COVID-19 outcomes among pregnant and nonpregnant women at reproductive age in Egypt

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ABSTRACT

Background To describe demographic, clinical and epidemiological characteristics of pregnant and nonpregnant women with confirmed COVID-19 at reproductive age and determine risk factors of COVID-19 severe outcomes during pregnancy.

Methods A retrospective study for females aged 18–49 with confirmed COVID-19 by RT-PCR in Egypt, February–July 2020. Data were obtained from Egypt National Surveillance, bivariate and multivariate analysis for demographic and clinical characteristics and outcomes of COVID-19 between pregnant and nonpregnant women including ICU admission, need for ventilator and death was performed.

Results A total of 23 095 females were identified, with mean (SD) age of 35.1 (8.1) year. Of those, 408 (1.8%) were pregnant, with mean (SD) age of 29.3 (8.1) years. Compared to nonpregnant, pregnant patients were more likely to be admitted to hospital (OR = 1.7 CI = 1.4–2.1), ICU (OR = 2.4, CI = 1.3–4.3), need ventilator (OR = 3.9, CI = 2.1–7.4) and have severe outcome (OR = 3.0, CI = 1.9–4.7). Factors associated with severe outcome included: pregnancy, age > 30 years, underlying medical conditions, and living in rural areas.

Conclusion Pregnant women with COVID-19 are at higher risk of severe symptoms and outcome including ICU admission, requiring ventilator and death. To reduce risk of severe outcome, counseling about for seeking medical care and health education about COVID-19 preventive measures should be performed.

Keywords Pregnancy and childbirth disorders, public health, women's health

Introduction

The novel coronavirus disease 2019 COVID-19 is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a newly emergent coronavirus, that was first recognized in Wuhan, China in December 2019.[1] Coronavirus causes respiratory and gastrointestinal infections that might range from mild to severe disorders such as viral pneumonia with systemic impairment.[2] Globally, more than 85.1 million laboratory-confirmed cases and more than 1.8 million deaths were reported as of 31 December 2020.[3] In Egypt, the first case of COVID-19 was announced in 14 February 2020.[4] As of 31 December 2020, a total of 136 644 cases of COVID-19 and 7576 deaths were reported.[5]

Emerging infections have been shown to have an important impact on pregnant females and their fetuses.[6] Since the beginning of the COVID-19 pandemic, it has been argued that pregnant females are at increased risk of severe infection.[7] Studies suggested that pregnant females with COVID-19 are more likely to develop respiratory complications, require intensive care unit admission and require invasive ventilator, while maternal mortality due to COVID-19 was uncommon.[8]

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Currently, no sufficient evidence is available to conclude the definite effect of COVID-19 on pregnant females given the novelty of the virus. Most of the studies were performed on small numbers of pregnant females with no comparison groups. Additional studies with larger sample sizes and comparison group are required to fill the gap in the available knowledge.[9] In Egypt, specific hospitals at all Egyptian governorates are designated for screening and isolation of COVID-19 confirmed cases. Data on pregnant females are entered in the National Electronic Disease Surveillance System (NEDSS) database during patient evaluation and confirmation before referral to hospital or sent home for home treatment and self-isolation. This study aimed to describe the demographic, clinical and epidemiological characteristics of pregnant and nonpregnant women at reproductive age with COVID-19 and determine the association between pregnancy and COVID-19 severe outcomes.

Methods

Study setting and design

This is a retrospective study of all pregnant women with confirmed COVID-19 infection in Egypt during the period February–July 2020. Data were extracted from the NEDSS. NEDSS is an electronic system first established in 2006 for reporting communicable diseases of public health impact in Egypt. COVID-19 was added to the list of 40 reportable diseases in December 2019. Demographic data, clinical data, COVID-19 severity risk factors, status of pregnancy and outcome data were obtained for all women aged 18–49 year during the period of the study. The study was approved by the Ethical Committee at Egypt Ministry of Health and Population (MoHP). The reported cases were anonymous in the surveillance records.

