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Extended Abstract
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Predictor Factor of Maternal Death Related Covid-19 : A Case Control Study

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Nowadays, Covid-19 has become our concern, included its impact to pregnant women. The rate of maternal mortality related Covid-19 increased. Early detection of significant factor related to clinical worsening of pregnant women with Covid-19 can be a rationale to do aggressive treatment and closed monitoring. The aim of study is to analyze the risks and predictor factor of maternal death with Covid-19. Material and method : Case control study, case grup consists of all maternal death related Covid-19 till August 2020 (15 patients) in Soetomo Hospital, tertiary hospital in Indonesia. Control grup consists of all pregnant women survived with Covid-19 confirmed till August 2020 (30 patients). We used bivariat analysis and multivariat using logistic regression. Result : We found five significant factors of maternal death related Covid-19. They are respiration rate p=0,04 CI 95% 3,75 (1-14), D-dimer >2400 with p=0,035 CI 95% 4,12 (1,06-16,03), SpO2 p=0,001 CI 95% 18 (3,61-89,5), CRP >7,15 p=0,003 CI 95% 7,5 (1,86-30,7) Obesity p=0,09 CI 95% 4,5 (0,9-22,3), A simple scoring is made based on probability equation of 5 factors and can predict the probability of level severity cause death from 3,9% (score 1) to 98,3% (score 5) with AUC (ROC) 94,7%. Conclusion : the risk and predictor factors of maternal death related covid included respiration rate, perifer saturation, CRP, D-dimer and Obesity. This simple prediction score can be used to define pregnant women with Covid-19 that need closed monitoring and aggressive treatment to avoid maternal morbidity and mortality.

COVID-19 is an infection with predominant respiratory features caused by the novel coronavirus SARS-CoV-2. The disease rapidly spread worldwide and was declared a worldwide pandemic on 11 March 2020, by the planet Health Organization (WHO). By 20 July 2020, COVID-19 had affected quite 14 million people in 188 territories, with quite 608 000 deaths. Despite the magnitude of incidence and mortality, how the infection impacts pregnancy and whether pregnancy and therefore the postpartum period would cause more vulnerability remain uncertain.

Initial case series from China didn't identify increased risk of adverse outcomes among obstetric patients in comparison with the overall population, and no maternal deaths were reported. However, physiological adaptations in normal pregnancies, mainly cardio-respiratory and immune, are known to extend the susceptibility of pregnant women to many infectious agents, viral infection especially . Thus, clinicians worldwide remained worried about the impact of COVID-19 during this population. Subsequent data emerging from Europe and North America also concluded that pregnant women were at no increased risk of severe COVID-19 or death. More recently, further studies reported higher risk of ICU admission and mechanical ventilation during pregnancy and therefore the first cases of mishap and maternal deaths have emerged from Iran, US, UK, France, Mexico and Spain.

When a lady with a COVID-19 diagnosis was identified antenatally, 2 women without COVID-19 diagnosis of comparable fetal age (±2 weeks) receiving standard antenatal care were enrolled that day. If impossible or if those women without COVID-19 diagnosis were lost to follow-up, we enrolled 2 women without COVID-19 diagnosis who delivered immediately after the lady with COVID-19 diagnosis. an equivalent selection strategy was used when a lady with COVID-19 diagnosis was identified at hospital admission and delivery was likely during that admission. If a lady without COVID-19 diagnosis declined participation, subsequent woman was approached until 2 women without COVID-19 diagnosis were enrolled per woman with COVID-19 diagnosis. We sought confirmation from a biweekly random 10% sample that the two women without COVID-19 diagnosis were appropriately chosen; we excluded 5 women who had a COVID-19 diagnosis and therefore the corresponding 10 women without a COVID-19 diagnosis, without such confirmation. Live and stillborn singleton and multiple pregnancies were included, including those with congenital anomalies. However, keep with reporting requirements during the pandemic,12 we excluded women/neonates from the ultimate analysis if their data were already published in

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any comparative study with women without COVID-19 diagnosis.

The primary outcomes24 were 3 unweighted indices: maternal morbidity and mortality index including a minimum of 1 of the subsequent pregnancy-related morbidities: third-trimester vaginal bleeding, pregnancy-induced hypertension, preeclampsia/eclampsia/hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, preterm labor, infections requiring antibiotics, or the other pregnancy-related conditions requiring treatment or referral; maternal admission to the medical care unit (ICU); referral to a better level of care; or death; severe neonatal morbidity index (SNMI) including a minimum of 3 of the subsequent severe complications: bronchopulmonary dysplasia, hypoxic-ischemic encephalopathy, sepsis, anemia requiring transfusion, patent blood vessel requiring treatment or surgery, intraventricular hemorrhage, and NEC or retinopathy of prematurity diagnosed before hospital discharge; and severe perinatal morbidity and mortality index (SPMMI) including fetal death, a minimum of 1 of the severe neonatal conditions listed above, admission to the neonatal ICU (NICU) for 7 days or longer, or death before hospital discharge. Secondary outcomes were each individual component of the indices described above considered as separate conditions.

