Original Article

Evaluation of Mortality Risk Factors of COVID-19 in Jakarta Tertiary Hospital During Peak of Second Wave and Predictive Utility of Community RT-PCR Low CT Values

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Abstract

Background: The Delta variant of SARS-CoV-2 led to a surge in COVID-19 cases in Indonesia. This study aimed to assess the demographic profile and mortality rates of hospitalized COVID-19 patients in YARSI referral hospital, Jakarta, comparing pre-Delta and Delta wave periods. The study also investigated whether low CT values in RT-PCR tests indicated heightened viral transmission before the Delta wave surge.

Method: A retrospective analysis was conducted on 1,457 COVID-19 patients hospitalized at YARSI (January-August 2021) and 25,279 RT-PCR test results from walk-in patients (April-August 17, 2021). Differences were evaluated using Chi-square or Fisher's Exact Tests while binary logistic regression was used to assess mortality risk factors.

Results: There were increased proportions of pregnant women, patients aged 20-29 and those with coronary artery disease during the Delta wave. This period also showed a significant increase in mortality rates, with the highest seen in patients >60 years old or those with multiple comorbidities. Notably, most of the deceased patients (131 of 139) were unvaccinated. Analysis of RT-PCR data showed rising percentages of positive results with low CT values (below 21 or 15) from April to June.

Conclusion: The Delta wave saw a higher risk of hospitalization among young individuals and pregnant women, despite their low mortality risk. The unvaccinated and those with multiple comorbidities faced higher mortality risks. Increases in RT-PCR positivity with low CT values preceded the July COVID-19 case surge.

Keywords: COVID-19, Delta variant, mortality risk factors, PCR CT values, vaccine status

INTRODUCTION

SARS-CoV-2 Delta variant is the fourth variant of concern (VOC) designated by WHO due to its effective transmission and short incubation period. Delta variant has quickly dominated circulating variants in Indonesia.[1] In Indonesia, genomic surveillance shows that Delta has become a major variant since the beginning of May 2021. This upsurge of Delta variant is followed by spike of COVID-19 cases and mortality in reaching a peak in July 2021, including Jakarta.[2]

Genomic surveillance in Indonesia shows that Delta variant has contributed up to 85% of COVID-19 cases setting off second wave of COVID-19. In July 2021, 56,767 new cases were recorded with up to 26% positivity rate. Jakarta, the capital city of Indonesia, has also experienced peak of COVID-19 cases at that time, setting off unprecedented crisis of health care facilities including shortage of trained staffs and oxygen supplies.[2]

Previous reports from Singapore and United Kingdom suggest that Delta infection increases risk of hospitalization and mortality.[3,4] However, the impact of Delta surge on mortality of hospitalized COVID-19 patients in Indonesia was largely unknown. Moreover, Indonesia has begun the COVID-19 vaccination drive using inactivated virus vaccine technology since January 2021, primarily targeting elderly (60 years and older) and healthcare workers.[5] In May 2021, two-dose vaccine coverage among elderly in Jakarta was 55% and increased to 80% in July.[6] The vaccine using inactivated COVID-19 virus manufactured by Sinovac is the most common COVID-19 vaccine used in Indonesia.[7]

There were three objectives in this study. First, to identify clinical profiles of COVID-19 patients which were disproportionately higher during Delta (June to August 2021) than previous (January to May) waves. Second, to describe and identify clinical predictors associated with mortality of COVID-19 patients during Delta wave. Lastly, explored the utility of RT-PCR CT values to predict viral transmission preceding the Delta wave. Clinical profile and vaccination status of deceased patients would be interesting to explore and may help in shaping future policy while facing future emergence of COVID-19 variants.

METHOD

This retrospective study was conducted following the approval of the Ethical Clearance Committee of YARSI Hospital, ensuring adherence to the ethical standards of research. Laboratory and clinical data from YARSI Hospital electronic medical record systems were collected for all patients treated with positive SARS-CoV-2 RNA test between January and August 17th 2021 (N=1,457 patients).

Parameters to be compared included demographics (age and gender), comorbidity, length of hospitalization, laboratory parameters (blood glucose, D-dimer, neutrophil-lymphocytes ratio/NLR and c-reactive protein/CRP) and mortality.

Case-fatality risk was calculated among patients with in-hospital mortality (ie, COVID-19 deceased patients divided by COVID-19 deaths plus survivors of COVID-19).