Study variables

Data obtained included demographic characteristics (age, residence, occupation and nationality), clinical signs and symptoms of COVID-19, radiological imaging, pregnancy status, contact with COVID-19 confirmed cases, underlying medical conditions, COVID-19 outcomes (recovery, Intensive Care Unit (ICU) admission, ventilation and death). Underlying medical conditions included diabetes, chronic pulmonary disease, cardiovascular disease, renal disease, hepatic disease, immunocompromised and obesity. Severe outcome was defined as ICU admission or placing on ventilator or death during hospitalization. The 27 governorates in Egypt were categorized into 3 categories: Mostly rural governorates, mostly urban governorates and metropolitan governorates.[10]

Laboratory confirmation

Patients with respiratory symptoms seen at the designated hospitals are interviewed with standardized surveillance data collection form after providing nasopharyngeal swab. Specimens are transferred to the Central Public Health Laboratory to be tested for SARS-CoV-2 by RT-PCR (Viasure Sars-CoV-2 Real Time PCR Detection Kit (CerTest Biotec, Spain).

Statistical analysis

Statistical analysis was carried out using IBM SPSS version 20. Categorical variables were described using percentages, while continuous variables were described using mean and standard deviation. We compared demographic and clinical characteristics of COVID-19 between pregnant and nonpregnant women to describe the risk factors of COVID-19 infection among pregnant women, and we compared severe outcomes between the two groups to identify risk factors for severe outcome. We used Chi-square test or Fisher's exact tests to identify significant factors, wherever appropriate. Crude odds ratios were calculated for each variable of interest through bivariate analysis. Multivariate analysis using binary logistic regression was conducted to assess the association between pregnancy and severe COVID-19 outcomes. A P-value of < 0.05 was considered as statistically significant.

Results

Demographic and epidemiologic characteristics

A total of 23 095 women of reproductive age had confirmed COVID-19 between February and July 2020 in Egypt. Their mean (SD) age was 35.1 (8.1) year. Of those, 408 (1.8%) were pregnant, with mean (SD) age of 29.3 (8.1) year. More than half of them (52.9%) aged less than 30 year (Table 1). Compared with nonpregnant COVID-19 confirmed patients, pregnant were significantly younger, and more likely to live in rural areas rather than urban areas or large cities and contacted confirmed COVID-19 case. Proportion of cases with underlying medical conditions was higher in nonpregnant than pregnant women. The most frequently reported underlying medical conditions in pregnant and nonpregnant COVID-19-infected women were diabetes (2.0 and 5.4%, respectively), followed by chronic lung disease (1.0 and 3.1%, respectively) and cardiovascular diseases (1.0 and 1.9%, respectively).

Clinical picture and disease severity

No significant differences were observed between pregnant and nonpregnant COVID-19 patients in the general,

Table 1 Demographic characteristics of women at the reproductive age with COVID-19 according to pregnancy status, Egypt

Characteristics	Pregnant N = 408		Nonpregnant N = 22 687		P-value
	n	%	n	%	
Age (year)					<0.001
18–24	98	24	2636	11.6	
25–29	118	28.9	3514	15.5	
30–34	113	27.7	4248	18.7	
35–39	62	15.2	4421	19.5	
40–44	15	3.7	4078	18	
45–49	2	0.5	3790	16.7	
Residence					<0.001
Mostly rural governorates	287	70.3	12 298	54.2	
Metropolitan Governorates	85	20.8	6811	30.0	
Mostly urban governorates	36	8.8	3578	15.8	
Underlying medical condition	24	5.9	2772	12.2	<0.001
Hospitalized	223	54.7	9320	41.1	<0.001
Contact with confirmed case	98	24.0	310	15.8	<0.001
Healthcare worker	71	17.4	4516	19.9	0.104

Table 2 Clinical characteristics of women at the reproductive age with COVID-19 according to pregnancy status, Egypt

