BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-070688
Article Type:	Original research
Date Submitted by the Author:	10-Dec-2022

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Keywords:	COVID-19, EPIDEMIOLOGIC STUDIES, Public health < INFECTIOUS DISEASES, OBSTETRICS

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Factors Associated with Having COVID-19 Among Pregnant and Non-Pregnant Women in Metro Manila, Philippines: A Multi-Center Longitudinal Cohort Study

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WORD COUNT: 1938 words

ABSTRACT

Objective. To determine potential risk factors associated with having COVID-19 among unvaccinated pregnant and non-pregnant women.

Design. A multicenter prospective cohort study among eligible women in Metro Manila, Philippines, from 2020 to 2022.

Setting. Five national and local hospital research sites altogether recruited and screened 500 consenting eligible individuals.

Participants. Pregnant and non-pregnant participants meeting the eligibility criteria were admitted for an RT-PCR determination of SARS-CoV-2, pregnancy testing and ultrasound, and an interview with an administered questionnaire.

Exposures. Primary exposure was pregnancy; secondary exposures involve sociodemographic, lifestyle, and obstetric-gynecologic factors.

Outcome measure. Outcome being measured was COVID-19 status.

Results. Pregnancy was found to be a significant risk factor (PR=1.184, 95CI[1.096,1.279]), as was being a white-collar worker (PR=1.123, 95CI[1.02,1.235]), traveling outside the country (PR=1.369, 95CI[1.083, 1.173]), and being infected by at least one vaccine-preventable disease (VPD) (PR=1.208, 95CI[1.113,1.310]). Protective factors included having graduate-level education (PR=0.787, 95CI[0.649,0.954]), immunization against a VPD (PR=0.795, 95CI[0.733,0.862]), and practicing contraception (PR=0.889, 95CI[0.824,0.960]).

Conclusion. This study is the first in the country to determine the risks influencing COVID-19 infection among unvaccinated pregnant and non-pregnant women. Pregnancy is a significant risk for the disease among women in Metro Manila, and other risk and protective factors may be said to lie along socioeconomic lines. Further studies are needed to elucidate the development of the disease in pregnant women, and the maternal and neonatal effects of COVID-19 via potential vertical mechanisms of transmission.

KEYWORDS COVID-19, Pregnancy, Prospective studies, Risk factors

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This article provides the first multi-center determination study in public hospitals in the Philippines to serve as a baseline for the determination of risk factors of COVID-19 in women.
- This article also incorporates in the analysis, some of the pre-existing conditions and pressures experienced by Filipino women as a driving force behind COVID-19 risk.

- Further studies with an emphasis on the longitudinal nature of the disease throughout the gestation period are recommended to determine the differential progression of the disease in terms of changes brought about by pregnancy.
- Research on clinical manifestations, progression, and outcomes of COVID-19 among women is recommended.

INTRODUCTION

Background. The rapid transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) caused cases of Coronavirus Disease 2019 (COVID-19) to rise in many countries since it was first reported in Wuhan, China, in December 2019[1]. By the time the WHO declared it a pandemic, significant repercussions were already observed in worldwide social and economic life[2]. The multifaceted nature of this pandemic gives rise to concerns about identifying relevant risk factors, especially for vulnerable populations. Men have higher mortality risks when infected, but women may have higher risks of worse health outcomes and less healthcare access due to pre-existing socioeconomic gaps exacerbated by the pandemic[3,4]. At par or possibly greater risks are pregnant women and their unborn; both susceptible to infection due to their weakened immune system[5]. Evidence of sex- and pregnancy-based differences in COVID-19 vulnerability indicate a need to determine the relevant socio-demographic, lifestyle, and obstetric-gynecologic risk factors. This is especially urgent in countries whose pandemic response policies prioritize universal community health over the needs of vulnerable populations like women because of scarce resources.

Objective. To our knowledge, there is scant local literature describing the risk factors of COVID-19 among unvaccinated women in the Philippines during the pandemic. Furthermore, studies on the matter are yet to incorporate the intersectionality of pre-existing socioeconomic pressures on women which may compound the risk determination for the disease. In conducting this research, we provided baseline information and comparison between pregnant and non-pregnant populations in this pandemic and validated the findings of relevant literature while offering new and local insights into the characteristics of unvaccinated women admitted to public hospitals in a highly populous and heterogenous city. This study thus aimed to identify the risk factors associated with COVID-19 in unvaccinated pregnant and non-pregnant women in five hospitals in the City of Manila, Philippines.

METHODS

Study design and setting. This prospective multicenter cohort study is part of a comprehensive protocol to determine the risk factors, clinical manifestations, progression, and maternal-neonatal outcomes of COVID-19 vertical transmission among pregnant and non-pregnant women in Metro Manila[6]. Specific details on the procedures such as detailed eligibility criteria, data sources, handling of bias, missing data, and non-response, and sensitivity analyses can be found in said protocol. Cases were recruited from the study population consisting of all pregnant or non-pregnant women who will consult among the five public hospital research sites under the Department of Health (DOH) or the Manila City Government, ranging from November 30, 2020, to March 31, 2022. The Research Institute of Tropical Medicine (RITM) processed the collected samples using reverse-transcription PCR for diagnosis and analyses of unconventional samples. All study participants meeting the inclusion criteria were admitted to the study following a thorough briefing and with their written and continuing consent.

Patient and public involvement. Patients and(or) the public were not involved in the design. All participants were recruited with informed and continuing consent from research hospital sites.

Data collection. Laboratory determination of SARS-CoV-2 and pregnancy status were carried out after collection of samples from the participants. They were also given a validated self-administered structured COVID-19 infection in adults questionnaire adapted from the New South Wales Department of Health[6]. The questionnaire will profile the socio-demographic, lifestyle, obstetric-gynecologic, medical history, and pregnancy-related characteristics of each participant.

Outcome and exposures. Outcome measurement was COVID-19 status, which is confirmed from the RT-PCR test. Primary exposure was pregnancy status, determined from pregnancy test and(or) ultrasound. Secondary exposures were socio-demographic, lifestyle, and obstetric-gynecologic factors, as will be discussed in later sections.