In addition, records of RT-PCR test results were also accessed from 25,279 individuals referred to YARSI Hospital from surrounding community such as clinics and drive-thru sites from the period of April to August 2021. Parameters to be evaluated were positivity rates, median CT values and percentages of low CT values set arbitrarily at <15 and <21.

Descriptive data were presented as percentage comparing clinical parameters of all COVID-19 patients admitted to YARSI Hospital between January to May 2021 (pre-Delta variant) and June to August 2021 (Delta variant). No statistical sample size calculation was made and sample size was equal to the number of laboratory confirmed COVID-19 patients admitted at YARSI hospital during the study period to evaluate risk factors of hospitalization and mortality.

Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as medians (interquartile ranges/IQR). Differences between groups were assessed using chi-square or Fisher's exact tests for categorical variables. Differences were considered significant when p values were <0.05 for a two-tailed test. A binary logistic regression was used to evaluate risk factors associated with mortality including the variable of interest (wave) to assess differences in mortality between study waves. Factors included in the model were those with statistical significance in the univariable analysis. The results of the multivariable analysis were reported as odds ratios (OR) with the 95% confidence intervals (CI). StatPlus (AnalystSoft Inc) was used to perform statistical calculation.

RESULTS

Overall, there were 1,457 COVID-19 patients confirmed by laboratory tests between January to August 2021. As shown in Table 1, during the first five months of 2021 (January to May), there were 736 COVID-19 patients, with 721 patients added in just three months (June to August) which coincided with rising prevalence of COVID-19 Delta variant of concern (VOC). Comparative study revealed significant demographic differences between pre-Delta wav e (January to May) and Delta wave (June to August).

During Delta wave, there were more cases of pregnant women (0.5% vs 1.8%; OR=3.36; 95% CI=1.09-10.35; P=0.019), patients belonging to age group 20-29 years old (7% vs 13%; OR=1.99; 95% CI=1.39-2.86; P=0.0002) and patients with coronary artery disease comorbidities (5.3% vs 8.5%; OR=1.85; 95% CI=1.19-2.87; P=0.02) using univariate analysis. However, after adjusted to age and comorbidities, pregnancy variable reached borderline significant (aOR=2.99; 95% CI=0.96-9.32; P=0.05).

Table 1. Univariate and multivariate analysis of factors associated with admission to YARSI hospital in the pre-Delta (January to May 2021) and Delta (June to August 2021) waves

Parameters	Pre-Delta wave (N=736)	Delta wave (N=721)	OR (95% CI)	P	aOR (95% CI)	P
Gender						
Male	387 (53%)	378 (52%)	0.99 (0.81-1.22)	0.95	---	---
Female	349 (47%)	343 (48%)				
Age groups						
0-4	13 (1.8%)	7 (1.0%)	0.55 (0.22-1.37)	0.18	---	---
5-9	7 (1.0%)	6 (0.8%)	0.87 (0.29-2.61)	0.81	---	---
10-19	22 (3.0%)	25 (3.5%)	1.17 (0.65-2.09)	0.61	---	---
20-29	52 (7.1%)	94 (13.0%)	1.97 (1.38-2.81)	0.0001*	1.99 (1.39-2.86)	0.002*
30-39	113 (15.4%)	102 (14.1%)	0.91 (0.68-1.21)	0.52	---	---
40-49	137 (18.6%)	137 (19.0%)	1.03 (0.79-1.33)	0.85	---	---
50-59	192 (26.1%)	180 (25.0%)	0.94 (0.74-1.19)	0.62	---	---
60-69	127 (17.3%)	105 (14.6%)	0.82 (0.62-1.08)	0.16	---	---
70 and older	73 (9.9%)	65 (9.0%)	0.90 (0.63-1.28)	0.56	---	---
Comorbidities						
None	322 (43.8%)	307 (42.6%)	0.95 (0.77-1.17)	0.65	---	---
Single	236 (32.1%)	261 (36.2%)	1.2 (0.97-1.49)	0.10	---	---
Multiple	178 (24.2%)	153 (21.2%)	0.66 (1.08-0.18)	0.18	---	---
Type of comorbidities						
Diabetes	179 (24.3%)	152 (21.1%)	0.83 (0.65-1.06)	0.14	---	---
Hypertension	270 (36.7%)	231 (32.0%)	1.0 (0.66-1.01)	0.06	---	---
Obesity	33 (4.5%)	35 (4.9%)	1.09 (0.67-1.77)	0.74	---	---
CAD	39 (5.3%)	61 (8.5%)	1.65 (1.09-2.5)	0.02*	1.85 (1.19-2.87)	0.01*
CKD	14 (1.9%)	19 (2.6%)	1.4 (0.69-2.81)	0.35	---	---
Malignancy	8 (1.1%)	7 (1.0%)	0.89 (0.32-2.47)	0.83	---	---
TB	11 (1.5%)	12 (1.7%)	1.12 (0.49-2.54)	0.79	---	---
Alzheimer	2 (0.3%)	2 (0.3%)	1.02 (0.14-7.27)	0.98	---	---
Geriatric	9 (1.2%)	5 (0.7%)	0.56 (0.19-1.69)	0.30	---	---
Pregnancy	4 (0.5%)	13 (1.8%)	3.36 (1.09-10.35)	0.02*	2.99 (0.96-9.32)	0.05*
HIV	1 (0.1%)	3 (0.4%)	3.07 (0.32-29.6)	0.30	---	---
Asthma	25 (3.4%)	22 (3.1%)	0.9 (0.5-1.6)	0.71	---	---
Others	37 (5.0%)	44 (6.1%)	1.23 (0.78-1.93)	0.37	---	---

