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Outcomes of Critically Ill Pregnant Women with COVID-19 Pneumonia at Rhuh in Lebanon

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ABSTRACT

Introduction: Since its declaration, the novel COVID-19 has been the center stage of worldwide concern as an international public health emergency due to its immense morbidity and mortality. Pregnant women are considered the most vulnerable population when encountering a SARS-COV2 infection and so extensive studies regarding risk factors, level of severity as well as maternal & neonatal outcomes are crucial to optimize the approach and management of a pregnant infected female.

Methods: This is a case-control retrospective study of women with COVID infection (pregnant and non-pregnant) admitted to ICU in Rafik Hariri Hospital between February 2020 and June 2021. Data were collected from digitized records including demographic characteristics, oxygen requirement, vitals, laboratory results, and imaging, management lines, maternal and neonatal outcomes. The latter was analyzed using SPSS Statistics Version 19.0, Armonk, NY: IBM Corp.

Results: No significant difference was found concerning the severity of the disease and its course, length of hospital stay, ICU admission, complications during hospitalization, and treatment administration. Non-pregnant women did exhibit more chronic illnesses, mainly HTN and DM, presented with more severe hypoxemia, higher ferritin levels, more lung involvement on CT chest on admission, and were primarily given heparin as anticoagulation. Neonatal death was significant in cases of pregnancy termination with a lack of follow-up after discharge.

Conclusion: Pregnant women were hospitalized for less severe indications due to controversy on management and scarcity of evidence. No difference in morbidity and mortality between the two groups and further research is indicated for optimization of treatment and prognosis.

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Introduction

Since its declaration as the first coronavirus pandemic on the 3rd of November 2020 by the WHO, the novel COVID-19 has been the center stage of worldwide concern as an international public health emergency. SARS-CoV-2 has already been the primary culprit for the death of 1.35 million and 55 million infection cases, heavily burdening the global healthcare system with its significant morbidity and mortality [1]. In Lebanon, around 380000 people have recovered to this date and approximately 679 have succumbed to SARS-CoV-2 infection [2].

Among the affected population, pregnant women are considered more susceptible to severe viral respiratory infections since their physiological and anatomical alterations render them more vulnerable to complications. At first, the primary reports of pregnant women diagnosed with COVID-19 pneumonia in China suggested that the clinical picture was mild, with favorable outcomes as observed amongst similarly-aged patients [3].

However, new literature suggested otherwise with more severe pregnancy cases documented. In fact, pregnant females are more likely to contract corona infection and it has been associated with a substantial risk of morbidity and mortality, especially in the third trimester and postpartum phase along with their infants, compared with their not- infected pregnant counterparts. The latter is evidently true when pregnant individuals are symptomatic or have chronic illnesses… Same as with other viral illnesses, including influenza and varicella [4].

When dissecting COVID-19 as an infection, according to The WHO, there are four clinical stages: a mild form with non-specific symptoms(fatigue, cough, muscle pain, nasal congestion, headache, fever, sore throat, nausea, diarrhea, vomiting and anosmia);a moderate form with pneumonia and oxygen saturation below 94% requiring minimal oxygen supplementation; a severe form of pneumonia with prominent tachypnea and more than 50% lung implication on CT chest asking for high oxygen therapy and a very severe form calling for mechanical ventilation, usually associated with multi-organ failure and shock [5].

In regard to comorbidities apparent during the second trimester of pregnancy (hypertension, cholestasis, diabetes), as well as obesity and elevated maternal age, they all place pregnant women in jeopardy of the last 2 clinical stages of COVID-19, necessitating their admission to the intensive care unit with invasive ventilation compared to the general population [6].

The basic principles for diagnosis and treatment mirror the non-pregnant and so pregnant patients should be provided with all means of investigation and management options without delay or disregard.

Fortunately, most management lines available for COVID-19 pneumonia are considered safe during pregnancy and lactation with no teratogenicity, but their effectiveness remains uncertain or even minimal. As mentioned earlier, pregnancy is a vulnerability status that comprises hypercoagulability predisposing females to exacerbated COVID-19 pneumonia. The consensus reached so far is that low molecular weight heparin and steroids are the mainstay of treatment and are recommended for both fetal pulmonary maturation between 24+0 and 33+6 weeks of gestation and hindrance of SARS-COV2 lung involvement progression.