Statistical analysis. Descriptive statistics profiled the socio-demographic, lifestyle, and obstetric-gynegologic characteristics of pregnant and non-pregnant cohorts. The crude prevalence ratio (cPR) and the corresponding 95% confidence interval (95CI) were calculated after regressing a bivariable generalized linear model using a Poisson distribution with robust variance correction and a log link function between the characteristics as predictors, and COVID-19 status as the outcome. This model was used as the best option to minimize the overestimation of the true prevalence ratio among other alternatives[7]. The same regression model was used to create adjusted prevalence ratios (aPRs) and to determine which among the

characteristics are better risk indicators of COVID-19 susceptibility among the women in the study.

RESULTS

Five hundred respondents were included from the five hospitals throughout the study period. Of them, 233 (46.6%) were COVID-19-positive and 267 (53.5) were pregnant. After omitting missing observations in the variables of interest, only 352 (70.4%) cases remained for regression analyses and calculation of prevalence ratios. Most participants were lost to follow-up, particularly during delivery, when most of them preferred to deliver out of the hospital research sites. **Table 1** shows the socio-demographic and lifestyle characteristics of the respondents.

Table 1. Characteristics of respondents included in the present study, stratified by pregnancy status.

Characteristics	Total, n=500	Non-pregnant, n=233	Pregnant, n=267
SOCIODEMOGRAPHIC FACTORS			
Admitting hospital			
DJFMH	166 (33.2)	78 (15.6)	88 (17.6)
JRRMMC	168 (33.6)	78 (15.6)	90 (18.0)
OMMC	58 (11.6)	26 (5.2)	32 (6.4)
SAH	59 (11.8)	29 (5.8)	30 (6.0)
JJASGH	49 (9.8)	22 (4.4)	27 (5.4)
Age			
18-30	246 (49.2)	77 (15.4)	169 (33.8)
31-48	202 (40.4)	105 (21.0)	97 (19.4)
>49	52 (10.4)	51 (10.2)	1 (0.2)
Resides in Manila			
No	226 (45.7)	89 (17.9)	137 (27.7)
Yes	269 (54.3)	139 (28.1)	130 (26.3)
Missing	5	5	0
Address type			
Household	494 (98.9)	228 (45.7)	266 (53.3)
Aged care facility	1 (0.2)	1 (0.2)	0 (0.0)
Other residence type	4 (0.8)	3 (0.6)	1 (0.2)
Missing	1	1	0
Educational attainment			
Elementary	33 (6.6)	18 (3.6)	15 (3.0)
High school	234 (46.8)	100 (20.0)	134 (26.8)
College	195 (39.0)	85 (17.0)	110 (22.0)
Graduate school	35 (7.0)	30 (6.0)	5 (1.0)
Vocational	3 (0.6)	0 (0.0)	3 (0.6)
Type of occupation			
Unemployed/Unstable	306 (64.3)	116 (24.4)	190 (39.9)
Blue-collar job	42 (8.8)	25 (5.3)	17 (3.6)
White-collar job	128 (26.9)	87 (18.3)	41 (8.6)
Missing	24	5	19
Marital status			
Single	278 (55.6)	103 (20.6)	175 (35.0)

Married	189 (37.8)	109 (21.8)	80 (16.0)
Cohabiting	27 (5.4)	15 (3.0)	12 (2.4)
Widowed	6 (1.2)	6 (1.2)	0 (0.0)
Religion			
Catholic	440 (89.8)	196 (40.0)	244 (49.8)
Protestant	11 (2.2)	8 (1.6)	3 (0.6)
Muslim	15 (3.1)	9 (1.8)	6 (1.2)
Others	24 (4.9)	13 (2.7)	11 (2.2)
Missing	10	7	3
Socioeconomic status			
Less than Php5,000	250 (50.3)	96 (19.3)	154 (30.9)
Php5,001 to Php20,000	159 (31.9)	71 (14.3)	88 (17.7)
Php20,001 and above	88 (17.7)	64 (12.9)	23 (4.8)
Missing	3	2	1
LIFESTYLE FACTORS			
Use of contraceptive			
No	338 (77.6)	168 (33.6)	220 (44.0)
Yes	112 (22.4)	65 (13.0)	47 (9.4)
Smoking history			
Never smoker	468 (93.8)	207 (41.5)	261 (52.3)
Ever smoker	31 (6.2)	25 (5.0)	6 (1.2)
Missing	1	1	0
Alcohol use			
Never alcoholic	412 (82.6)	170 (34.1)	242 (48.5)
Ever alcoholic	87 (17.4)	62 (12.4)	25 (5.0)
Missing	1	1	0
Illicit drug use			
No	496 (99.4)	230 (46.1)	266 (53.3)
Yes	3 (0.6)	2 (0.4)	1 (0.2)
Missing	1	1	0
Immunized from at least one VPD			
No	260 (64.4)	106 (26.2)	154 (38.1)
Yes	144 (35.6)	37 (9.2)	107 (26.5)
Missing	96	90	6
History of at least one VPD			
No	344 (69.8)	160 (32.5)	184 (37.3)
Yes	149 (30.2)	68 (13.8)	81 (16.4)
Missing	7	5	2
Blood type			
A	113 (24.1)	43 (9.2)	70 (14.9)
B	88 (18.8)	37 (7.9)	51 (10.9)
O	237 (50.5)	113 (24.1)	124 (26.4)
AB	31 (6.6)	15 (3.2)	16 (3.4)
Unrecalled	31	25	6
Travel history			
No	484 (96.8)	219 (43.8)	265 (53.0)
Yes	16 (3.2)	14 (2.8)	2 (0.4)
OBSTETRIC-GYNECOLOGIC FACTORS			
Gravidity			
Two at most	320 (64.1)	153 (30.7)	167 (33.5)
At least 3	179 (35.9)	79 (15.8)	100 (20.0)
Missing	1	1	0
Parity			
Two at most	376 (75.4)	161 (32.3)	215 (43.1)
At least 3	123 (24.6)	71 (14.2)	52 (10.4)
Missing	1	1	0
COVID-19 EXPOSURE			
Negative	267 (53.4)	120 (24.0)	147 (29.4)

Positive	233 (46.6)	113 (22.6)	120 (24.0)

*Unless otherwise specified, all summary statistics are expressed in counts and percentage of the total, *n (%)*.