Note: *significant (P<0.05); CAD=Coronary Artery Disease; CKD=Chronic Kidney Disease; TB=Tuberculosis; HIV=*Human Immunodeficiency Viruses*

Mortality rates during pre-Delta and Delta waves were 7.2% and 11.9% respectively (Table 2). Mortality risks were higher in Delta wave for individuals with advanced age (>60 years, OR=1.81; 95% CI=1.19-2.76; P<0.05) or having multiple comorbidities (OR=2.3; 95% CI 1.57-3.35; P=0,0001). The most common comorbidities associated with higher risk of mortality in Delta wave were hypertension, diabetes, obesity, chronic kidney disease and geriatry. Interestingly, young age (20-29 years old) and individuals with coronary artery disease were not associated with mortality risk during Delta wave despite having significantly higher cases.

Table 2. Univariate and multivariate analysis of factors associated with in-hospital mortality in YARSI Hospital between pre-Delta wave versus Delta wave

Parameters	Pre-Delta wave	Delta wave	OR (95% CI)	P	aOR (95% CI)	P
Total	53 (7.2%)	86 (11.9%)	1.75 (1.22-2.5)	0.0001*	1.95 (1.35-2.83)	0.0001*
Gender						
Males	24 (45.3%)	45 (52.3%)	0.88 (0.62-1.25)	0.4787	---	---
Females	29 (54.7%)	41 (47.7%)	1.1352	0.4787	---	---
Age groups (years)						
0-4	0 (0.0%)	0 (0.0%)	---	---	---	---
5-9	0 (0.0%)	0 (0.0%)	---	---	---	---
10-19	0 (0.0%)	0 (0.0%)	---	---	---	---
20-29	1 (1.9%)	2 (2.3%)	0.16 (0.05-0.52)	0.0001*	0.22 (0.07-0.70)	0.0001*
30-39	4 (7.5%)	5 (5.8%)	0.38 (0.19-0.75)	0.01*	0.56 (0.27-1.14)	0.01*
40-49	8 (15.1%)	15 (17.4%)	0.84 (0.52-1.34)	0.46	---	---
50-59	12 (22.6%)	29 (33.7%)	1.26 (0.86-1.85)	0.24	---	---
60-69	17 (32.1%)	21 (24.4%)	2.26 (1.51-3.39)	0.0001*	1.81 (1.19-2.76)	0.0001*
70 and older	11 (20.8%)	14 (16.3%)	2.39	0.0001*	1.81 (1.11-2.96)	0.002*
Comorbidities						
None	7 (13.2%)	10 (11.6%)	0.16 (0.095-0.269)	5E-12*	0.24 (0.14-0.41)	2.2E-7*
Single	18 (34.0%)	42 (48.8%)	1.50 (1.05-2.14)	0.026	1.21 (0.84-1.74)	0.31*
Multiple	28 (52.8%)	34 (39.5%)	3.26 (2.27-4.69)	0.0001*	2.3 (1.57-3.35)	0.0001*
Types of comorbid						
Diabetes	26 (49.1%)	31 (36.0%)	2.75 (1.91-3.96)	0.0001*	2.01 (1.38-2.93)	0.0001*
Hypertension	33 (62.3%)	45 (52.3%)	2.82 (1.97-4.03)	0.0001*	1.76 (1.20-2.59)	0.0001*
Obesities	6 (11.3%)	11 (12.8%)	3.46 (1.93-6.21)	0.0001*	4.80 (2.58-8.91)	0.0001*
CAD	4 (7.5%)	11 (12.8%)	1.65 (0.92-2.96)	0.09	---	---
CKD	2 (3.8%)	7 (8.1%)	3.62 (1.64-7.99)	0.0001*	3.0 (1.33-6.80)	0.01*
Malignancy	0 (0.0%)	2 (2.3%)	1.49 (0.33-6.73)	---	---	---
TB	2 (3.8%)	1 (1.2%)	1.41 (0.41-4.84)	0.58	---	---
Alzheimer	1 (1.9%)	1 (1.2%)	---	---	---	---
Geriatric	2 (3.8%)	2 (2.3%)	4.27 (1.31-13.96)	0.02*	2.01 (0.6-6.72)	0.26
Pregnancy	0 (0.0%)	2 (2.3%)	1.10 (0.25-4.90)	0.90	---	---
HIV	1 (1.9%)	1 (1.2%)	---	---	---	---
Asthma	3 (5.7%)	1 (1.2%)	0.89 (0.31-2.53)	0.83	---	---
Others	1 (1.9%)	2 (2.3%)	0.34 (0.11-1.09)	0.07	---	---