Antibiotics are still reserved for confirmed co-bacterial or superimposed infections. Therapies like tocilizumab, interferon beta B1, and convalescent plasma have been mentioned and are employed in critical and life-threatening cases, but the data is still restricted and sparse [7].

It is vital to state that a multi-disciplinary expert team must be employed when approaching a severe case of corona in pregnancy for adequate and effective management. Immediate and fast escalation to the appropriate treatment lines are needed to elevate outcomes for both women and their off-springs.

Corticosteroid therapy should be altered during pregnancy with non- fluorinated glucocorticoids. Il-6 inhibitors and monoclonal antibodies, together with certain antiviral therapies, may also be considered. At any point, pregnant patients might be placed on supportive oxygen therapy, non-invasive ventilation, ventilation in the prone position, intubation, and ECMO. None of the mentioned supportive therapies were contraindicated during pregnancy with the same criteria applied to the general population. In some clinical situations, especially later in the third trimester, early delivery of the baby may facilitate improvement of the maternal condition.

However, decisions regarding timing and mode of delivery should be taken with a holistic approach, ideally in a center with appropriate expertise [8].

Of course, vaccination with COVID-19 is of supreme importance prior and during pregnancy and should be strongly advised, with appropriate guidance and signposting of reliable data. It has already been shown to be safe for the mother as well as the born child with no adverse events or undesirable short term neonatal outcomes with the recommended mRNA vaccine [9].

Novel research concerning the course of the disease during pregnancy as well as the repercussions of applied therapies is of paramount value to tailor the most optimal management for pregnant females with COVID-19 infection, hence, this study.

Primary Outcome

- Assess the maternal outcome in severe COVID-19 pneumonia at RHUH in Lebanon.

Secondary Outcomes

- Compare the characteristics of these pregnant women with those of women who were not pregnant at the time of ICU admission.
- Determine the treatment and complications of covid-19 infection in pregnant women.
- Evaluate the outcome and prognosis of COVID-19 infection, along with the mortality rate and length of hospital stay.

Subjects & Methods

Study Design

An epidemiological, case-control, retrospective study about pregnancy was conducted from February 23th, 2020 to June 30th, 2021 in a single public hospital in Beirut, Lebanon, Rafic Hariri University Hospital-RHUH, a referral center for covid-19.

Study Population

Sample Size

The sample size considered all female patients diagnosed with COVID-19 admitted to ICU, 440 patients were then selected based on the inclusion and exclusion criteria.

Inclusion criteria

- Women between 18-51 years old who are in reproductive age.
- Diagnosis of covid-19 pneumonia was documented by positive polymerase chain reaction (PCR) testing of nasopharyngeal swab sampling, according to WHO guidelines.
- Severe cases, according to WHO, defined by: Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to the fraction of inspired oxygen (PaO2/FiO2) <300, respiratory rate >30 breaths/minute, or lung infiltrates >50% on chest CT scan.
- *Exclusion criteria*
- Younger than 18 or older than 51 years old.
- History of major psychiatric disorders (e.g., schizophrenia, bipolar disorder).

Therefore, the sample size was decreased to 58, including all eligible subjects (19 cases and 39 controls).

Data Collection

Chart Review

Medical charts were reviewed employing a consistent data set to assemble demographic characteristics (age, sex, comorbidities, smoking habits..), vital signs at ICU admission, laboratory findings such as white blood cell count, lymphocyte and neutrophils count, platelet count, lactate concentration,

crp, procalcitonin, D-dimer, Il-6, ferritin, pro-bnp as well as arterial blood gas analysis, partial pressure of oxygen (PaO2)/ fraction inspired of oxygen (FiO2), treatment (oxygen therapy, antimicrobial agents, corticosteroids, anticoagulation, vasopressor use) and outcomes (death, acute kidney injury, mechniacal ventilation, dialysis, neonatal/fetal demise).

Ethical Considerations

It is an epidemiological study that received approval from Rafic Hariri University Hospital-Institutional Review Board that complies with the membership requirements in the US Code of Federal Regulations (21CFR56 and 45CFR46) of the Food and Drug Administration. The participant's privacy has been protected at any respected of time. All data collected has been kept confidential. All information collected has been completely anonymous. The info has been transcribed and then destroyed. There have been safeguards in situ to protect the participant's confidentiality.