Most respondents tested negative for COVID-19 during the study, which is also consistent for pregnant (29.4%) and nonpregnant (24.0%) cohorts. More than half of all respondents reside in Manila City and were admitted to DOH partner hospitals, which are among the highest-capacity tertiary institutions in the country. Furthermore, most respondents live in households, are Catholic, have never smoked nor drank alcoholic beverages, have not consumed illicit drugs, have an O blood type or have never left the country during the pandemic. Among pregnant respondents, the majority were younger, high school graduates, unemployed, single, making less than PHP5,000.00 (USD84.94) per month, not practicing contraception, have been infected or immunized against at least one vaccine-preventable disease (VPD), have been twice pregnant at most, or with up to two viable pregnancies.

Table 2 shows crude and adjusted prevalence ratios for potential risk factors of COVID-19. Significant risk factors among unvaccinated women include being pregnant, white-collar worker, having been infected with at least one VPD, and leaving the country during the pandemic. Protective factors appear to be having graduate-level education, practicing contraception, and being immunized for at least one VPD. Blood type does not seem to be a significant predictor of COVID-19 among women, as well as gravidity, parity, smoking history, and alcohol use.

Table 2. Crude (cPR) and adjusted (aPR) prevalence ratios with 95% confidence intervals for associations between COVID-19 and covariates.

Characteristics	Total, n=352	COVID-19-negative, n=220	COVID-19-positive, n=132	cPR[95CI]	aPR[95CI]
OBSTETRIC-GYNECOLOGIC FACTORS					
Pregnancy status					
Non-pregnant	120 (34.1)	85 (24.1)	35 (9.9)	1.000	1.000
Pregnant	232 (65.9)	135 (38.4)	97 (27.6)	1.149 [1.063, 1.242]*	1.184[1.096, 1.279]*
Gravidity					
Two at most	225 (63.9)	142 (40.3)	83 (23.6)	1.000	1.000
At least 3	127 (36.1)	78 (22.2)	49 (13.9)	1.012 [0.938, 1.093]	1.075 [0.975, 1.185]
Parity					
Two at most	270 (76.7)	165 (46.9)	105 (29.8)	1.000	1.000
At least 3	82 (23.3)	55 (15.6)	27 (7.7)	0.957 [0.877, 1.044	0.934 [0.842, 1.036]
SOCIODEMOGRAPHIC FACTORS					
Age					

18-30	189 (53.7)	118 (33.5)	71 (20.2)	1.000	1.000
31-48	140 (39.8)	87 (24.7)	53 (15.1)	1.002 [0.928, 1.082]	0.968 [0.896, 1.045]
>49	23 (6.5)	15 (4.3)	8 (2.3)	0.980 [0.841, 1.142]	0.999 [0.857, 1.163]
Resides in Manila					
No	175 (51.0)	128 (36.4)	48 (13.6)	1.000	1.000
Yes	168 (48.9)	92 (26.1)	84 (23.9)	1.161 [1.080, 1.247]*	1.055 [0.990, 1.123]
Educational attainment					
Elementary	16 (4.5)	9 (2.6)	7 (1.9)	1.000	1.000
High school	171 (48.6)	110 (31.3)	61 (17.3)	0.944 [0.791, 1.127]	0.917 [0.807, 1.043]
College	143 (40.6)	83 (23.6)	60 (17.0)	0.988 [0.826, 1.180]	0.927 [0.809, 1.063]
Post-graduate	19 (5.4)	16 (4.5)	3 (0.9)	0.805 [0.646, 1.004]	0.787 [0.649, 0.954]*
Vocational	3 (0.9)	2 (0.6)	1 (0.3)	0.928 [0.601, 1.432]	0.798 [0.62, 1.027]
Type of occupation					
Unemployed/Unstable	243 (69.0)	160 (45.5)	83 (23.6)	1.000	1.000
Blue-collar job	25 (7.1)	14 (3.9)	11 (3.1)	1.073 [0.931, 1.237]	1.02 [0.889, 1.169]
White-collar job	84 (23.9)	46 (13.1)	38 (10.8)	1.083 [0.994, 1.179]	1.123 [1.02, 1.235]*
Marital status					
Single	207 (58.8)	133 (37.8)	74 (21.0)	1.000	1.000
Married	126 (35.8)	73 (20.7)	53 (15.1)	1.047 [0.969, 1.131]	1.057 [0.979, 1.142]
Cohabiting	15 (4.3)	12 (3.4)	12 (0.9)	0.884 [0.742, 1.053]	0.906 [0.759, 1.082]
Widowed	4 (1.1)	2 (0.6)	2 (0.6)	1.105 [0.794, 1.537]	0.990 [0.610, 1.606]
Religion					
Catholic	324 (92.0)	202 (57.4)	122 (34.7)	1.000	1.000
Protestant	5 (1.4)	2 (0.6)	3 (0.9)	1.162 [0.886, 1.524]	1.193 [0.913, 1.558]
Muslim	9 (2.6)	6 (1.7)	3 (0.9)	0.969 [0.766, 1.224]	1.056 [0.896, 1.244]
Others	14 (3.9)	10 (2.8)	4 (1.1)	0.934 [0.774, 1.127]	0.982 [0.841, 1.147]
Socioeconomic status					
Less than Php5,000	198 (56.3)	136 (38.6)	62 (17.6)	1.000	1.000
Php5,001 to Php20,000	101 (28.7)	54 (15.3)	47 (13.4)	1.116 [1.027, 1.212]*	1.060 [0.985, 1.141]
Php20,001 and above	53 (15.1)	30 (8.5)	23 (6.5)	1.092 [0.983, 1.213]	1.048 [0.935, 1.174]
LIFESTYLE FACTORS					
Using contraception					
No	282 (80.1)	166 (47.2)	116 (32.9)	1.000	1.000
Yes	70 (19.9)	54 (15.3)	16 (4.5)	0.870 [0.796, 0.952]*	0.889 [0.824, 0.960]*
Smoking history					
Never smoker	337 (95.7)	209 (59.4)	128 (36.4)	1.000	1.000
Ever smoker	15 (4.3)	11 (3.1)	4 (1.1)	0.918 [0.766, 1.100]	1.124 [0.955, 1.324]
Alcohol use					
Never smoker	301 (85.5)	185 (52.6)	116 (32.9)	1.000	1.000
Ever smoker	51 (14.5)	35 (9.9)	16 (4.5)	0.948 [0.854, 1.053]	1.002 [0.909, 1.104]