Note: *significant (P<0.05); CAD=Coronary Artery Disease; CKD=Chronic Kidney Disease; TB=Tuberculosis; HIV=*Human Immunodeficiency Viruses*

The age of deceased patients in Delta wave (57 years old) was younger than previous wave (60 years old) but did not reach statistical significance (Table 3). Furthermore, there were no significant differences in terms of measured blood glucose, CRP, D-dimers and NLR. The number of deaths from each causes such as acute respiratory distress syndrome (ARDS), cardiac arrest and thromboembolism/coagulopathy were also similar to each other, except there was less incidence of sepsis during Delta wave (P=0.0413). Most deceased patients were not vaccinated as shown in both pre-Delta wave (98%) and Delta wave (90.6%).

Table 3. Clinical and laboratory parameters in deceased patients

Parameters	Pre Delta wave	Delta wave	P
Age [media (min-max)]	60 (51-68)	57 (49-66)	0.231
Blood glucose (mg/dL) [media (min-max)]	158 (118-283)	131 (108-192)	0.099
CRP (mg/dL) [media (min-max)]	8.7 (1.45-17.4)	9.32 (3.52-15.4)	0.574
D-Dimer (ug/mL) [media (min-max)]	1.5 (0.5-5.8)	0.9 (0.43-2.7)	0.15
NLR [media (min-max)]	6.43 (3.74-13.1)	7.2 (4.12-13.1)	0.76
Vaccine status			
None	52 (98%)	78 (90.6%)	0.022*
Completion	1 (1.9%)	8 (9.3%)	--
Length of stay	7 (4-13)	7 (3-12)	0.488
Cause of death			
ARDS	36 (68%)	64 (75%)	0.407
Cardiac arrest	43 (81%)	69 (80%)	0.896
Thromboembolism/Coagulopathy	20 (37%)	40 (46%)	0.31
Sepsis shock	31 (59%)	35 (41%)	0.0413*
WHO Clinical Progression scales			
Mild	21 (39.6%)	44 (51.1%)	0.185
Moderate	25 (47.1%)	40 (46.5%)	0.939
Severe	5 (9.4%)	2 (2.32%)	0.0627

Note: CRP=C-Reactive Protein; NLR=Neutrophil Lymphocyte Ratio; ARDS=Acute Respiratory Distress Syndrome

Table 4 CT values of population RTPCR test results performed by YARSI Hospital serving surrounding community

Months	COVID-19 cases in YARSI Hospital (N=865)	RT-PCR tests surrounding community (N=25,279)	Median of RT-PCR CT values in the community	Positivity Rate of RT-PCR testing in the community	Percent of CT Values <21	Percent of CT values <15
April	74	2339	29	16,7%	1,9%	0,04%
May	70	2183	32	18,3%	3,3%	0,55%
June	227	7379	23	46,0%	17,4%	1,88%
July	406	10748	26	57,3%	14,5%	0,76%
August	88	2630	32	25,9%	4,2%	1,14%

Note: RT-PCR=Real Time Polymerase Chain Reaction

The proportion of mortality in vaccinated patients was significantly higher in Delta wave (P=0.0413). Lastly, length of hospital stay (median 7 days) was similar between two waves (P=0.488).