Data Statement: No additional Data is available.

Statistical Analysis

The data collected was analyzed using Statistical Package for the Social Sciences software (Version 19.0. Armonk, NY: IBM Corp) and was described using frequencies (N), percentages (%), means, and standard deviations. Absolute number and percentage reported categorical variables. Chi-square distribution was accustomed to determine the association between categorical variables. The differences within the average value of the numeric variables were assessed using t-test for independent samples. All data were two sided analyzed and a p value of $\leq$ 0.05 designated statistical significance.

Results

Demographic variables results are as follows: the mean age of the pregnant patients was 41.59 (± 7.56) years while that of the controls was 33.32(± 6.71) years (p< 0.001).

General health issues data are presented in Table 1. Concerning weight and daily routine, the BMI mean was 30.31 (±8.16) and 30.21 (±6.13) for the cases and controls, respectively (p= 0.964). Concerning smoking, 10.5% of the cases are smokers compared to a percentage of 30.8% among controls (p= 0.091). Among the cases, 10.5% complained of chronic disease, compared to 56.4% for those among controls. (p= 0.001).

Table 1: General Health Issues among Pregnant and Non-pregnant Women

Characteristic	Pregnancy		p value
	Yes	No	
Total Number	19	39	
Age (years)	41.59 ± 7.56	33.32 ± 6.71	<0.001
BMI (kg/m^2)	30.31 ±8.16	30.21 ±6.13	0.964
Smoking n (%)	2 (10.5%)	12 (30.8%)	0.091
Alcohol n (%)	0 (0.0%)	2 (5.1%)	0.315
Nationality			0.106
Lebanese	12 (63.2%)	16 (41.0%)	
Syrian	5 (26.3%)	13 (33.3%)	
Bangladeshi	0 (0.0%)	5 (12.8%)	
Iraqi	2 (10.5%)	0 (0.0%)	
Others	0 (0.0%)	5 (12.8%)	
Chronic diseases n (%)	2 (10.5%)	22 (56.4%)	0.001
Type of chronic disease n (%)			
Hypertension	0 (0.0%)	12 (30.8%)	0.007
Diabetes	0 (0.0%)	10 (25.6%)	0.015
Lung diseases	2 (10.5%)	3 (7.7%)	0.718
End Stage Renal Disease	0 (0.0%)	2 (5.1%)	0.315
Others	1 (5.2%)	9 (23.1%)	0.732

The time from onset of symptoms to ICU admission ranged from 2 to 14 days with a mean duration of 7.89 (±3.01) and 7.56 (±3.20) for the cases and controls, respectively (p= 0.708). The vital signs varied between patients, with a mean shown in Table 2.

Regarding the PO2/FiO2 ratio on admission to ICU, the pregnant patients had a mean ratio of 170.11 (±32.15) compared to 93.77 (±5.69) for the non-pregnant (p=0.002).

Table 2: Vitals Signs among Pregnant and Non-pregnant Women

Vitals	Pregnancy		p value
	Yes	No	
Total Number	19	39	
T (◦C)	36.49 ± 0.62	36.79 ± 0.56	0.076
SBP (mmHg)	112.47 ± 14.66	121.33 ± 18.18	0.070
DBP (mmHg)	69.26 ± 9.04	72.41 ± 12.94	0.346
HR (bpm)	102.94 ± 21.62	95.97 ± 16.92	0.185
RR (bpm)	24.05 ± 4.66	24.87 ± 5.29	0.586
SpO2 (%)	79.47 ± 10.47	71.21 ± 14.74	0.033

The different laboratory abnormalities are shown in Table 3. The acute inflammatory markers (D-dimer, ferritin, interleukin-6 (IL-6), procalcitonin, LDH, pro-BNP, and CRP) were significantly elevated in both groups.