	Pregnant (n = 408)		Nonpregnant (n = 22 687)		P-value
Variable	n	%	n	%	
Temperature > 38 °C	328	80.4	17 354	76.5	**0.031**
Cough	285	69.9	15 330	67.6	0.330
Sore throat	192	47.1	10 712	47.2	0.950
Difficulty of breathing	177	43.4	9474	41.8	0.225
Joint pain	156	38.2	7752	34.2	0.440
Vomiting	41	10.0	1966	8.7	0.163
Diarrhea	40	9.8	2931	12.9	**0.028**
Loss of smell and taste	30	7.4	711	3.1	<**0.001**
Myalgia	22	5.4	688	3	**0.006**
Headache	13	3.2	466	2.1	0.066
Pneumonia	177	43.4	8018	35.3	<**0.001**
Asymptomatic	9	2.2	1896	8.4	<**0.001**

respiratory or gastrointestinal symptoms. However, pregnant patients tended to complain more of anosmia and myalgia. Pregnant women tended to have more severe symptoms in the form of clinical pneumonia (43.4 vs. 35.3%, $P < 0.001$), while nonpregnant were more likely to be asymptomatic cases (8.4 vs. 2.2%, $P < 0.001$) (Table 2).

Compared to nonpregnant women, pregnant patients were more likely to be admitted to hospital (OR = 1.7, 95% CI: 1.4–2.1, P-value == < 0.001), ICU admitted (OR = 2.4, 95% CI: 1.3–4.3, P-value = < 0.001), need invasive mechanical ventilator (OR = 3.9, 95% CI: 2.1–7.4, P-value == < 0.001) and have severe outcome (OR = 3.0, 95% CI: 1.9–4.7, P-value == < 0.001). Case fatality rate was not significantly different between pregnant and nonpregnant women (OR = 1.6, 95% CI: 0.9–3.0, P-value =0.079) (Table 3).

Table 3 Hospitalization and disease outcome of women at the reproductive age admitted with COVID-19, Egypt, February–July 2020

Characteristics	Pregnant (n = 408)		Nonpregnant (n = 22 687)		Crude OR (pregnant vs. nonpregnant)	95% CI	P value
	n	%	n	%			
Hospitalized	223	54.7	9320	41.1	1.7	1.4–2.1	**<0.001**
ICU Admission	12	2.9	281	1.2	2.4	1.3–4.3	**<0.001**
On ventilator	11	2.7	157	0.7	3.9	2.1–7.4	**<0.001**
Death	10	2.5	348	1.5	1.6	0.9–3.0	0.079
Severe outcome	20	4.9	388	1.7	3.0	1.9–4.7	**<0.001**

Pregnant women with underlying conditions were more likely to have severe outcome than nonpregnant women with underlying conditions (3/24 (12.5%) vs. 186/2772 (6.7%), $P = 0.146$). However, this was not statistically significant. Out of 10 pregnant women who died of COVID-19, 2 (20.0%) had underlying medical conditions.

Multivariate analysis of the association between pregnancy and COVID-19 severe outcomes

In the multivariate analysis, pregnancy was significantly associated with increased odds of severe COVID-19 outcomes after adjusting for age, residency and underlying medical conditions. Pregnant women with confirmed COVID-19 were almost four times (OR = 3.96, 95% CI: 3.62–5.26; $P < 0.001$) more likely to have severe COVID-19 outcome compared to nonpregnant women with COVID-19. In the multivariate analysis, age > 30 year, having underling medical condition, and living in rural areas were significantly associated with increased COVID-19 severity (Table 4).

