Young pregnant women are also at an increased risk of mortality and severe illness due to COVID-19: Analysis of the Mexican National Surveillance Program

Raigam Jafet Martinez Portilla, Emily R. Smith, Siran He, Johnatan Torres Torres, Salvador Espino-Y-Sosa, Juan Mario Solis-Paredes, Liona C. Poon

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I am an author on this submission, have adhered to all editorial policies for submission as described in the Information for Authors, attest to having met all authorship criteria, and all potential conflicts of interest / financial disclosures appears on the title page of the submission.

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Objective

There is conflicting information as to whether pregnant women are at increased risk of severe complications from SARS-CoV-2. **We sought to understand whether pregnant women are at increased risk of death or severe illness due to COVID-19 as compared to non-pregnant women and whether that risk varies by age.**

Study Design

Data were extracted from the epidemiological surveillance system of viral respiratory diseases of Mexico, that includes 475 monitoring hospitals are components of the Mexican Public Health Network which includes the National Mexican Institute of Social Security, Institute of Security and Social Services for State Workers, Secretary of National Defense, Secretary of the Navy of the Mexican Republic, and National Health Department. These monitoring hospitals are approved to perform reverse transcription-polymerase chain reaction (rt-PCR) analysis for SARS-CoV-2 in Mexico and are, therefore, the reference centers for all patients with suspected COVID-19. We included 7,028 pregnant and 255,721 non-pregnant women aged 15-45 diagnosed with COVID-19 between February 1st and October 27^{th,} 2020.

Results

We find that the risk of death and pneumonia increases with age for both pregnant and non-pregnant women (Figure 1A, 1C). Adjusted case fatality rate for pregnant women was 1.3% overall, but rose to 2.1% and 5.9% for those aged 35-39 and 40-44, respectively. Pregnant women with COVID-19 consistently had a higher risk of death and pneumonia as compared to similarly aged, non-pregnant women with COVID-19 (adjusted relative risk [RR] death: 1.68, 95% CI: 1.36-2.08; adjusted RR pneumonia: 1.97, 95% CI: 1.82-2.13) (Figure 1, Table 1). While the risk is highest among older pregnant women, the highest RRs appear among both younger and older pregnant women (Figure 1B, 1D).

Conclusion

Earlier reports suggested mortality may not be higher in pregnant women with COVID-19[1]. However, a recent US study found a 1.7-fold increased risk of death in pregnant women (n=34) with COVID-19 when compared to non-pregnant women (n=447)[1]. We confirm that pregnancy puts the women at increased risk of COVID-19-related death and pneumonia as we have already suggested in our previous manuscript using a propensity score matching analysis[2]. What is striking about our results, is that although the risk o highest amongst older pregnant women, the RR is high among younger pregnant women between 20 and 30 years old. This likely reflects both the excess risk conferred by pregnancy and the low baseline risk of death and severe disease among younger non-pregnant women. This finding is concerning. Younger populations have been reassured that they are at lower risk for COVID-19-related complications, and pregnant women may falsely believe their young age protects against severe disease. Such inadequate health advice may render this vulnerable group to seek medical care too late, and care may not be prioritized appropriately if they are perceived to be at lower risk.

Therefore, pregnancy puts the woman at an increased risk of COVID-19-related death and pneumonia. All pregnant women, irrespective of age, should be informed about the health risks associated with COVID-19 and should seek medical help at the earliest opportunity.