Table 3: Laboratory Tests among Pregnant and Non-pregnant Women

Vitals	Pregnancy		p value
	Yes	No	
Total Number	19	39	
WBC (10^9/L)	10.77 ± 5.16	11.95 ± 6.60	0.497
Neutrophils (%)	85.58 ± 5.31	84.13 ± 8.63	0.503
Lymphocytes (%)	9.66 ± 4.66	11.30 ± 7.54	0.387
Platelets (10^9/L)	199.66 ± 22.88	244.87 ± 14.93	0.096
Creatinine (mg/dl)	0.68 ± 0.13	1.34 ± 0.43	0.262
D-dimer /FEU (mcg/ml)	3.47 ± 0.80	2.31 ± 0.56	0.229
Ferritin (ng/ml)	307.67 ± 58.09	620.75 ± 106.44	0.043
IL6 (ng/ml))	73.95 ± 12.89	112.60 ± 34.03	0.399
LDH (IU/L)	631.42 ± 209.24	467.52 ± 39.24	0.328
Procalcitonin (ng/ml)	3.29 ± 1.59	25.96 ± 5.11	0.506
CRP (mg/L)	106.59 ± 10.81	179.99 ± 19.34	0.002
Pro-BNP (pg/ml)	2124.81 ± 1489.39	1686.56 ± 803.60	0.778

Upon admission to ICU, CT scan chest showed a percentage of 56.76 ± 4.58 involvement with ground glass opacities in the pregnant group compared to a percentage of 67.90 ± 3.35 among non-pregnant group (p= 0.055).

During ICU stay, the oxygen requirements varied between patients, using different types such as face mask, non-rebreather face mask, high flow nasal cannula and intubation with mechanical ventilation. The maximum requirement between both groups was detailed in Table 4.

The duration of oxygen therapy was 14.68 ± 2.3 days among cases compared to 16.59 ± 2.29 among controls (p= 0.561). In addition, the time needed for mechanical ventilation for cases and control was 10.71 ± 2.93 days and 11.73 ± 2.89 days, respectively (p= 0.809).

All patients were also treated with antibiotics, steroids, anticoagulation, and many other medical therapies, shown in Table 4. The duration of steroid therapy was approximatively the same between both groups with a mean of 12.74 ± 1.78 days for cases and 12.21 ± 1.15 days for controls (p= 0.798).

Table 4: Treatment among Pregnant and Non-pregnant Women

Treatment	Pregnancy		p value
	Yes	No	
Total Number	19	39	
FM	6 (31.6%)	5 (12.8%)	0.087
NRFM	0 (0%)	12 (30.8%)	0.007
HFNC	6 (31.6%)	11 (28.2%)	0.791
MV	7 (36.8%)	10 (25.6%)	0.379
Steroids			
Dexamethasone	15 (78.9%)	27 (69.2%)	0.437
Solumedrol	11 (57.9%)	27 (69.2%)	0.394
Anticoagulation			
Heparin	8 (42.1%)	32 (82.1%)	0.002
Enoxaparin	19 (100%)	23 (59%)	0.001
Fundaparinux	1 (5.3%)	1 (2.6%)	0.597
Antimicrobials			
Ceftriaxone	17 (89.5%)	34 (87.2%)	0.801
Levofloxacin	3 (15.8%)	28 (71.8%)	<0.001
Azithromycin	9 (47.4%)	11 (28.2%)	0.150
Meropenem	7 (36.8%)	18 (46.2%)	0.502
Vancomycin	7 (36.8%)	15 (38.5%)	0.905
Colistin	5 (26.3%)	6 (15.4%)	0.319
Voriconazole	2 (10.5%)	3 (7.7%)	0.718
Fluconazole	4 (21.1%)	6 (15.4%)	0.592
Others	10 (52.6%)	16 (41%)	0.630
Medical Trials			
Remdesivir	1 (5.3%)	6 (15.4%)	0.267
Tocilizumab	0 (0%)	3 (7.7%)	0.214
Ivermectin	0 (0%)	1 (2.6%)	0.481
Convalescent Plasma	0 (0%)	5 (12.8%)	0.103
Others	0 (0%)	2 (5.1%)	0.604
Prone	6 (31.6%)	5 (12.8%)	0.087
Vasopressors	4 (21.1%)	10 (25.6%)	0.702
Neuromuscular Blockers	7 (36.8%)	7 (17.9%)	0.115

Some complications were noted, like arrhythmia that was seen only in 6 patients (15.4%) of the control group (p= 0.071), and acute kidney injury that was documented in 5 pregnant patients (26.3%) compared to 6 in non-pregnant patients (15.4%) (p=0.319). Among the patient who developed acute kidney injury, 50% of the control group were started on dialysis while 0% in the case group (p= 0.214). No case of thrombosis was documented between both groups.