Immunized VPD > 1					
No	219 (62.2)	103 (29.3)	116 (32.9)	1.000	1.000
Yes	133 (37.8)	117 (33.2)	16 (4.4)	0.732 [0.686, 0.782]*	0.795 [0.733, 0.862]*
History VPD > 1					
No	238 (67.6)	181 (51.4)	57 (16.2)	1.000	1.000
Yes	114 (32.4)	39 (11.1)	75 (21.3)	1.338 [1.249, 1.432]*	1.208 [1.113, 1.310]*
Blood type					
A	82 (23.3)	58 (16.5)	24 (6.8)	1.000	1.000
B	68 (19.3)	42 (11.9)	26 (7.4)	1.069 [0.955, 1.197]	1.047 [0.958, 1.146]
O	181 (51.4)	106 (30.1)	75 (21.3)	1.094 [0.998, 1.199]	1.028 [0.958, 1.103]
AB	21 (5.9)	14 (3.9)	7 (1.9)	1.031 [0.871, 1.222]	0.967 [0.837, 1.117]
Travel history					
No	349 (99.1)	220 (62.5)	129 (36.6)	1.000	1.000
Yes	3 (0.9)	0 (0.0)	3 (0.9)	1.460 [1.407, 1.515]*	1.369 [1.083, 1.173]*

*Significant at 5% level of significance.

DISCUSSION

This is the first multicenter study in the country to address relevant gaps in the literature by elucidating the systemic inequities and circumstances that contextualize the differential risks in sociodemographic, lifestyle, and obstetric-gynecologic factors between pregnant and non-pregnant women during the early pandemic when vaccines were still unavailable. Further research with consideration of the temporal interaction of the disease with pregnancy is suggested in view of the cumulative nature of this cohort study.

What are the living conditions of pregnant women in the Philippines during the pandemic? Pregnant women were more likely younger, single, unemployed or hold unstable jobs, or make lesser monthly income. Before the pandemic, there were already fewer women in the Philippine labor force in 2015[8]. Filipinas also had a higher incidence of vulnerable employment like self-employment and unpaid home duties, often associated with insufficient income and unsafe working conditions. Prevailing conservative gender roles also translate to women usually being housemakers, even as the Philippines ranks first in gender equality among Asian countries in 2022[4,9]. This cultural practice relegates women from the job market, causing insecure, lower-income employment with lesser bargaining power in most national economies[4]. Pregnancy ultimately compounds these intersecting inequities due to behavioral tendencies to take lesser risks even in decisions that may benefit their physical or financial wellbeing [10,11].

How is COVID-19 risk different among women during the pandemic? Multivariable analysis found that COVID-19-positive women may more likely present as pregnant, white-collar workers, have had at least one VPD infection, or have traveled outside the country during the pandemic. Pregnancy, as a risk factor, supports other studies' findings which have variously been attributed to a more vulnerable immune constitution during gestation[5]. On the other hand, white-collar workers being at higher risk may be explained by the general nature of their occupations in healthcare, essential bureaucracy as part of a skeleton workforce, and similar jobs that result in increased interaction with suspect cases of the disease. For this reason, it is also rational, as other studies found to varying significance, to expect international travel as a risk factor for COVID-19 infection and its consequent spread [12,13]. Having a history of VPD infection as a risk is a novel finding that warrants further research. The researchers hypothesize that the social and environmental influences that led to a prior VPD infection may have been the same conditions that caused COVID-19 transmission, especially among the densely populated shanty towns of Manila City with poor sanitation systems and ventilation. In the same vein, immunization for at least one VPD appears to be protective against COVID-19, which likewise requires further immunologic and socio-behavioral investigations. Furthermore, graduate-level education also lowers infection risk, suggesting a positive effect of higher education in forming informed decisions among individuals. Subsequently, contraception also lowers the risk of COVID-19 presumably due to the positive health outcomes inherent in the behavior that could have translated into COVID-19-safe practices. Furthermore, some studies suggest that higher or physiologic estrogen levels, especially during consumption of combined hormonal contraceptives (CHCs) confer a humoral immune-reactive response by inducing higher antibody levels [14,15].

CONCLUSION

Pregnancy is a significant risk factor for COVID-19 infection among women, as is being a white-collar worker, being infected by at least one VPD, and traveling outside the country during the pandemic. On the other hand, protective factors include graduate-level education, practicing contraception, and being immunized for at least one VPD.

Our findings are useful in providing baseline findings on the characteristics that exacerbate and relieve the susceptibility of unvaccinated Filipinas to COVID-19. This will inform the development of public health response and vaccination efforts with consideration to vulnerable populations, including pregnant women. Further investigations as to the clinical

manifestations, maternal and neonatal outcomes, and the possibility of vertical transmission of COVID-19 are recommended.

COMPETING INTERESTS

The authors declare no potential conflicts of interest regarding the research, authorship, and publication of this article.

AUTHOR CONTRIBUTIONS

EL-C is the principal investigator and first author of this study who gave instrumental contributions to the concept, research design and methodology including the implementation and management of this study. FMH, ESB, METV-U, MSFC, MUL and PJR-U assisted in specific components of the study. LCC-C, EIV, HJDC, LBHE, CUA, MLDA, CPCM, PVS, JBB, VDG, RBC, ARD, and ALR implemented the research methodology and provided practical insights and discussion which were considered in the study. ESB, JFF and ELC conducted statistical data analyses and interpretation. JFF and EL-C drafted the article and visualization, and provided contextual interpretations into the study findings. All have critically revised and approved the final version of the manuscript.