Discussion

Main findings of the study

The health of pregnant women should be considered during this rapidly changing coronavirus pandemic as they experience physiological and psychological changes, which can alter their immune systems.[11]

Most studies did not find significant differences between pregnant and nonpregnant women regarding the development of the clinical features of SARS-CoV-2.[12,13] A recent review indicated that most reported symptoms of COVID-19 in pregnant women included fever (40%) and cough (39%), whereas each of dyspnea, myalgia, loss of sense of taste and diarrhea were reported in less than 10% of pregnant women.[14] Whereas other studies suggested that pregnant women have a different clinical presentation of and morbidity from COVID-19 compared with the nonpregnant

Table 4 Multivariate analysis of risk factors for severe COVID-19 outcomes among COVID-19 confirmed women patients at the reproductive age, Egypt

Variable	OR	95% CI	P-value
Age (year)			
> 30	1.52	1.18–1.96	0.001
≤ 30	1		
Pregnancy (yes vs. no)	3.96	2.47–6.35	<0.001
Underlying medical condition (yes vs. no)	4.36	3.62–5.26	<0.001
Residency			
Living in urban areas	1.0		
Living in rural areas	1.78	1.32–2.39	<0.001
Living in metropolitan areas	1.72	0.93–1.73	0.131

with lower prevalence of fever and higher rates of fatigue, and headaches.[15] This study reported fever and cough as the most common symptoms in pregnant and nonpregnant women, whereas myalgia and anosmia were significantly more reported in pregnant women than nonpregnant women. Much less is known about the underlying mechanisms that may explain taste problems in COVID-19. Studies suggested that dysfunction of the olfactory receptor neurons or difference of susceptibility in different populations could be the reason.[16] More studies are needed to better describe the clinical characteristics of COVID-19 in pregnant women to help case early detection.

We also found that clinically diagnosed pneumonia occurs more in pregnant than nonpregnant COVID-19-infected patients. A recent study reported a pneumonia prevalence of 61.5% in pregnant women.[17] The physiologic changes occurring during pregnancy that leads to increased heart rate and oxygen consumption and decreased lung capacity

could be a reason.[18] Pneumonia could indicate COVID-19 symptoms severity in pregnant women.

Asymptomatic cases ratio in this study was lower than what reported from other studies conducted in countries performing routine SARS-CoV-2 testing upon admission to labor and delivery units.[19,20] Testing for COVID-19 should be done before labor regardless of the symptoms, to protect healthcare workers.

Available data on the severity of COVID-19 in pregnant women are controversial. Small studies reported no difference in the course of illness between pregnant and nonpregnant women.[21−23] Other studies suggested that pregnant women have slightly higher severity when compared to the general population.[22,24,25] Alternatively, other studies reported that pregnant women are more likely to have severe illness, be admitted to ICU and require mechanical ventilation compared to nonpregnant women even after adjusting for age, race and co-morbidities.[20,26] In addition, studies found that the rate of ICU admission rises with increasing gestational age, with one study reported more than 90% of pregnant patients requiring ICU in their third trimester.[25]

This study showed disproportionately higher rates of COVID-19 hospitalizations among pregnant women compared to nonpregnant women in accordance with other studies.[27] Furthermore, higher rates of ICU admission, mechanical ventilator and death were found in pregnant women with COVID-19 compared to nonpregnant. After adjusting for age, residence and underlying medical conditions, the study showed that pregnant women with COVID-19 are more likely to be hospitalized, ICU admitted, require ventilator and die than nonpregnant women. The difference in severity of COVID-19 illness and outcome between pregnant and nonpregnant patients could be attributed to the physiological and mechanical changes that lead to a state of relative immunosuppression to prevent rejection of the semi-allogenic fetus. These changes predispose pregnant women to a more severe and prolonged disease course.[28] These findings highlight the need for counseling about the importance of seeking medical care if they feel any symptom and measures to prevent COVID-19 should be strongly emphasized for pregnant women and their families during antenatal care visits.