Considering pregnant patients, the gestational age upon admission to ICU varied between 18 and 35 weeks with a mean age of 27.79 weeks, while the mean gestational age at delivery for pregnancy termination was 28.67 weeks. 15 pregnant patients delivered by c-section, none via vaginal delivery, while only 4 cases recovered without termination of the pregnancy.

Finally, the maternal outcome was shown in Figure 1. A percentage of 21.1 of pregnant women died compared to 35.9% of non-pregnant women. As for fetal outcome, 9 (60%) were alive, while 6 (40%) were dead (p<0.001).

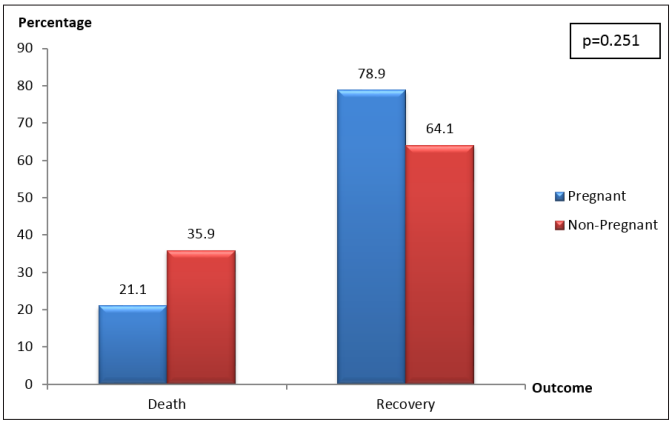

Figure 1: Maternal Outcomes among Pregnant and Non-pregnant Women

A percentage of 21.1 of pregnant women died compared to 35.9% of non-pregnant women. Regarding recovery, 78.9% versus 64.1% of pregnant and non-pregnant women recovered, respectively, p value 0.251

The mean duration of ICU stay was 12.47 ± 2.28 days among cases compared to 13.26 ± 1.99 days for controls (p= 0.797) , and the mean duration of total hospital stay was 15.58 ± 2.38 days and 17.26 ± 2.26 days for cases and controls respectively (p= 0.647).

Discussion

Bulky literature, including the latest study by the National Institute of Health, deduced that pregnant women who contracted COVID-19 appear to be more exposed to common pregnancy complications than their counterparts. This is probably due to caesarean delivery, preterm delivery, peripartum death, postpartum hemorrhage, or superimposed infections. Nonetheless, our results do not depict the previous statement [10].

The demographic characteristics were not significantly different between pregnant and non-pregnant women except for age and chronic diseases. The mean age among pregnant women was 41.59, higher than that of non-pregnant women, which were 33.32 with a p-value of less than 0.001. The latter reflects the mean age of patients who were hospitalized and admitted to ICU.

Such a prominent result highlights the fact that pregnant women at risk for ICU admission were at an advanced maternal age, but without a direct proportional correlation. An age exceeding 35 years in pregnancy was already showcased as a risk factor for ICU admission by Knight M et al [11].

BMI of pregnant and non-pregnant was in the overweight range above 30 kg/m2 which places them both on the front line for complications and ICU admission. This aligns with the finding of Sarah et al. study where both groups were in the overweight range [12].

Another eminent finding is the significant difference in the prevalence of chronic diseases as well as some types of diseases between the two groups. It was 56.4% and 10.5% in non-pregnant and pregnant women, respectively, with a P-value of 0.001. Such a discovery negates the suggestion that pregnancy is an isolated risk factor for hospitalization since there other contributing elements exist like comorbidities. This is also braced in a study by Melanie Nana and Catherine Nelson-Pierce stating that the majority of pregnant women who acquire COVID-19 will be asymptomatic or endure a mild clinical picture. However, small subsets of those women do develop a more severe course with increased rates of ICU admission, invasive ventilation, and preterm birth when compared with the non-pregnant population [6].

Among the mentioned illnesses in the collected data, hypertension and diabetes constituted a robust independent risk factor for admission among non-pregnant women while acknowledging that none of the pregnant women had these comorbidities compared to 30.8% for HTN and 25% for DM among non-pregnant women respectively.