References

1. Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**(44): 1641-7.
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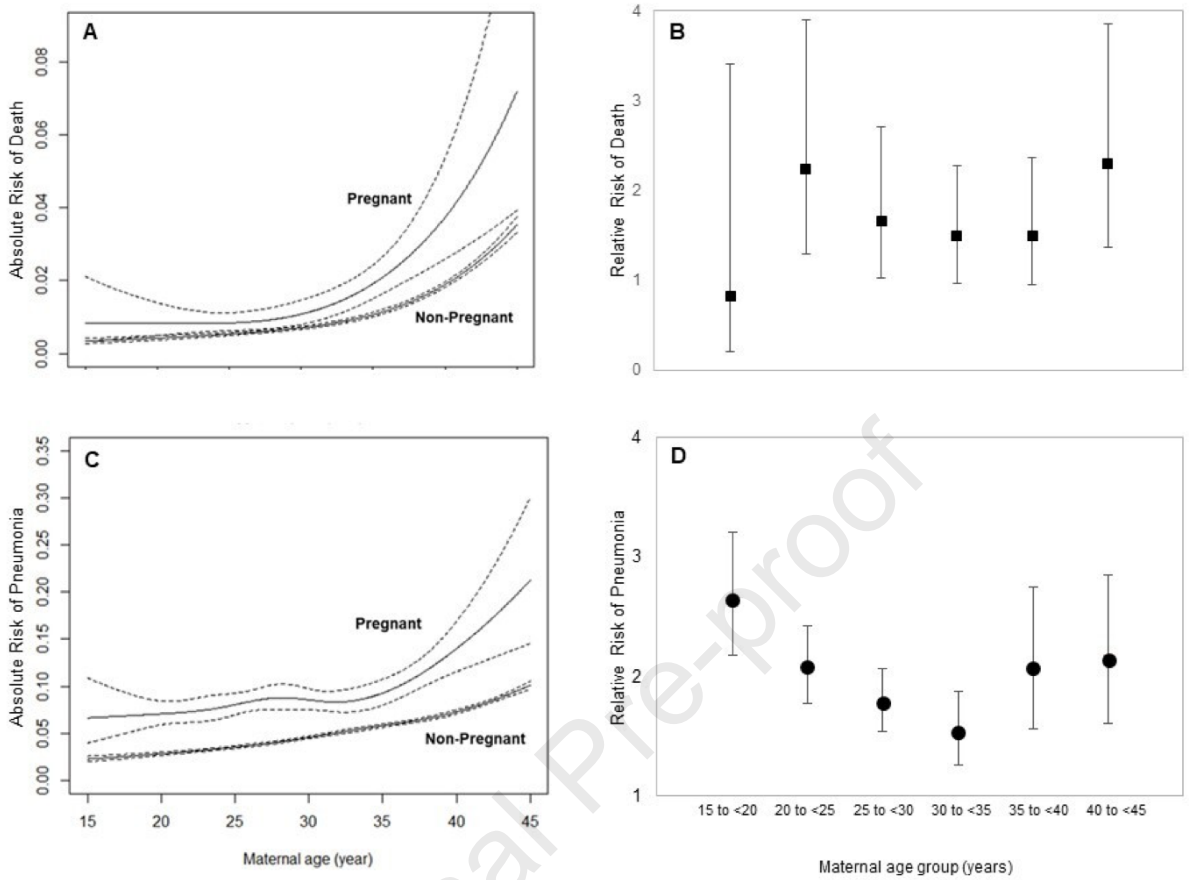
Table 1. Relative risk of death and pneumonia among pregnant vs non-pregnant women with COVID-19 (aged 15-44)

	Pregnancy			Non-Pregnant						
Death[2]	**Events**	**Total**	**Risk per 100k**	**Events**	**Total**	**Risk per 100k**	**Relative Risk (95% CI)**		**Adjusted Relative Risk[1] (95% CI)**	
Overall	93	7028	1320	3221	255721	1260	1.61 (1.28 , 2.02)	<0.001	1.68 (1.36 , 2.08)	<0.001
Age 15 to <20	2	451	444	58	10844	530	0.83 (0.20 , 3.38)	0.79	0.83 (0.20 , 3.41)	0.80
Age 20 to <25	16	1505	1060	128	29257	440	2.43 (1.45 , 4.08)	0.0008	2.24 (1.29 , 3.90)	0.004
Age 25 to <30	18	2102	860	255	49592	510	1.67 (1.03 , 2.68)	0.04	1.66 (1.02 , 2.71)	0.04
Age 30 to <35	23	1768	1300	474	53377	890	1.47 (0.97 , 2.22)	0.07	1.49 (0.97 2.27)	0.07
Age 35 to <40	20	963	2080	709	52246	1360	1.53 (0.99 , 2.38)	0.06	1.50 (0.95 , 2.36)	0.08
Age 40 to <45	14	239	5860	1597	60405	2640	2.22 (1.32 , 3.69)	0.002	2.30 (1.37 , 3.85)	0.002
Pneumonia[3]	**Events**	**Total**	**Percent**	**Events**	**Total**	**Percent**	**Relative Risk (95% CI)**		**Adjusted Relative Risk[1] (95% CI)**	
Overall	611	7028	8.7	14332	255716	5.6	1.96 (1.81 , 2.12)	<0.001	1.97 (1.82 , 2.13)	<0.001
Age 15 to <20	32	451	7.1	249	6804	3.66	2.45 (1.72 , 3.48)	<0.0001	2.42 (1.70 , 3.46)	<0.0001
Age 20 to <25	110	1505	7.3	627	18750	3.34	2.63 (2.17 , 3.19)	<0.0001	2.64 (2.18 , 3.21)	<0.0001
Age 25 to <30	169	2102	8.0	1508	34162	4.41	2.07 (1.78 , 2.41)	<0.0001	2.08 (1.78 , 2.42)	<0.0001
Age 30 to <35	167	1768	9.5	2285	37422	6.11	1.79 (1.54 , 2.08)	<0.0001	1.78 (1.54 , 2.07)	<0.0001
Age 35 to <40	91	963	9.5	2636	37134	7.1	1.52 (1.25 , 1.85)	<0.0001	1.54 (1.26 , 1.88)	<0.0001
Age 40 to <45	42	239	17.6	4271	43252	9.87	2.03 (1.54 , 2.68)	<0.0001	2.07 (1.56 , 2.75)	<0.0001