Fatality due to COVID-19 during pregnancy also is controversial. A small study reported death of 7 out of 9 pregnant women with COVID-19,[29] while other studies reported low rates of death in pregnant women with COVID-19.[30] Fatality rate in this study was higher than what have been reported from other countries.[27,30] A possible cause of higher mortality rate in pregnant women than their corresponding nonpregnant group could be explained by the increased estriol levels which interferes with production of CD4+ and CD8+ T cells, leading to an aggressive inflammatory response with

the release of a large amount of pro-inflammatory cytokines that causes a cytokine storm.[28] This reaction was directly correlated with lung injury, multi-organ failure and unfavorable prognosis of severe COVID-19.[31,32] Studies are needed to better describe the causes and risk factors of death from COVID-19 among pregnant women.

This study found that women at reproductive age with COVID-19 who were older than 30 years, women who were living in rural area and women who had underlying medical conditions were at increased risk of severe COVID-19. Studies suggested that living in an area of increased socioeconomic deprivation is a risk factor for COVID-19 infection severity.[33] This could be related to the limited healthcare facilities with ICU beds and ventilators in rural setting.[34]

Studies indicated that COVID-19 shows an increased number of cases and a greater risk of severe disease in the general population with increasing age.[35] It was found that susceptibility to infection in under-20s is approximately half that of older adults. The reason could be that younger ages experience more frequently mild upper respiratory infections resulting in immune cross-protection when in contact with an infectious person.[36]

Underlying medical conditions were identified as a risk factor for COVID-19 severity and poor outcome among general population in many studies.[37,38] Other studies reported that older maternal age, high body mass index, pre-existing medical condition were associated with ICU admission and mechanical ventilation.[24,25,39] Data suggest that 40% of pregnant women who died from COVID-19 had obesity, diabetes or maternal age greater than or equal to 40 years.[17,25] This study showed that underlying medical conditions were associated with unfavorable outcome from COVID-19 among women at reproductive age. We were unable to test association between comorbidities and severe disease outcome in pregnant women due to the small number of pregnant women with underlying conditions. The most prevalent conditions identified among pregnant women were diabetes and chronic pulmonary and cardiovascular disease in agreement with other studies.[40]

What is already known on this topic

Results of studies on the severity and fatality due to COVID-19 in pregnant women is controversial. Most studies conducted on smaller sample size to give significant evidence of pregnancy as risk for severe outcome in COVID-19 patients.[21−23,29] Also, few studies discussed risk factors for COVID-19 severity among females at reproductive age.

What this study adds

This is one of a few studies that enrolled sufficient number of pregnant and nonpregnant women at reproductive age

with COVID-19 to assess their demographic and epidemiologic characteristics and to determine the association between pregnancy and COVID-19 severity. The study discussed association between pregnancy and COVID-19 severe outcome using multivariate analysis to prove that pregnant women are at higher risk of hospitalization, ICU admission, mechanical ventilator and death if infected with COVID-19.

Study limitations

This is one of the few studies with sufficient sample size that describe the epidemiologic and clinical characteristics and outcomes of COVID-19 infection among women in the reproductive age and compare pregnant to nonpregnant women characteristics. Yet, some data were not available during patients' hospitalization such as specific clinical and investigations information, treatment received, delivery-related information and newborn outcomes.

Conclusions

Pregnant women with COVID-19 are at higher risk of severe COVID-19 outcomes including ICU admission, requiring mechanical ventilator and death due to COVID-19. Pregnant women should be counseled about the importance of seeking prompt medical care immediately when having symptoms during antenatal care visits to reduce risk of infection and mortality in this vulnerable group. They should be educated how to minimize the risk for acquiring COVID-19 infection including limiting unnecessary interactions with persons who might have been infected with SARS-CoV-2, wear a mask, comply with social distancing, avoid persons who are not wearing a mask and wash their hands frequently. Understanding disease severity risk factors can help clinicians in the early appropriate medical management of patients with COVID-19. Testing for SARS-COV-2 should be conducted upon admission to labor and delivery units to protect healthcare workers performing the process of labor. Additional studies are needed on COVID-19 severity during pregnancy to inform messaging and patient counseling.

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Conflict of interest

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