To note that lung disease, end-renal stage diseases, and others were not significantly different between both groups. This was also demonstrated by Sarah Easter et al. where hypertension and diabetes mellitus were significantly more prevalent among non-pregnant women [12]. The previous amplifies the conclusion reached by Manou Vouga et al. in the largest cohort of pregnant women tested for SARS-Cov-2 worldwide and the first analysis of primary data stratified by the severity of maternal disease. It was found that pulmonary diseases, hypertensive disorders, and diabetes mellitus were significantly associated with an elevated risk of severe maternal outcomes [13].

Further study is required to validate this correlation among non-pregnant women to assess the ramifications of hypertension and diabetes on disease severity.

As for the time length between the onset of symptoms to ICU admission, the statistics were of no significance between pregnant and non-pregnant women. The length was 7.89 days among pregnant women compared to 7.56 among non-pregnant patients. This in fact is illustrated in the cohort study by Pierce-Williams RAM et al [14].

In regard to vital measurements, there was no significant difference between the two groups except for SpO2 with its mean 79.47 in pregnant patients topping that of non-pregnant women, 71.21, with P-value of 0.033. To notice that both groups had SpO2 levels below 94%, necessitating admission. It also evinces that a higher threshold of SpO2 was adopted as a criterium for hospitalization in pregnant patients since practitioners meticulously and vigilantly approached cases of COVID infection in pregnancy with the scarcity of medical evidence.

No significant difference in laboratory parameters was demonstrated among the two groups except for ferritin among the other elevated acute inflammatory reactants (IL6, CRP) which was higher and double in value when compared to the pregnant patients. Both groups had a normal white count even though slightly more elevated in non-pregnant women. D-dimers were more elevated in pregnant women with no statistical difference, and this is an expected physiological elevation in pregnancy. Neutrophil count was not significantly different between both groups. This contradicts the assessment done by Cheng et al which found higher CRP levels and neutrophilia among pregnant women [15].

CT findings upon admission to ICU showed a 56.6% involvement in pregnant women compared to 67.9% in non-pregnant women with P-value of 0.055. This highlights again the tendency for admission in pregnant women with lung involvement since they were considered at higher risk for deterioration due to pregnancy-related physiological changes. This is controversial with the finding by Rachel. R et al. who found that pregnant women appear to present more commonly with advanced CT findings compared to the general population [16]. Rachel et al found as well that pregnant patients present with higher rates of lower ground-glass opacities, consolidation, and pleural effusion [16].

During ICU stay, the oxygen requirements varied between patients, encompassing a wide range of oxygenation means from nasal cannula, face mask, and high flow nasal cannula to non-rebreather and intubation to mechanical ventilation. Most pregnant women required high flow nasal cannula and mechanical ventilation with no statistical difference compared to the control group. This disputes the cohort UK study which demonstrated that pregnant women were more prone to invasive ventilation with an odds ratio 1.88 with 95% confidence interval 1.36 - 2.6. The type of use depends on the clinical judgement of health care providers upon admission and the clinical presentation of patients. There was no difference in the duration of oxygen administration between both groups as well as no difference in the time needed for mechanical ventilation with a mean time of almost 11 days for both groups [11].

There was no statistical difference in steroid use in both groups. Yet, steroids were more used among non-pregnant women. This could be explained by the side effects that long-term use of steroids could have on the fetus, treating this medication as a last resort when weighing risks and benefits. The duration of steroid use was almost 12 days for both groups. "The RECOVERY trial does not support the use of steroids in infected pregnant cases but not on oxygen therapy and, when legitimately indicated, it can be employed cautiously favoring methylprednisolone as the primary treatment for 10 days after the administration of dexamethasone for 2 days for fetal lung maturation [17].

There was a statistical difference in the use of anticoagulation among pregnant and non-pregnant women. Several modalities of anticoagulation were used including LMWH, enoxaparin, fondaparinux, and DOACs, with heparin more abundantly administered in the non-pregnant group. This is controversial since pregnancy represents a state of increased hypercoagulability necessitating anticoagulation, especially with infection or when bed-ridden.

Therefore far, there is't a consensus regarding thromboprophylaxis in COVID19 pregnant females as mentioned in Jahnavi DaruKatie et al. study; anticoagulation should be considered in line with existing risk stratification approaches [18].

