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# Risk factors associated with deaths among hospitalized pregnant women with COVID-19 in Uganda, June 2020-August 2021

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## Summary

**Background:** Pregnant women are at higher risk than other COVID-19 patients for severe COVID-19 disease. Few studies have been done to understand risk factors for death among COVID-19-infected pregnant women in Africa. We investigated risk factors for death among hospitalized pregnant women with COVID-19 in Uganda.

**Methods:** We abstracted demographic and clinical characteristics from files of pregnant women admitted during any trimester with confirmed SARS-CoV-2 infection at eleven hospitals in Uganda. We conducted an unmatched case-control study among hospitalized pregnant women with COVID-19 during June 2020-August 2021; cases were those who died while controls were those who recovered and were discharged during the same period. We enrolled 33 cases and 109 controls. We analysed risk factors for death using multivariable logistic regression adjusted for age, trimester, parity, and presence of comorbidities because these factors have previously been associated with COVID death or maternal death.

**Results:** Of 33 cases and 109 controls, 32 (97%) cases and 73 (67%) controls were hospitalised in 2021 (p=0.01). Thirty-two (97%) cases and 85 (78%) controls had COVID-19 symptoms at admission (p=0.04). Nineteen (58%) cases and nine (8%) controls had severe or critical COVID-19 disease at admission (p<0.001). The median length of hospitalisation for cases was 3 days (IQR: 1-6) while that for controls was 7 days (IQR: 4-11) (p<0.001). Odds of seeking care from another medical facility before admission were higher among cases than controls (OR unadjusted= 3.0, 95% CI: 1.1-7.9). Having severe disease at admission increased odds of death ($OR_{adj}$= 16, 95% CI: 3.9 -69), while admission for ⩾ 6 days was protective ($OR_{adj}$= 0.2, 95% CI: 0.1- 0.8).

**Conclusion:** Pregnant women with COVID-19 who died had higher odds of being admitted with symptomatic, severe disease compared with those who survived. Earlier facilities cases visited could have delayed referral to the hospitals where they died few days after hospitalisation. Orienting facilities on referral of pregnant women with COVID-19 could improve their clinical outcomes.

## Background

Uganda registered its first case of COVID-19 on 21 March, 2020. By the end of August 2021, nearly 100,000 cases of COVID-19 had been confirmed, with almost 3,000 deaths (1). During the first wave of COVID-19, which lasted from August to December 2020, several healthcare services, including maternal health, were affected; this negatively impacted pregnancy and neonatal outcomes in Uganda (2).

Pregnant women are at high-risk for developing severe COVID-19 due to immune changes that result from pregnancy (3). Studies outside of Uganda have shown that pregnant women with COVID-19 are at greater risk of maternal mortality, hypertensive disorders of pregnancy, severe infections, and intensive care admission compared to those without COVID-19 infection (4).

Other studies have shown risk factors for deaths among hospitalized pregnant women with COVID-19 infection to include smoking, cardiovascular disease, age group under 19 or over 38 years, diabetes, and increased body mass index(5).The above studies have been conducted in high resource countries or outside Africa. However, few studies have been done to understand risk factors for COVID-19 mortality among pregnant women in Africa. The identification of such factors would enable design of interventions to reduce mortality risk when a pregnant woman is found to be infected, such as targeted risk messaging. The total number of pregnant women with COVID-19 in Uganda as of September 2021 was unknown; however, deaths among women with COVID-19 were notified and investigated as part of maternal death surveillance. We investigated risk factors for deaths among pregnant women infected with COVID-19 in Uganda who were hospitalized in the period June 2020-August 2021to inform optimal quality of care hence reduce excess mortality from COVID-19.

## Methods

### Study setting

We conducted the study at eleven hospitals with COVID-19 treatment units in Uganda. The hospitals included included Arua Regional Referral Hospital (RRH), Fort Portal RRH, Hoima RRH, Jinja RRH, Mbale RRH, Mbarara RRH, Mubende RRH, Masaka RRH, St. Mary's Lacor Hospital, Naguru Hospital, and Entebbe Hospital. According to District Health Information Systems 2 (DHIS2) data, these hospitals notified and reviewed deaths of pregnant women with confirmed COVID-19 between June 2020 and August 2021. The DHIS2 is an electronic version of data from the Health Management Information System (HMIS). The HMIS is a paper-based reporting system in which integrated health facility data on several conditions are reported on a weekly and monthly basis. DHIS2 data on maternal deaths notification and review provides summaries of events surrounding deaths among pregnant women including investigations done, comorbidities, interventions, and possible cause(s) of death (6).