[1] Modified poisson model adjusted for obesity, hypertension, diabetes, smoking

[2] P value for interaction (maximum likelihood test comparing full and reduce model, 5 degrees of freedom) between pregnancy and age (5 year age bin categories) = 0.46

[3] P value for interaction (maximum likelihood test comparing full and reduce model, 5 degrees of freedom) between pregnancy and age (5 year age bin categories) = 0.002



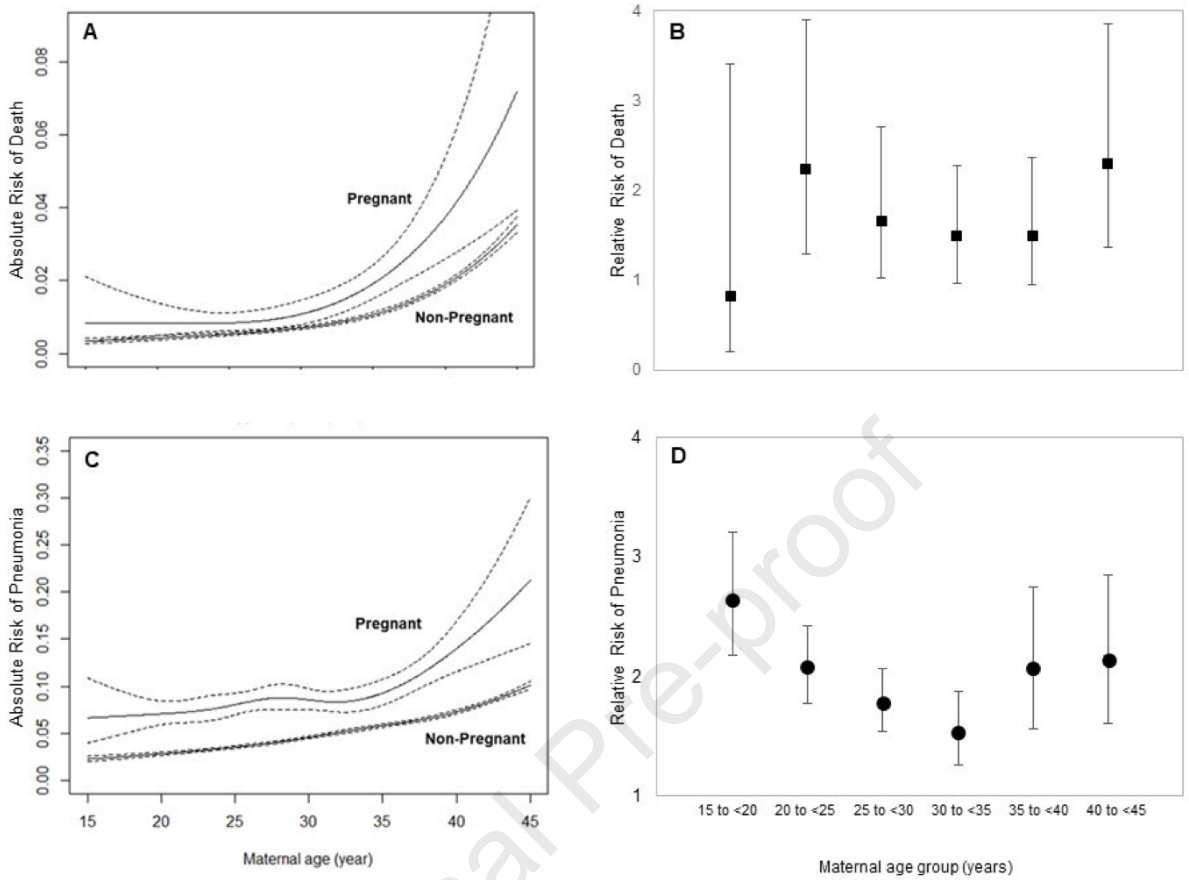


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Figure Description

Figure 1. Absolute risk of death or pneumonia and relative risk of death or pneumonia comparing pregnant and non-pregnant women age 15-45 years with PCR-confirmed SARS-CoV-2 infection in Mexico from March through October 2020. A. Absolute risk of death and 95% confidence limits by patient age, stratified by pregnant and non-pregnant women (non-linear relationship between the risk of death and age modeled using restricted cubic splines). B. Relative risk of death comparing pregnant and non-pregnant women with COVID-19, by age categories. C. Absolute risk of pneumonia and 95% confidence limits by patient age stratified by pregnant and non-pregnant women (non-linear relationship between the risk of death and age modeled using restricted cubic splines). D. Relative risk of pneumonia comparing pregnant and non-pregnant women with COVID-19, by age categories.