We used a centrally coordinated data management system developed for the INTERGROWTH-21st Project (MedSciNet).27 Associations between being diagnosed as having COVID-19 and morbidity/mortality indices expressed as binary outcomes were assessed using Poisson models with a log link function and robust standard errors expressed as relative risk (RR) and 95% CI. Associations with number of days in ICU were assessed using negative binomial models with robust standard errors (expressed as an incidence rate ratio and 95% CI). We set statistical significance at $P < .05$. Models for our primary outcomes were adjusted for country, month entering study, maternal age, and history of maternal morbidity (including diabetes, thyroid, and other endocrine disorders; cardiac disease; hypertension; chronic respiratory disease; kidney disease; malaria; or tuberculosis). Models with preterm birth as an outcome were also adjusted for previous preterm birth. We plotted Kaplan-Meier curves with the share of girls remaining pregnant by fetal age to match the distributions between women with and without COVID-19 diagnosis, consistent with symptom status. We evaluated women with COVID-19 diagnosis for the first and secondary outcomes using the ladies without COVID-19 diagnosis because the reference group. We further categorized women with COVID-19 diagnosis as asymptomatic or symptomatic supported type and duration of symptoms, also as consistent with past maternal morbidity and normal weight or overweight to explore effect modification. We assessed the association of neonates testing positive for SARS-CoV-2 infection. In separate sensitivity analyses, we adjusted for extra potential confounders, restricted the definition of girls with COVID-19 diagnosis to mothers with a positive laboratory test result, and excluded twins. We also performed separate meta-analyses for our primary outcomes of interest using the stratified results to estimate pooled effects and assess heterogeneity by country.

Women with COVID-19 diagnosis delivered before those without COVID-19 diagnosis after approximately 30 weeks' gestation, with the best difference but 37 weeks' gestation. The Figure illustrates the probability of remaining pregnant after 25 weeks' gestation for those women with COVID-19 diagnosis, stratified into those with and without symptoms. Using the log-rank test for trend of survivor curves, we observed a big downwards trend within the fetal age distributions that progressed from women without COVID-19 diagnosis, to asymptomatic women with COVID-19 diagnosis, to symptomatic women with COVID-19 diagnosis ($P < .001$ for this trend) (Figure). In regression models, the fetal age at delivery was 0.6 weeks shorter (95% CI, −0.9 to −0.3) altogether women with COVID-19 diagnosis and 0.8 weeks shorter (95% CI, −1.2 to −0.5) in symptomatic women with COVID-19 diagnosis than in women without COVID-19 diagnosis.

We demonstrated that ladies with COVID-19 diagnosis, compared with those without COVID-19 diagnosis, were at substantially increased risk of severe pregnancy complications, including preeclampsia/eclampsia/HELLP syndrome, ICU admission or referral to higher level of care, and infections requiring antibiotics, also as preterm birth and low birth weight. the danger of maternal mortality was 1.6%, ie, 22 times higher within the group of girls with COVID-19 diagnosis. These deaths were concentrated in institutions from less developed regions,

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implying that when comprehensive ICU services aren't fully available, COVID-19 in pregnancy are often lethal. Reassuringly, we also found that asymptomatic women with COVID-19 diagnosis had similar outcomes to women without COVID-19 diagnosis, apart from preeclampsia.

Our study has expected limitations. Ideally, we might have collected data prospectively from all pregnancies within the participating institutions, but this was impractical due to their sizable amount of deliveries. There was alittle risk of selection bias related to the reference group of girls without COVID-19 diagnosis, despite all efforts to make sure they represented an unbiased sample of the overall noninfected pregnant population. the choice of cases with COVID-19 diagnosis was suffering from whether routine testing was conducted, awareness of COVID-19 symptoms particularly early within the pandemic, and therefore the availability of test kits. Where universal testing in pregnancy has been introduced, real-time polymerase chain reaction positive rates are 0.5% to 14% in asymptomatic women. Hence, this group of girls without COVID-19 diagnosis may have included small numbers of asymptomatic infected women (a crossover effect when women without COVID-19 diagnosis were enrolled antenatally), which might end in more conservative estimates by reducing the differences between groups. Finally, we acknowledge a risk of reporting bias concerning maternal and neonatal morbidity because women with COVID-19 diagnosis and their newborns may are more carefully evaluated, tested, and have more events reported than within the sample of girls without COVID-19 diagnosis. However, we are reassured that the results reflect a real increased risk due to our careful data monitoring and use of severe morbidity markers.

Conclusion: In summary, during this study, COVID-19 infection during pregnancy was related to substantial risk of morbidity and mortality in postpartum parents and their infants worldwide, compared with their not-infected pregnant counterparts, especially if the these individuals were symptomatic or have comorbidities. there's an urgent got to follow up with these parents and infants due to possible long-term health effects, including long-term COVID-19.

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