### Study design

We conducted an unmatched case-control study and retrospectively extracted hospital data from files of pregnant women admitted with COVID-19 at the eleven hospitals. We defined a case as a pregnant woman who tested positive for COVID-19 by rapid diagnostic testing (RDT) or polymerase chain reaction (PCR) and was hospitalized between June 2020 and August 2021, and died at the health facility. Controls were pregnant women who had a positive COVID-19 test and were admitted during the study period but recovered (were discharged).

The outcome variables in this study were death or discharge from hospital. The independent variables included socio- demographic variables, clinical characteristics, data on seeking care elsewhere, and period of current admission. Socio-demographic variables were age, gestational age, and parity. Clinical characteristics were presence and number of COVID-19 symptoms, disease severity (clinical state at admission), presence of underlying comorbidities including hypertension, delivery status while hospitalised. Gestational age was classified according to the Ministry of Health grouping of trimesters (7). Hypertension was defined as a systolic blood pressure (BP) of $\geqslant$140 mmHg and/or diastolic blood pressure of 90 mmHg, pre-hypertension as systolic BP between 120 and 140 mmHg and/or diastolic BP between 80 and 90 mmHg. Length of hospital stay for cases was defined as the number of

days from admission date to date of death, while for controls, it was defined as days from admission to discharge dates. Length of hospital stay was dichotomised at the median value with one category being days below the median score and the other being days from the median upwards. Year of admission was used as a proxy for the first and second waves of COVID-19 in Uganda which periods were November-December 2020, and April-June 2021 respectively.

We used a standard questionnaire to retrieve data from patient files at the health facilities for both cases and controls.

**Data analysis**

We analysed data using Stata software version 14. We presented data on age groups, gestational age, parity, COVID-19 symptoms, clinical state at admission, presence of comorbidities, delivery status, and period of admission using frequencies and percentages. Age and gestational age were also presented using mean and standard deviation, as well as number of pregnancies carried and number of children. In bivariate analysis, llogistic regression was done for each independent variable and the outcome of variable of death.

Multivariable binary logistic regression was done to assess the association between variables that had a p-value of $p<0.2$ at bivariate analysis and the dependent variable of death. If two variables were highly correlated, only one was included in the final model. Age and gestational age were included in the final model to control for confounding as they are potential confounding factors. A p value cut off of $<0.05$ was used for statistical significance.

**Ethics approval and consent to participate**

A non-research determination form was submitted to US CDC for clearance before the commencement of the study. The Office of the Associate Director for Science, U.S. Centers for Disease Control and Prevention cleared the study. In the districts, we sought permission from the District Health Officers and the executive directors of the health facilities to retrieve data. We obtained verbal consent from hospital records department, COVID-19 treatment unit heads, and maternity unit In charges before retrieving data. During data collection, we used patient identification numbers and initials to protect their confidentiality. We stored the data in password-protected computers.

**Results**

**Socio-demographic and clinical characteristics of hospitalized pregnant women with COVID-19, Uganda, June 2020- August 2021**

This study compared pregnant women who were admitted with COVID-19 in ten hospitals and died with those who were discharged. A total of 143 patient's data were reviewed. We identified 33 cases and 109 controls. The mean age of pregnant women in the study was 29 years (± 7) while mean gestational age was 31 weeks (± 7). The average number of times each woman had been pregnant was 3(± 2) and the mean number of children per woman was 2 (±2). The median length of hospitalisation for cases was 3 days (IQR: 1-6) while that for controls was 7 days (IQR: 4-11) ($p<0.001$).

Thirty-two (97%) cases and 73 (67%) controls were hospitalised in 2021. Among 31 case-patients and 105 controls with trimester data, 22 (70%) case-patients and 71 (68%) controls were in the third trimester of pregnancy. Thirty-two (97%) case-patients and 85 (78%) controls had symptoms of COVID-19 ($p= 0.04$). Nineteen (58%) case-patients and nine (8%) controls had severe or critical COVID-19 disease at admission (Table 1).

