levels and COVID-19. Rev Panam Salud Publica. 2020; 1(44): e72.
25. Mahroum N, Alghory A, Kiyak Z, Alwani A, Seida R, Alrais M, et al. Ferritin - from iron, through inflammation and autoimmunity, to COVID-19. J Autoimmun. 2022; 126: 102778.
26. Cheng HY, Jian SW, Liu DP, Ng TC, Huang WT, Lin HH; Taiwan COVID-19 Outbreak Investigation Team. Contact Tracing Assessment of COVID-19 Transmission Dynamics in Taiwan and Risk at Different Exposure Periods Before and After Symptom Onset. JAMA Intern Med. 2020; 180(9): 1156-1163.
27. Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, Hochman JS, Berger JS. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J. 2021; 42(23): 2270-2279.
28. Stringer D, Braude P, Myint PK, Evans L, Collins JT, Verduri A, et al. The role of C-reactive protein as a prognostic marker in COVID-19. International Journal of Epidemiology. 2021; 50(2): 420–429.
29. Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: A systematic review on the current evidences. Diabetes Res Clin Pract. 2020; 166: 108347.
30. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et alLactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. Am J Emerg Med. 2020; 38(9): 1722-1726.
31. Li C, Ye J, Chen Q, Hu W, Wang L, Fan Y, et al. Elevated Lactate Dehydrogenase (LDH) level as an independent risk factor for the severity and mortality of COVID-19. Aging (Albany NY). 2020; 12(15): 15670-15681.
32. Han Y, Zhang H, Mu S, Wei W, Jin C, Tong C, et al. Lactate dehydrogenase, an independent risk factor of severe COVID-19 patients: a retrospective and observational study. Aging (Albany NY). 2020; 12(12): 11245-11258.
33. Miri C, Charii H, Bouazzaoui MA, Laouan Brem F, Boulouiz S, Abda N, et al. D-dimer Level and Diabetes in the COVID-19 Infection. Clin Appl Thromb Hemost. 2021; 27: 10760296211045902.
34. Ceriello A. Diabetes, D-dimer and COVID-19: The possible role of glucose control. Diabetes Metab Syndr. 2020; 14(6):1987.

How to cite this article: Cempaka Dewi NST, Dian Anindita Lubis, M. Aron Pase. Inflammation markers (CRP, LDH, D-Dimer, Ferritin) as a predictor of death in COVID-19 patients with type 2 DM at H. Adam Malik Hospital. *International Journal of Research and Review*. 2023; 10(8): 7-14. DOI: *https://doi.org/10.52403/ijrr.20230802*

******