To explore possible circumstances preceding second wave, obtained RT-PCR test results since April 2021 from the surrounding community. As shown in Table 4, the positivity rate of COVID-19 RT-PCR testing in the community mirrored the number of COVID-19 cases admitted to YARSI hospital each month. The positivity rate reached its peak in the month of July (57%) and went down to 25% in August. Furthermore, there was a trend of decreasing median of CT values in positive test results. The lowest median occurred in the month of June (CT value 23) which suggested low CT values could be more common in this month.

Low CT values had been thought to correlate with high viral load and may predict high level of infectiousness and epidemic trajectory.

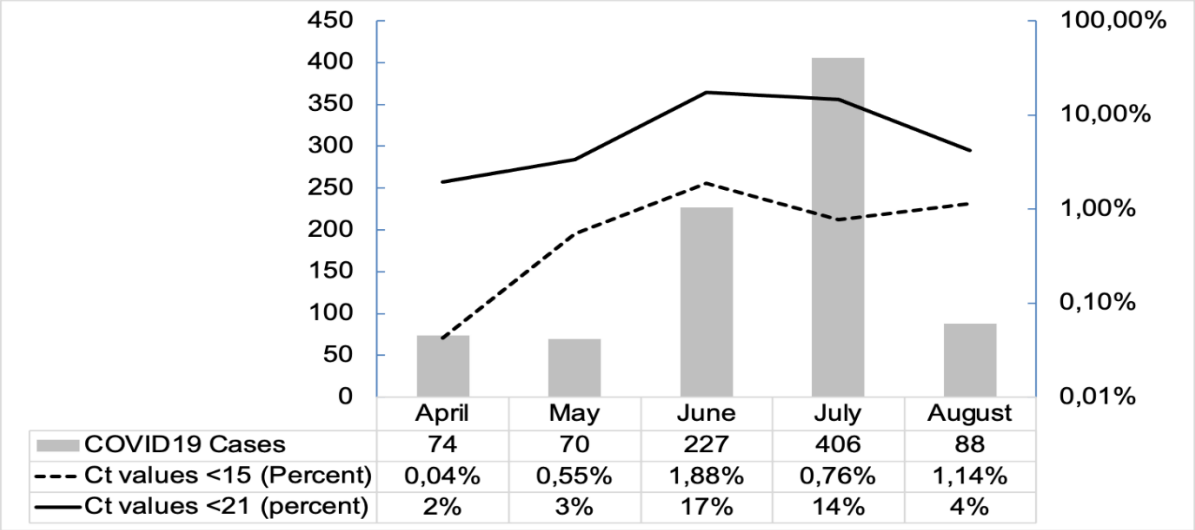

Figure 1. Relationship between monthly cases of COVID-19 patients and low RTPCR Ct values. Solid gray bars indicate the number of patients admitted to YARSI hospital. Solid line represents trend of low Ct values (under 21) and dashed line low Ct values (under 15). Left y-axis represents the number of COVID-19 cases. Right y-axis is percentage of low Ct values with respected cut-off 21 or 15. Low Ct values of RTPCR may be associated with relatively high viral load

The tracking the percentage of low CT values using two arbitrary cut-off CT values (15 and 21). As shown in Figure 1, low CT values (less than 21) were found in April and May 2021 (2% and 3% respectively). The percentage increased to 17% in June 2021 which preceded the doubling of COVID-19 cases in July.

On the other hand, while using 15 as the cut-off for CT values, the percentage increased from 0,04% in April to 0,55% in May. This tenfold rise of the percentage of low CT values in May was followed by significant surge of COVID-19 cases in June. Moreover, the percentage of low CT values dropped to 0.76% in June, followed by declining numbers of COVID-19 cases in August.

Pre-Delta wave was defined as January to May 2021, while Delta wave was June to August 2021. Categorical variables were presented as frequency and percentages. Chi-square or Fisher's exact test was applied to frequency distribution accordingly. Those with significant p values are indicated in bold ($P<0.05$ indicated that the difference was statistically significant). aOR means adjusted Odds Ratio.