**Table 1: Socio-demographic and clinical characteristics of hospitalized pregnant women with COVID-19, Uganda, June 2020- August 2021**

| Variable | Total | Cases (died) | Controls (discharged) |
|---|---|---|---|
| | Frequency (%) | Frequency (%) | Frequency (%) |
| **Age group (years) (n=142)** | | | |
| 15-34 | 106 (75) | 27 (82) | 79 (72) |
| 35-42 | 36 (25( | 6 (18) | 30 (28) |
| **Gestational age (weeks) (n=136)** | | | |
| 7 _21 | 43 (32) | 9 (29) | 34 (32) |
| 29-40 | 93 (68) | 22 (71) | 71 (68) |
| **COVID-19 symptoms (n=142)** | | | |
| No | 25 (18) | 1 (3) | 24 (22) |
| Yes | 117 (82) | 32 (97) | 85 (78) |
| **Number of COVID-19 symptoms** | | | |
| 0-1 | 37 (26) | 3 (9) | 34 (31) |
| 2 to 8 | 106 (74) | 30 (91) | 76 (69) |
| **Clinical state (n=142)** | | | |
| Mild-moderate disease | 114 (80) | 14 (42) | 100 (92) |
| Severe and critical disease | 28 (20) | 19 (58) | 9 (8) |
| **Mother delivered (n=142)** | | | |
| No | 97 (68) | 17 (52) | 80 (73) |
| Yes | 45 (32) | 16 (48) | 29 (27) |
| **Year of admission** | | | |
| 2020 | 37 (26) | 1 (3) | 36 (33) |
| 2021 | 105 (74) | 32 (97) | 73 (67) |
| **Systolic blood pressure (n=132)** | | | |
| <120 | 79 (60) | 14 (45) | 65 (64) |
| 120-139 | 42 (32) | 12 (39) | 30 (30) |
| ≥140 | 11 (8) | 5 (16) | 6 (6) |
| **Diastolic blood pressure (n=132)** | | | |
| <80 | 93 (71) | 21 (68) | 72 (71) |
| 80-89 | 27 (20) | 6 (19) | 21 (21) |
| ≥90 | 12 (9) | 4 (13) | 8 (8) |

**Distribution of symptoms of COVID-19 among hospitalized pregnant women at 19 hospitals, Uganda, June 2020-August 2021**

Cough was the most common symptom among both cases (81%) and controls (84%) whereas difficulty in breathing was more than twice as common among cases than controls (81% versus 35%). An equal proportion of cases and controls (38%) had fever (Table 2).

**Table 2: Distribution of symptoms of COVID-19 among hospitalized pregnant women at 19 hospitals, Uganda, June 2020-August 2021**

| Symptom | Total (n=117) | | Cases (n= 32) | | Controls (n=85) | |
|---|---|---|---|---|---|---|
| | Frequency | % | Frequency | % | Frequency | % |
| Cough | 98 | 83 | 26 | 81 | 72 | 84 |
| Difficulty in breathing | 55 | 47 | 26 | 81 | 29 | 34 |
| Fever | 45 | 38 | 13 | 41 | 34 | 40 |
| Chest pain | 40 | 34 | 12 | 38 | 28 | 33 |
| Runny nose | 28 | 24 | 3 | 9 | 25 | 29 |
| Body weakness | 26 | 22 | 2 | 6 | 24 | 28 |
| Headache | 23 | 19 | 4 | 13 | 19 | 22 |
| Sorethroat | 18 | 15 | 6 | 19 | 12 | 14 |
| Poor appetite | 12 | 10 | 2 | 6 | 10 | 12 |
| Shortness of breath | 7 | 6 | 4 | 13 | 3 | 3 |
| Chills/ rigors | 6 | 5 | 1 | 3 | 5 | 6 |
| Loss of smell | 6 | 5 | 1 | 3 | 5 | 6 |
| Loss of taste | 5 | 4 | 1 | 3 | 4 | 5 |

**Factors associated with deaths among pregnant women with COVID-19**

At bivariate analysis, several factors were associated with deaths among pregnant women. However, after adjusting for maternal age, weeks of gestation, parity, and having comorbidities in the multivariable model, clinical state at admission and length of hospital stay were the factors independently associated with deaths. Nineteen case-patients (58%) and 9 controls (8%) had severe or critical disease at admission ($OR_{adj}$= 16, 95% CI: 3.9 -69). Ten case-patients (30%) were admitted at the hospital for 6 or more days compared to 70 controls (64%) ($OR_{adj}$= 0.2, 95% CI: 0.1- 0.8). Having severe disease at admission increased odds of death, while admission for 6 or more days was protective (Table 3).