FUNDING

This study was made possible by grants from the Australian Awards and Alumni Engagement Program, Department of Science and Technology - Philippine Council for Health Research and Development (DOST-PCHRD), and the Philippine Obstetrical and Gynecological Society (POGS).

ACKNOWLEDGEMENTS

The authors would like to thank the following: Research Institute of Tropical Medicine—Dr Celia Carlos; Manila City Officials headed by former Mayor Francisco 'Isko Moreno' Domagoso; Office of the Mayor Honorable Honey Lacuna-Pangan, the Manila City Councilors headed by Councilor Joel Chua, and Manila City Health Department Staff—Dr Arnold Pangan, Dr Gina Pardilla, and Dr Rosalina R Tan and other public health staff. Our gratitude to the administrators, resident physicians and medical officers and staff of the project site hospitals including the research staff and all participants who contributed in this multicenter COVID19 and women study for the Philippines.

PATIENT CONSENT FOR PUBLICATION

Obtained.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request.

ETHICS APPROVAL

The study was approved by the DOH Single Joint Research Ethics Board (DOH-SJREB Protocol Code 2020-30) and the University of the Philippines Manila Research Ethics Board (UPMREB Code 2020-0320-01-SJREB).

REFERENCES

1. She J, Jiang J, Ye L, Hu L, Bai C, Song Y. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. *Clin. Transl. Med.* 2020;9(1). doi:10.1186/s40169-020-00271-z
2. Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. *BMJ*. Published online March 12, 2020:m1036. doi:10.1136/bmj.m1036
3. Connor J, Madhavan S, Mokashi M, et al. Health risks and outcomes that disproportionately affect women during the Covid-19 pandemic: A review. *Soc. Sci. Med*. 2020;266:113364. doi:10.1016/j.socscimed.2020.113364
4. Fortier N. COVID-19, gender inequality, and the responsibility of the state. *Int. J. Wellbeing*. 2020;10(3):77-93. doi:10.5502/ijw.v10i3.1305
5. Phoswa WN, Khaliq OP. Is pregnancy a risk factor of COVID-19? *Eur. J. Obstet. Gynecol. Reprod. Biol*. 2020;252:605-609. doi:10.1016/j.ejogrb.2020.06.058
6. Llamas-Clark EF, Singson RB, Heralde FM, et al. Risk factors of COVID-19 vertical transmission among pregnant and non-pregnant Filipinos in Metro Manila: a multicentre cohort study protocol. *BMJ Open*. 2022;12(4):e053389. doi:10.1136/bmjopen-2021-053389
7. Petersen MR, Deddens JA. A comparison of two methods for estimating prevalence ratios. *BMC Med. Res. Methodol*. 2008;8(1). doi:10.1186/1471-2288-8-9
8. Albert, JRG, Vizmanos JFV. Do men and women in the Philippines have equal economic opportunities?. *Philippine Institute for Development Studies Policy Notes*.

2017;2017(9). https://www.pids.gov.ph/publication/policy-notes/do-men-and-women-in-the-philippines-have-equal-economic-opportunities

9. World Economic Forum. *Global gender gap report 2022*. https://www3.weforum.org/docs/WEF_GGGR_2022.pdf. Published 2022. Accessed July 14, 2022.
10. Mielcarska K, Żelaźniewicz A, Pawłowski B. Risk taking propensity in pregnancy — Longitudinal study. Pers. Individ. Differ. 2017;110:7-11. doi:10.1016/j.paid.2017.01.012
11. Lyerly AD, Mitchell LM, Armstrong EM, et al. Risk and the Pregnant Body. *Hastings Center Report*. 2009;39(6):34-42. doi:10.1353/hcr.0.0211
12. Burns J, Movsisyan A, Stratil JM, et al. International travel-related control measures to contain the COVID-19 pandemic: a rapid review. *CDSR*. 2021;2021(3). doi:10.1002/14651858.cd013717.pub2
13. Klinger C, Burns J, Movsisyan A, et al. Unintended health and societal consequences of international travel measures during the COVID-19 pandemic: a scoping review. *J. of Travel Med*. 2021;28(7). doi:10.1093/jtm/taab123
14. The gendered impact of coronavirus disease (COVID-19): do estrogens play a role? The Eur. *J. Contracept. Reprod. Health Care*. Published 2020. Accessed October 24, 2022. https://www.tandfonline.com/doi/full/10.1080/13625187.2020.1766017
15. Kaushic C, Roth KL, Anipindi V, Xiu F. Increased prevalence of sexually transmitted viral infections in women: the role of female sex hormones in regulating susceptibility and immune responses. *J. Reprod. Immunol*. 2011;88(2):204-209. doi:10.1016/j.jri.2010.12.004

Reporting checklist for cohort study.

Based on the STROBE cohort guidelines.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary	2

		of what was done and what was found	
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	#4	Present key elements of study design early in the paper	4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	4
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	4
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4

Bias	#9	Describe any efforts to address potential sources of bias	4
Study size	#10	Explain how the study size was arrived at	4
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	4
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	4
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	4
Statistical methods	#12c	Explain how missing data were addressed	4
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	4
Statistical methods	#12e	Describe any sensitivity analyses	4
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and	5

		unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	5
Participants	#13c	Consider use of a flow diagram	5
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	7
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	5
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	5
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	6
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7
Main results	#16b	Report category boundaries when continuous variables were	7

		categorized	
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	7
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	8
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	8-10
Generalisability	#21	Discuss the generalisability (external validity) of the study results	8-10
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