DISCUSSION

Several countries including Indonesia have been impacted by the surge of new COVID-19 cases associated with Delta variant of SARS-CoV-2. This observations in a single tertiary hospital not only showed several key results regarding affected population and mortality rates, but also offered insights regarding vaccination status and potential utility of low CT values to predict active transmission in the community. First, during second wave there was a significant rise of hospitalization among young patients and those without known comorbidities. A study from the UK demonstrates that Delta variant mostly infected younger patients, which is consistent with this finding.[4]

Moreover, unvaccinated population was more susceptible to Delta infection. Another recent study in Singapore comparing three VOCs (Alpha, Beta and Delta) found that the median age of Delta infected patients in Singapore was around 48 which is highly similar to this cohort.[3] Furthermore, Delta might cause more severe cases compared to other variants.

However, it could not evaluate the virulence impact of Delta variant in this cohort because it did not genotype patients for VOCs. Interestingly, a hospital study in Yogyakarta, Indonesia suggests that the mortality risk between Delta and non-Delta variants were not significantly different.[8] Nevertheless, old age and comorbidity continue to be consistent predictors of poor outcome regardless of variants.

There were more pregnant female patients during the second wave in this cohort compared to the first. In the United States, during the surge of Delta variant between May to July 2021, the numbers of pregnant women with COVID-19 had been increasing with up to 25% requiring hospitalization due to severe or critical symptoms.[9] In addition to the rising number of pregnant COVID-19 patients during Delta wave, this cohort also showed mortality rate of 22%. While the pathophysiology was not clear, the deceased patients had pregnancy related comorbidity especially hypertension which might exacerbate the symptoms.[10]

COVID-19 cases generally affect older population with high prevalence of comorbidities, but it observed an increasing proportion of young patients without comorbidities during Delta wave. This shift in COVID-19 proportion has been previously described in Brazil during the wave associated with Gamma variant in February 2021 and was attributed to young population doing more rigorous daily activities due to economic necessity while having relatively smaller coverage of vaccination, which mainly prioritized the elderly population.[11] Although there was no fatalities in children (age 0-18 years old) in this cohort, they remained susceptible to Delta variants. Recent outbreak in California elementary school showed that an unmasked, symptomatic teacher reading a book out loud caused up to 50% infection among 22 students.[12]

Comparison of mortality rates revealed that males and hypertension remained consistent as risk factors for poor outcome in COVID-19. This was also seen in the second wave. While there was increased number of hospitalization in young adults and children, no fatalities were found. However, the possibility of long term effect of COVID-19 among surviving children and young adults should be monitored closely. Recent reports showed that the frequency of persistent symptoms may affect between 15%-46% of children within 2-4 months post COVID-19 infection.[13,14]

In this cohort, pregnant women showed mortality rates of 20%. Although not statistically significant, some pregnancy may induce hypertension, a comorbid which also causes higher rates of mortality during the Delta wave. Many studies found that COVID-19 patients with hypertension

tend to have worse prognosis than normotensive patients. As many as 23.7% hypertensive patients suffered from severe COVID-19, compared to 13.4% of non-hypertensive patients.[15]

Another study showed that 35.8% of COVID-19 patients with hypertension needed to be admitted to ICU, received mechanical ventilation or resulted to death, compared to 13.7% in patients with normal blood pressure.[16] Another study that examined 138 patients who tested positive for COVID-19 in China described that 58.3% of patients with hypertension were admitted to ICU, higher than patients with normal blood pressure (21.6%).[15] In a large-scale cohort study with 1590 sample size from 575 hospitals, hypertension showed an independent association to severe covid with hazard ratio=1.575; 95% CI=1.07-2.32.[16]

Since there were high mortality rates in patients aged 60 years old and under, it examined laboratory parameters in deceased patients and compared the results between young (<60) and old patients. There were no significant differences in NLR, blood glucose and D-dimer among deceased patients during Delta wave. Previous literature review suggests that these laboratory parameters have been associated with poor outcomes in COVID-19 in Asian patients.[17]

The role of ethnicity has been investigated in a study from the United Kingdom where it's found that elevated (ALP × ALT)/albumin ratio is a reliable mortality predictor for Caucasian patients while NLR (>7.8) is poor prognostic marker for all ethnicity.[18]

Recent study has compared laboratory parameters among patients infected with alpha, beta and delta variants and found similar values of NLR across all variants, but the level of CRP (median 28 mg/L) in significantly higher in Delta infected patients.[3] This study could not corroborate the CRP value because it did not have access to variant genotyping within this cohort.[19]