**Table 3: Risk factors for deaths among hospitalised pregnant women with COVID-19, Uganda, June 2020- August 2021**

| Variable | Cases (%) | Controls (%) | uOR (95% CI) | aOR (95% CI) |
|---|---|---|---|---|
| **Clinical state (n=142)** | | | | |
| Mild-moderate disease | 14 (42) | 100 (92) | 1 | 1 |
| Severe and critical disease | 19 (58) | 9 (8) | 15(5.7-40) | 16 (3.9-69) |
| **Length of hospital stay (days) (n=142)** | | | | |
| 0-5 | 23 (70) | 39 (36) | 1 | 1 |
| 6- 149 | 10 (30) | 70 (64) | 0.2(0.1-0.6) | 0.2(0.1-0.8) |
| **Year of admission (n=142)** | | | | |
| 2020 | 1 (3) | 36 (33) | 1 | 1 |
| 2021 | 32 (97) | 73 (67) | 16(2.1-120) | 6.2(0.1-439) |
| **Number of comorbidities(n=142)** | | | | |
| 0 | 28 (85) | 101 (93) | 1 | 1 |
| 1 to 2 | 5 (15) | 8 (7) | 2.3(0.7-7.4) | 2.5(0.2-28) |

| | | | | |
|---|---|---|---|---|
| **Age group (years) (n=142)** | | | | |
| 15-34 | 27 (82) | 79 (72) | 1 | 1 |
| 35-42 | 6 (18) | 30 (28) | 0.6(0.2-1.6) | 0.1(0.004-2) |
| **Gestational age (weeks) (n=136)** | | | | |
| 7_28 | 9 (29) | 34 (32) | 1 | 1 |
| 29-40 | 22 (71) | 71 (68) | 1.2(0.5-2.8) | 3.1(0.3-28) |
| **Parity (n=125)** | | | | |
| 0 | 7 (23) | 19 (20) | 1 | 1 |
| 1 to 9 | 23 (77) | 76 (80) | 0.8(0.3-2.2) | 1.2(0.1-10) |
| **Care from other health facility before admission (n=105)** | | | | |
| No | 7 (26) | 40 | 1 | 1 |
| Yes | 20 (74) | 38 | 3.0(1.1-7.9) | 0.1 (0.01-0.8) |
| **COVID-19 symptoms (n=142)** | 1 (3) | 24 (22) | 1 | |
| Yes | 32 (97) | 85 (78) | 9.0(1.2-70) | |
| **Difficulty in breathing (n=117)** | | | | |
| No | 6 (19) | 56 (66) | 1 | |
| Yes | 26 (81) | 29 (34) | 8.4(3.1-23) | |
| **Runny nose (n=117)** | | | | |
| No | 29 (91) | 60 (71) | 1 | |
| Yes | 3 (9) | 25 (29) | 0.2(0.1-0.9) | |
| **General malaise (n=117)** | | | | |
| No | 30 (94) | 61 (72) | 1 | |
| Yes | 2 (6) | 24 (28) | 0.2(0.04-0.8) | |
| **Mechanical ventilation(n=124)** | | | | |
| **Yes** | 2 (11) | 1 (1) | 1 | |
| No | 17 (89) | 104 (99) | 0.1(0.01-1.0) | |
| **Systolic blood pressure (n=131)** | | | | |
| < 140 | 26 (84) | 94 (94) | 1 | |
| ≥140 | 5 (16) | 6 (6) | 3.0(0.9-11) | |
| **Diastolic blood pressure (n=131)** | | | | |
| <90 | 27 (87) | 92 (92) | 1 | |
| ≥90 | 4 (13) | 8 (8) | 1.7(0.5-6.1) | |

## Discussion

This study revealed that pregnant women with COVID-19 who died (cases) were more likely to be admitted with symptomatic, severe disease, and died few days after hospitalization. On the other hand, few pregnant women who survived had severe COVID-19 disease at admission although they spent more days in hospital on average than cases. Having severe disease at admission increased odds of death, while admission for 6 or more days was

protective. However, the admission time is likely to be related to death before that time period. That is, survivors survived for at least 6 days while those who died did not.