BMJ Open

Factors Associated with Having COVID-19 Among Unvaccinated Pregnant and Non-Pregnant Women in Metro Manila, Philippines: A Multi-Center Longitudinal Cohort Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-070688.R1
Article Type:	Original research
Date Submitted by the Author:	08-Mar-2023
Complete List of Authors:	Llamas-Clark, Erlidia; University of the Philippines Manila, Heralde, Francisco M.; University of the Philippines Manila College of Medicine, Department of Molecular Biology and Biochemistry Lumandas, Mayan U.; Research Institute for Tropical Medicine, Department of Virology Cagayan, Maria Stephanie Fay; University of the Philippines Manila College of Medicine, Department of Pharmacology and Toxicology Villanueva-Uy, Maria Esterlita T.; University of the Philippines Manila, Institute of Child Health and Human Development, National Institutes of Health Chavez-Coloma, Leilani; Jose R Reyes Memorial Medical Center Valencia, Eleyneth; Jose R Reyes Memorial Medical Center Cabana, Charizze Anne; Jose R Reyes Memorial Medical Center Espinosa, Lea Bernadette; Jose R Reyes Memorial Medical Center Anzures, Cynthia; Dr Jose Fabella Memorial Hospital, Department of Obstetrics and Gynecology Andal, Maria Lu; Dr Jose Fabella Memorial Hospital Martin, Carolina Paula; Ospital ng Maynila Medical Center Suarez, Patricia Nevira; Ospital ng Maynila Medical Center Quanico, Celine; Ospital ng Maynila Medical Center Beltran, Julia; Ospital ng Maynila Medical Center de Guzman, Vanessa; Justice Jose Abad Santos General Hospital Capitulo, Ryan; Justice Jose Abad Santos General Hospital Dominguez, Arlene; Sta. Ana Hospital Recio, Abygail; Sta. Ana Hospital Feliciano, Jeremiah; University of the Philippines Manila College of Medicine Baja, Emmanuel; University of the Philippines Manila, Exposure Assessment, Epidemiology, and Risk Lab Institute of Clinical Epidemiology; University of the Philippines Manila, Department of Clinical Epidemiology Rosell-Ubial, Paulyn Jean; University of the Philippines Manila College of Public Health
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Public health, Infectious diseases, Epidemiology

Keywords:	COVID-19, EPIDEMIOLOGIC STUDIES, Public health < INFECTIOUS DISEASES, OBSTETRICS

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Factors Associated with Having COVID-19 Among Unvaccinated Pregnant and Non-Pregnant Women in Metro Manila, Philippines: A Multi-Center Longitudinal Cohort Study

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WORD COUNT: 2,357 words
ABSTRACT: 244 words
TABLE AND FIGURE: 1 Table, 1 Supplementary Table
REFERENCES: 27

ABSTRACT

Objective. To determine potential risk factors associated with having COVID-19 among unvaccinated pregnant and non-pregnant women.

Design. A multicenter prospective cohort study among eligible women in Metro Manila, Philippines, from 2020 to 2022.

Setting. Five national and local hospital research sites altogether recruited and screened 500 consenting eligible individuals.

Participants. Pregnant and non-pregnant participants meeting the eligibility criteria were admitted for an RT-PCR determination of SARS-CoV-2, pregnancy testing and ultrasound, and an interview with an administered questionnaire.

Exposures. Primary exposure was pregnancy; secondary exposures involve sociodemographic, lifestyle, and obstetric-gynecologic factors.

Outcome measure. Outcome being measured was COVID-19 status.

Results. The significant COVID-19 risk factors were: pregnancy (PR=1.184, 95CI[1.096,1.279]), having a white-collar job (PR=1.123, 95CI[1.02,1.235]), traveling abroad (PR=1.369, 95CI[1.083, 1.173]), and being infected by at least one vaccine-preventable disease (VPD) (PR=1.208, 95CI[1.113,1.310]). Protective factors included having graduate-level education (PR=0.787, 95CI[0.649,0.954]), immunization against a VPD (PR=0.795, 95CI[0.733,0.862]), and practicing contraception (PR=0.889, 95CI[0.824,0.960]).

Conclusion. This study is the first in the country to determine the risks influencing COVID-19 infection among unvaccinated pregnant and non-pregnant women. Pregnancy is a significant risk for COVID-19 among women in Metro Manila. Educational attainment and positive health behaviors seem to confer protection. Occupations and activities that increase the frequency of interactions, as well as prior history of communicable diseases may predispose women to COVID-19. Further studies are needed to elucidate the development of the disease in pregnant women, including the maternal and neonatal effects of COVID-19 via potential vertical mechanisms of transmission.

KEYWORDS COVID-19, Pregnancy, Prospective studies, Risk factors

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This article provides the first Philippine multi-center study in public hospitals in the National Capital Region to serve as a baseline for the determination of risk factors of

COVID-19 in women that incorporates in the analysis the pre-existing conditions and pressures experienced by Filipino women as a driving force behind COVID-19 risk.

- The study was conducted during the unpredictable height of the pandemic which may have introduced variability in the collection of exposed respondents, owing to the duration of the study which spanned six surges with three different prevailing variants, and pre-existing burdens of healthcare which may have caused consistently few enrollments.
- Further studies with an emphasis on the longitudinal nature of the disease throughout the gestation period to determine the differential progression of the disease in terms of gestational development may supplement the methodological approaches of the study.

INTRODUCTION

Background. The rapid transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) caused cases of Coronavirus Disease 2019 (COVID-19) to rise in many countries since it was first reported in Wuhan, China, in December 2019[1]. By the time the WHO declared it a pandemic, significant repercussions were already observed in worldwide social and economic life[2]. The multifaceted nature of this pandemic gives rise to concerns about identifying relevant risk factors, especially for the vulnerable and underrepresented groups. Men have higher mortality risks when infected, but women may have higher risks of worse health outcomes and less healthcare access due to pre-existing socioeconomic gaps exacerbated by the pandemic[3,4]. At par or greater risks are pregnant women and their unborn; both susceptible to infection due to their weakened immune system[5]. However, these findings are largely dominated by white/Caucasian populations resulting in the underrepresentation of other races and ethnic minorities[6]. Evidence of sex- and pregnancy-based differences in COVID-19 vulnerability indicate a need to determine the relevant socio-demographic, lifestyle, and obstetric-gynecologic risk factors, especially in the Philippine context.