The majority of deceased patients in this cohort was not vaccinated. As per July 2021, up to 80% of elderly citizens in Jakarta have been vaccinated. This implies protective effect of vaccination which had begun in January 2021.[6] A retrospective study from Canada showed that Delta variant imposed higher risk of mortality in unvaccinated population.[20]

Within this cohort, there was significantly higher proportion of deceased patients who had been vaccinated during Delta than pre-Delta wave. The increased proportion may reflect the increasing vaccination coverage during the Delta wave period in Jakarta. Alternatively, there is a possibility of lower vaccine effectiveness against Delta as suggested by in vitro neutralization study of Delta variant using serum of vaccinated individuals.[21]

The effectiveness of COVID-19 vaccine using inactivated virus platform against Delta variant has been studied in China.[22] In spite of the presence of many mutations in Spike protein in Delta and lower titre of neutralizing antibody induced by vaccine, this study indirectly suggests

that unvaccinated individuals remain at high risk of mortality regardless of the type of variant causing COVID-19 infection.[21] Therefore, vaccination program should remain a priority targeting high risk population especially the elderly and individuals with comorbidities.

This study also had observed increased proportion of low CT values within the surrounding community in the month of April and May, or at least two months before the surge occured in July. Hospital bed occupancy and RT-PCR testing positivity rates have been used to estimate epidemiologic trajectory. However there might be limitations due to delay in reporting and bias in sampling. Hay et al found that CT values found in population may offer better prediction of epidemiologic trajectory. High proportion of individuals with positive RT-PCR and low CT values at a given time suggests an increase in epidemic trajectory.[23]

The utility of low CT values to predict epidemiologic trajectory has been validated in Hong Kong, which is able to estimate real time viral transmission within the community. This CT value approach is useful even in areas with limited testing capacity or surveillance.[24] Another study from UK which encompassed period of high transmission of Alpha variant also shows that variation in CT values within confirmed cases may be useful as early warning indicator because the rising or declining proportion of low CT values in the community preceded the higher or lower incidences of COVID-19, respectively.[19] Similar to UK study, the inverse association of low CT values and increasing viral transmission in the population is also observed in Italy.[25]

In the month of August, the number of COVID-19 patients decreased significantly. Interestingly, there was a slight rise of low CT value percentage in the community, i.e. 0,76% in July to 1,14% in August. However, this rising percentage was not followed by another surge in the following month of September onwards.[26]

There were two possible explanations, namely massive vaccination drive and PPKM (restricted public activities) that had been enforced within Jakarta and other cities around Jakarta. Recent modelling study suggests that combination of vaccination drive and non-pharmaceutical intervention may mitigate impact of Delta variant in the community.[26] This data of CT values from the community may help in making decision to initiate, prolong or end PPKM based on continuous monitoring of proportion of low CT values.

CONCLUSION

The surge of variant of Delta in Indonesia also affects the city of Jakarta. Compared to profile of hospitalized patients in previous period, the Delta period (June to August 2021) yielded higher proportions of young population, pregnant women and individuals with heart problem. While COVID-19 vaccine coverage was between 55% (May 2021) and 80% (July 2021) among elderly, mortality during Delta

period was dominated by unvaccinated individuals.

Preceding the Delta period, surveillance data showed that the proportion of low CT values from surrounding community was increasing. Therefore, vaccination program and continuous monitoring of CT values may be helpful to mitigate risk of COVID-19 cases in developing countries.