A study conducted in Uganda in the Kampala Metropolitan area revealed that 94% of the reported deaths among all persons with confirmed COVID-19 occurred among people who had advanced disease at hospital admission (3). Hantoushzadehet al. (4) studied nine women seven of whom died, and reported a potential for maternal death due to COVID-19 in the second and third trimester; all these women presented with severe COVID-19 at admission, similar to the pregnant women who died in this study.

The finding in this study of difficulty in breathing being a risk factor for death is similar to what was found in Ethiopia where shortness of breath was a significant predictor of death among patients with severe COVID-19 (5). A study in France and Belgium revealed that pregnant women were at higher risk for hospital admission than non-pregnant women because of respiratory distress (6). Pregnancy results in compression of the diaphragm upwards and hormonal changes alter the upper airway tract; additionally, during the third trimester, there is limited expansion of the chest wall and total respiratory compliance reduces (7). Pregnant women diagnosed with COVID-19 should be therefore monitored closely for signs of respiratory distress so that appropriate interventions are promptly instituted.

Age in this study was not a risk factor for death among hospitalised pregnant women. This finding differs from that of Laopaiboonet al. (8) that advanced maternal age above 35 years increases the risk of maternal death and from what Liet al. (9) found that older age was associated with death among patients with COVID-19. In this study, 8% of women had systolic blood pressure $\geqslant$ 140 mmHg while 9% had diastolic blood pressure $\geqslant$ 90 mmHg which are indicative of hypertension. The prevalence of hypertension in this study is lower than that of 27 % that was found among hospitalised patients in Uganda byElayeeteet al. (10) in an earlier study. Although prevalence of hypertension in this study was similar between cases and controls, in Brazil, hypertension was higher among pregnant women who died than those who had COVID-19 and recovered (11).

**Study limitations**

Our findings should be interpreted in line with the following limitations. We could note evaluate clinical characteristics fully because of missing information in patient files such as laboratory reports, weight and height measurements, and information on comorbidities. Although we included patients from eleven hospitals, the sample size of 143 was still small and could have affected the direction of the study outcomes in either direction.

**Conclusion**

Women who died were also more likely to have sought care at another medical facility before reaching the admitting hospital for care. This suggests that the earlier facilities these women visited could have delayed to refer them to the hospitals where they eventually died a few days after admission. This possibly explains why they presented with severe disease. This study demonstrates the importance of prompt referral of pregnant women with COVID-19 before disease advances to severe stage. Even amidst lockdown, there should be a strategy that encourages pregnant women to utilise advanced health care services at the earliest opportunity. This optimises the utility of therapeutic interventions.

**Conflict of interest**

The authors declare that they had no competing interests.

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**References**

1. MOH. Corona Virus Disease (COVID-19) case confirmed Uganda: Ministry of Health; 2021 [Available from: https://www.health.go.ug/covid/category/press-release/page/2/.
2. Burt JF, Ouma J, Amone A, Aol L, Sekikubo M, Nakimuli A, et al. Indirect Effects of COVID-19 on Maternal, Neonatal, Child, Sexual and Reproductive Health Services in Kampala, Uganda. medRxiv. 2021.
3. Phoswa WN, Khaliq OP. Is pregnancy a risk factor of COVID-19? European Journal of Obstetrics & Gynecology and Reproductive Biology. 2020;252:605-9.
4. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. JAMA pediatrics. 2021.
5. Mendez-Dominguez N, Santos-Zaldívar K, Gomez-Carro S, Datta-Banik S, Carrillo G. Maternal mortality during the COVID-19 pandemic in Mexico: a preliminary analysis during the first year. BMC Public Health. 2021;21(1):1-9.
6. MOH. National Technical Guidelines for Integrated Disease Surveillance and Response. Third ed2021.
7. MOH. Goal Oriented Antenatal Care Protocol Uganda: Ministry of Health, Uganda; 2018 [Available from: https://platform.who.int/docs/default-source/mca-documents/policy-documents/operational-guidance/UGA-MN-21-02-OPERATIONAL-GUIDANCE-2018-eng-Goal-Oriented-ANC.pdf.