Two years have passed since the pandemic started, with several variants emerging such as the Alpha, Beta, Delta, and Omicron, that resulted in several surges that took the lives of millions[7]. In the Philippines, the Delta variant dominated COVID-19 cases in 2021 while the Omicron variant dominated in 2022[8,9]. Despite the numerous variants circulating in the country, genomic sequencing of COVID-19 variants remains limited and not part of routine case reporting of the Department of Health[10]. Regardless of this limitation, there are limited studies that identified the common risks attributed to COVID-19 infection in the local

population, especially with unvaccinated pregnant women and their unborn. Furthermore, studies on the matter are yet to incorporate the intersectionality of pre-existing socioeconomic pressures on women which may compound the risk determination for the disease.

Objective. This study aimed to identify the risk factors associated with COVID-19 in unvaccinated pregnant and non-pregnant women in five hospitals in the City of Manila, Philippines. More specifically, this explored the sociodemographic and lifestyle factors that potentially predisposed women to COVID-19 infection.

METHODS

Study design and setting. This study is part of a comprehensive prospective multicenter cohort study protocol to determine the risk factors, clinical manifestations, progression, and maternal-neonatal outcomes of COVID-19 vertical transmission among pregnant and non-pregnant women in Metro Manila[11]. Specific details on the procedures can be found in the said protocol.

Target population and eligibility criteria. Women at least 18 years old regardless of pregnancy status who consulted among the five public hospital research sites under the Department of Health (DOH) or the Manila City Government, ranging from November 30, 2020, to March 31, 2022. Included are women who will consult for any medical or Ob-Gyn condition at the Departments of Internal Medicine, Ob-Gyn emergency room, labor, or delivery rooms without any uterine or adnexal lesions which would influence the course of the disease. Excluded are those who are less than 18 years old, who cannot or are not able to provide informed consent, who cannot commit to the length of time of the study, who will not deliver in any of the five hospital sites, or those with malignant or congenital reproductive tract abnormalities or infection as seen on ultrasound. Incidental findings were referred to appropriate subspecialty services. All study participants meeting the inclusion criteria were admitted to the study following a thorough briefing and with their written and continuing consent. Respondents were informed of their right to withdraw at any time without fear of compromising medical care and are encouraged to state their reasons for documentation.

Sample size calculation, handling of bias, and nonresponse. A two-sided 95% CI with an 80% power and a ratio of 1, and a least extreme OR to be detected at around 2.0, the computed sample size was 576. To accommodate a 10% nonresponse rate, the final sample size was 640, of which 320 were to be pregnant, and which were proportionately allocated to the hospital sites. The hospital sites were selected because they have the highest capacities of public healthcare institutions and were anticipated to admit individuals representing the target

population. Pregnant women were all invited regardless of age of gestation, provided they met the inclusion criteria, to comprehensively capture information about COVID-19 at all developmental stages of pregnancy. The duration of the study has exposed the population to at least three prevailing COVID-19 variants and their corresponding surges. However, as the Department of Health has not made genomic surveillance routine operation on identification of cases, and that during the height of the pandemic, such operations were beyond the capacity of the study, further stratification of respondents according to SARS-CoV-2 strain were not carried out. The researchers were cognizant of the differing virulence and progressions of these strains. However, more pressing was the need to determine the common denominator of predisposing risks and protective factors to the local population.

Sampling and data collection. The Research Institute of Tropical Medicine (RITM) processed the collected samples using reverse-transcription PCR for diagnosis and analyses of unconventional samples. Laboratory determination of SARS-CoV-2 and pregnancy status were carried out after collection of samples from the participants. They were also given a validated self-administered structured COVID-19 infection in adults questionnaire adapted from the New South Wales Department of Health[11]. The questionnaire will profile the socio-demographic, lifestyle, obstetric-gynecologic, medical history, and pregnancy-related characteristics of each participant.

Patient and public involvement. Patients and(or) the public were not involved in the design.

Outcome and exposures. Outcome measurement was COVID-19 status, which is confirmed from the RT-PCR test. Primary exposure was pregnancy status, determined from pregnancy test and(or) ultrasound. Secondary exposures were socio-demographic, lifestyle, and obstetric-gynecologic factors, as will be discussed in later sections.

Statistical analysis. The data is expressed as the summation of all respondents that exhibited either infected or uninfected outcomes throughout the entire study duration as the prevalence period. Quantitative variables (i.e. age, income) were categorized following the protocol for this study[11]. Descriptive statistics profiled the socio-demographic, lifestyle, and obstetric-gynecologic characteristics of pregnant and non-pregnant cohorts. The crude prevalence ratio (cPR) and the corresponding 95% confidence interval (95CI) were calculated after regressing a bivariable generalized linear model using a Poisson distribution with robust variance correction and a log link function between the characteristics as predictors, and COVID-19 status as the outcome. This model was the best option to minimize the overestimation of the true prevalence ratio among other alternatives[12]. The same regression

model was used to create adjusted prevalence ratios (aPRs) and to determine which among the characteristics are better risk indicators of COVID-19 susceptibility among the women in the study.

RESULTS

Five hundred respondents were included from the five hospitals throughout the study period. Of them, 267 (53.5%) were pregnant. Among pregnant women, the median age of gestation was 39 weeks [QD=1 week], with the most recent being 16 weeks and the oldest being 40 weeks and 5 days. After omitting missing observations in the variables of interest, only 352 (70.4%) cases remained for regression analyses and calculation of prevalence ratios. Most participants were lost to follow-up, particularly during delivery, when most of them preferred to deliver out of the hospital research sites. **Supplemental Table 1** shows the socio-demographic and lifestyle characteristics of the respondents. Most respondents tested negative for COVID-19 during the study, which is also consistent for pregnant (29.4%) and nonpregnant (24.0%) cohorts. More than half of all respondents reside in Manila City (n=269, 54.3%) and were admitted to DOH partner hospitals, which are among the highest-capacity tertiary institutions in the country. Furthermore, most respondents live in households, are Catholic, have never smoked nor drank alcoholic beverages, have not consumed illicit drugs, have an O blood type or have never left the country during the pandemic. Among pregnant respondents, the majority were younger, high school graduates, unemployed, single, making less than USD90.91 (PHP5,000) per month, not practicing contraception, have been infected or immunized against at least one vaccine-preventable disease (VPD), have been twice pregnant at most, or with up to two viable pregnancies.