There was no statistical difference in antibiotics use except for levofloxacin which was more used in non-pregnant women. This is expected due to the contra-indicated use of fluoroquinolones in pregnancy. Pregnant women received mostly ceftriaxone, a third generation broad-spectrum cephalosporin safe to be used in pregnancy and breastfeeding as well.

Remdesivir was used in one pregnant woman compared to 6 non-pregnant women with no statistical difference. Such a finding is explained by the obscurity surrounding the use of this drug in pregnancy. This actually was not evident in the prospective study conducted by Sarah Easter et al. in the US where Remdesivir was used more among pregnant women. Tocilizumab, Ivermectin, and convalescent plasma were never used in pregnant women of this group. This is justified by the cautious use of novel treatments in pregnant women. Prone position was done in 4 pregnant women compared to 10 non-pregnant women with no statistical difference. Gravid uterus may represent a limitation for this position, yet benefits to outweigh the risks in certain individual cases. Use of vasopressors and neuromuscular blockers was also not statistically different between the two groups [12].

No complications of significant difference were noted between the two groups. Arrhythmias, acute kidney injury, and thrombosis rates were almost similar in both groups. No pregnant woman with kidney injury required dialysis compared to 50% of non-pregnant women with kidney injury. The mean gestational age at admission was 27.79 weeks (the earliest admission was at 18 weeks), with a mean gestational age of 28 weeks at delivery. To note that 88% of pregnant women in the study done by Sarah et al. were delivered at a gestational age more than 30 weeks [12]. All deliveries were done by caesarean section, none by normal delivery. The route of delivery is justified by the early preterm gestational age and the emergent need to terminate pregnancy to prevent regression and complications for the mother. This was consistent with previous COVID studies' findings.

Only 4 cases improved without the need to terminate pregnancy. Even though pregnancy by itself did not represent a risk factor for severe disease, termination of pregnancy was recommended for better maternal outcomes in the Lebanese practice. Yet, no unanimity exists regarding the decision for the optimal timing for delivery or clear indications for that matter, especially when COVID19 infection arises in late preterm and early term gestation. What is agreed upon is that the infection itself should not be considered a sole reason for delivery [19].

Moving on to neonatal death, it was common among delivered mothers (40% with P-value less than 0.001) given the preterm gestational age, lack of neonatal resuscitation equipment in the hospital and the worsening maternal clinical status. To note that COVID status of delivered neonates was not studied and was not considered a secondary outcome of this study.

Most cases in both groups recovered. Death was more common in non-pregnant women yet with no significant statistical difference. Mortality rate was 35.9% among non-pregnant women compared to 21.1% among pregnant. The larger prevalence of chronic illnesses could have contributed to this difference. It is insinuated that the decision for pregnancy termination could have contributed to the amelioration of the clinical conditions among pregnant women despite the fact that the duration of ICU admission and hospital stay did not significantly differ between the two groups.

Limitations

Considering the limitations impeding this study, it is retrospective meaning data collection was founded on accurate documentation and charting.

It is also a small single center study limiting the ability to extrapolate the results to the general Lebanese population and to do a multivariate analysis. Therefore, future studies should include multiple centers with a larger data pool using test negative design.

Management lines were not unified among all encountered cases and there is not data stressing the effect of the infection on preterm labor since previous studies did highlight the matter. The delivery process itself was not described either if it was spontaneous or induced or if its indications were maternal or fetal in origin.

Another prominent point to mention is that pregnant women as well as delivered neonates were not followed up after discharge from ICU.

Conclusion

In summary, this is a case-control retrospective study of severely-ill women with COVID infection (pregnant and non-pregnant) admitted to ICU in Rafik Hariri Hospital between February 2020 and June 2021. There was no significant difference in ICU and hospital stay between pregnant and non-pregnant women. Mortality and complication rates did not differ as well between the two groups. Steroids were used less frequently in comparison with anticoagulation that was administered more generously in the pregnant group. Management was somewhat similar with minute alterations in antibiotic administration and of course the indication for delivery that resulted in significant neonatal death.

Declarations

Competing Interests and Funding

The authors declare that they have no competing interests and the research is not funded by any funding agency.