REFERENCES

1. Mallapaty S. Delta threatens rural regions that dodged earlier COVID waves. Nature. 2021;596(7872):325–6.
2. Dyer O. Covid-19: Indonesia becomes Asia's new pandemic epicentre as delta variant spreads. BMJ. 2021;374:n1815.
3. Ong SWX, Chiew CJ, Ang LW, Mak TM, Cui L, Toh MPHS, et al. Clinical and Virological Features of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Variants of Concern: A Retrospective Cohort Study Comparing B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta). Clinical Infectious Diseases. 2022;75(1):e1128–36.
4. Twohig KA, Nyberg T, Zaidi A, Thelwall S, Sinnathamby MA, Aliabadi S, et al. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. Lancet Infect Dis. 2022;22(1):35–42.
5. Nugraha RR, Miranda AV, Ahmadi A, Lucero-Prisno DE. Accelerating Indonesian COVID-19 vaccination rollout: a critical task amid the second wave. Trop Med Health. 2021;49(1):76.
6. World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report - 63. Geneva: World Health Organization; 2021.
7. Cucunawangsih C, Wijaya RS, Lugito NPH, Suriapranata I. Post-vaccination cases of COVID-19 among healthcare workers at Siloam Teaching Hospital, Indonesia. International Journal of Infectious Diseases. 2021;107:268–70.
8. Gunadi, Hakim MS, Wibawa H, Marcellus, Setiawaty V, Slamet, et al. Is the Infection of the SARS-CoV-2 Delta Variant Associated With the Outcomes of COVID-19 Patients? Front Med (Lausanne). 2021;8:780611.
9. Adhikari EH, SoRelle JA, McIntire DD, Spong CY. Increasing severity of COVID-19 in pregnancy with Delta (B.1.617.2) variant surge. Am J Obstet Gynecol. 2022;226(1):149–51.
10. Magee LA, Khalil A, von Dadelszen P. Pregnancy hypertension diagnosis and care in COVID-19 era and beyond. Ultrasound in Obstetrics & Gynecology. 2020;56(1):7–10.
11. Nonaka CKV, Gräf T, Barcia CA de L, Costa VF, de Oliveira JL, Passos R da H, et al. SARS-CoV-2 variant of concern P.1 (Gamma) infection in young and middle-aged patients

admitted to the intensive care units of a single hospital in Salvador, Northeast Brazil, February 2021. International Journal of Infectious Diseases. 2021;111:47–54.

12. Lam-Hine T, McCurdy SA, Santora L, Duncan L, Corbett-Detig R, Kapusinszky B, et al. Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School — Marin County, California, May–June 2021. MMWR Morb Mortal Wkly Rep. 2021;70(35):1214–9.
13. Wise J. Long covid: One in seven children may still have symptoms 15 weeks after infection, data show. BMJ. 2021;374:n2157.
14. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, et al. Preliminary evidence on long COVID in children. Acta Paediatr. 2021;110(7):2208–11.
15. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.
16. Guan W jie, Ni Z yi, Hu Y, Liang W hua, Ou C quan, He J xing, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708–20.
17. Ghahramani S, Tabrizi R, Lankarani KB, Kashani SMA, Rezaei S, Zeidi N, et al. Laboratory features of severe vs. non-severe COVID-19 patients in Asian populations: a systematic review and meta-analysis. Eur J Med Res. 2020;25(1):30.
18. Marwah M, Marwah S, Blann A, Morrissey H, Ball P, Wandroo FA. Analysis of laboratory blood parameter results for patients diagnosed with COVID-19, from all ethnic group populations: A single centre study. Int J Lab Hematol. 2021;43(5):1243–51.
19. Walker AS, Pritchard E, House T, Robotham J V, Birrell PJ, Bell I, et al. Ct threshold values, a proxy for viral load in community SARS-CoV-2 cases, demonstrate wide variation across populations and over time. Elife. 2021;10:e64683.
20. Fisman DN, Tuite AR. Evaluation of the relative virulence of novel SARS-CoV-2 variants: a retrospective cohort study in Ontario, Canada. Can Med Assoc J. 2021;193(42):E1619–25.
21. Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature. 2021;596(7871):276–80.
22. Li XN, Huang Y, Wang W, Jing QL, Zhang CH, Qin PZ, et al. Effectiveness of inactivated SARS-CoV-2 vaccines against the Delta variant infection in Guangzhou: a test-negative case–control real-world study. Emerg Microbes Infect. 2021;10(1):1751–9.
23. Hay JA, Kennedy-Shaffer L, Kanjilal S, Lennon NJ, Gabriel SB, Lipsitch M, et al. Estimating epidemiologic dynamics

from cross-sectional viral load distributions. Science (1979). 2021;373(6552):eabh0635.

24. Lin Y, Yang B, Cobey S, Lau EHY, Adam DC, Wong JY, et al. Incorporating temporal distribution of population-level viral load enables real-time estimation of COVID-19 transmission. Nat Commun. 2022;13(1):1155.
25. Calistri P, Danzetta ML, Amato L, Cito F, Di Giuseppe A, Zenobio V, et al. Epidemiological Significance of SARS-CoV-2 RNA Dynamic in Naso-Pharyngeal Swabs. Microorganisms. 2021;9(6):1264.
26. Sonabend R, Whittles LK, Imai N, Perez-Guzman PN, Knock ES, Rawson T, et al. Non-pharmaceutical interventions, vaccination, and the SARS-CoV-2 delta variant in England: a mathematical modelling study. The Lancet. 2021;398(10313):1825–35.