Authors' Contributions

EL MAWLA Zeinab and EL SADDIK Ghaidaa collected the data. EL MAWLA Zeinab and SALAMEH Pascale contributed to its analysis. EL MAWLA Zeinab, EL SADDIK Ghaidaa, ASSAF Sara, HASSOUN Mahmoud contributed to the management of the patients, planning of the study, and the preparation of manuscript. All authors read and approved the final manuscript.

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References

1. Mahendra M, Nuchin A, Kumar R, Shreedhar S, Mahesh PA (2021) Predictors of mortality in patients with severe COVID-19 pneumonia - a retrospective study. Adv Respir Med 89: 135-144.
2. COVID19 [Internet]. Available from: https://covid19.moph.gov.qa/EN/Pages/default.aspx.
3. San-Juan R, Barbero P, Fernández-Ruiz M, López-Medrano F, Lizasoáin M, et al. (2020) Incidence and clinical profiles of COVID-19 pneumonia in pregnant women: A single-centre cohort study from Spain. EClinicalMedicine 23: 100407.
4. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, et al. (2021) Maternal and Neonatal Morbidity and Mortality among Pregnant Women with and without COVID-19 Infection: The INTERCOVID Multinational Cohort Study. JAMA Pediatr 175: 817-826.
5. Clinical Spectrum|COVID-19 Treatment Guidelines [Internet]. Available from: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/%0A.
6. Nana M, Nelson-Piercy C (2021) COVID-19 in pregnancy. Clin Med J R Coll Physicians London 21: e446-e450.
7. Emanoil A-R, Stochino Loi E, Feki A, Ben Ali N (2021) Focusing Treatment on Pregnant Women With COVID Disease. Front Glob Women's Heal 2: 590945.
8. Melanie Nana, Kenneth Hodson, Nuala Lucas, Luigi Camporota, Marian Knight, et al. (2022) Diagnosis and management of covid-19 in pregnancy. BMJ 377: e069739.
9. Favre G, Maisonneuve E, Pomar L, Winterfeld U, Daire C, et al. (2022) COVID-19 mRNA vaccine in pregnancy: Results of the Swiss COVI-PREG registry, an observational prospective cohort study. Lancet Reg Heal – Eur 18: 100410.
10. NIH-funded study suggests COVID-19 increases risk of pregnancy complications [Internet]. 2022. Available from: https://www.nih.gov/news-events/news-releases/nih-funded-study-suggests-covid-19-increases-risk-pregnancy-complications.
11. Knight M, Bunch K, Vousden N, Morris E, Simpson N, et al. (2020) Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: National population based cohort study. BMJ 369: m2107.
12. Easter SR, Gupta S, Brenner SK, Leaf DE (2021) Outcomes of Critically Ill Pregnant Women with COVID-19 in the United States. American Journal of Respiratory and Critical Care Medicine 203: 122-125.
13. Vouga M, Favre G, Martinez-Perez O, Pomar L, Acebal LF, et al. (2021) Maternal outcomes and risk factors for COVID-19 severity among pregnant women. Sci Rep 11: 13898
14. RAM P-W, JB, LF, RK, PS B, et al. (2020) Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. Am J Obstet Gynecol MFM 2: 100134.
15. Cheng B, Jiang T, Zhang L, Hu R, Tian J, et al. (2020) Clinical characteristics of pregnant women with coronavirus disease 2019 in Wuhan, China. Open Forum Infect Dis 7: ofaa294.
16. Oshay RR, Chen MYC, Fields BKK, Demirjian NL, Lee RS, et al. (2021) COVID-19 in pregnancy: a systematic review of chest CT findings and associated clinical features in 427 patients. Clinical Imaging 75: 75-82.
17. Saad AF, Chappell L, Saade GR, Pacheco LD (2020) Corticosteroids in the Management of Pregnant Patients with Coronavirus Disease (COVID-19). Obstet Gynecol 136: 823-826.
18. Daru J, White K, Hunt BJ (2021) COVID-19, thrombosis and pregnancy. Thrombosis Update 5: 100077.
19. Mokhtari NB, Drassinower D, Orr LA, Cobb NK, Mims OL, et al. (2021) Expectant management of severe covid-19 pneumonia in late preterm pregnancy and subsequent cholecystitis: Lessons learned. AJP Rep 11: e29-e33.