Table 1 shows crude and adjusted prevalence ratios for potential risk factors of COVID-19. Significant risk factors among unvaccinated women include being pregnant, white-collar worker, having been infected with at least one VPD, and leaving the country during the pandemic. Protective factors are having graduate-level education, practicing contraception, and being immunized for at least one VPD. Blood type does not seem to be a significant predictor of COVID-19 among women, as well as gravidity, parity, smoking history, and alcohol use.

Table 1. Crude (cPR) and adjusted (aPR) prevalence ratios with 95% confidence intervals for associations between COVID-19 and covariates.

Characteristics	Total, n=352	COVID-19-negative, n=220	COVID-19-positive, n=132	cPR[95CI]	aPR[95CI]
OBSTETRIC-GYNECOLOGIC FACTORS					
Pregnancy status					
Non-pregnant	120 (34.1)	85 (24.1)	35 (9.9)	1.000	1.000
Pregnant	232 (65.9)	135 (38.4)	97 (27.6)	1.149 [1.063, 1.242]*	1.184[1.096, 1.279]*
Gravidity					
Two at most	225 (63.9)	142 (40.3)	83 (23.6)	1.000	1.000
At least 3	127 (36.1)	78 (22.2)	49 (13.9)	1.012 [0.938, 1.093]	1.075 [0.975, 1.185]
Parity					
Two at most	270 (76.7)	165 (46.9)	105 (29.8)	1.000	1.000
At least 3	82 (23.3)	55 (15.6)	27 (7.7)	0.957 [0.877, 1.044	0.934 [0.842, 1.036]
SOCIODEMOGRAPHIC FACTORS					
Age					
18-30	189 (53.7)	118 (33.5)	71 (20.2)	1.000	1.000
31-48	140 (39.8)	87 (24.7)	53 (15.1)	1.002 [0.928, 1.082]	0.968 [0.896, 1.045]
>49	23 (6.5)	15 (4.3)	8 (2.3)	0.980 [0.841, 1.142]	0.999 [0.857, 1.163]
Resides in Manila					
No	175 (51.0)	128 (36.4)	48 (13.6)	1.000	1.000
Yes	168 (48.9)	92 (26.1)	84 (23.9)	1.161 [1.080, 1.247]*	1.055 [0.990, 1.123]
Educational attainment					
Elementary	16 (4.5)	9 (2.6)	7 (1.9)	1.000	1.000
High school	171 (48.6)	110 (31.3)	61 (17.3)	0.944 [0.791, 1.127]	0.917 [0.807, 1.043]
College	143 (40.6)	83 (23.6)	60 (17.0)	0.988 [0.826, 1.180]	0.927 [0.809, 1.063]
Post-graduate	19 (5.4)	16 (4.5)	3 (0.9)	0.805 [0.646, 1.004]	0.787 [0.649, 0.954]*
Vocational**	3 (0.9)	2 (0.6)	1 (0.3)	0.928 [0.601, 1.432]	0.798 [0.62, 1.027]
Type of occupation*					
Unemployed/Unstable	243 (69.0)	160 (45.5)	83 (23.6)	1.000	1.000
Blue-collar job	25 (7.1)	14 (3.9)	11 (3.1)	1.073 [0.931, 1.237]	1.02 [0.889, 1.169]
White-collar job	84 (23.9)	46 (13.1)	38 (10.8)	1.083 [0.994, 1.179]	1.123 [1.02, 1.235]*
Marital status					
Single	207 (58.8)	133 (37.8)	74 (21.0)	1.000	1.000
Married	126 (35.8)	73 (20.7)	53 (15.1)	1.047 [0.969, 1.131]	1.057 [0.979, 1.142]
Cohabiting	15 (4.3)	12 (3.4)	12 (0.9)	0.884 [0.742, 1.053]	0.906 [0.759, 1.082]
Widowed	4 (1.1)	2 (0.6)	2 (0.6)	1.105 [0.794, 1.537]	0.990 [0.610, 1.606]
Religion					
Catholic	324 (92.0)	202 (57.4)	122 (34.7)	1.000	1.000
Protestant	5 (1.4)	2 (0.6)	3 (0.9)	1.162 [0.886, 1.524]	1.193 [0.913, 1.558]
Muslim	9 (2.6)	6 (1.7)	3 (0.9)	0.969 [0.766, 1.224]	1.056 [0.896, 1.244]
Others	14 (3.9)	10 (2.8)	4 (1.1)	0.934 [0.774, 1.127]	0.982 [0.841, 1.147]
Socioeconomic status					
Less than 90.91 USD (5,000 PHP)	198 (56.3)	136 (38.6)	62 (17.6)	1.000	1.000
90.91 USD to 363.62 USD (5,000 to 20,000 PHP)	101 (28.7)	54 (15.3)	47 (13.4)	1.116 [1.027, 1.212]*	1.060 [0.985, 1.141]
Above 363.62 USD (20,000 PHP)	53 (15.1)	30 (8.5)	23 (6.5)	1.092 [0.983, 1.213]	1.048 [0.935, 1.174]
LIFESTYLE FACTORS					

Using contraception					
No	282 (80.1)	166 (47.2)	116 (32.9)	1.000	1.000
Yes	70 (19.9)	54 (15.3)	16 (4.5)	0.870 [0.796, 0.952]*	0.889 [0.824, 0.960]*
Smoking history					
Never smoker	337 (95.7)	209 (59.4)	128 (36.4)	1.000	1.000
Ever smoker	15 (4.3)	11 (3.1)	4 (1.1)	0.918 [0.766, 1.100]	1.124 [0.955, 1.324]
Alcohol use					
Never alcoholic	301 (85.5)	185 (52.6)	116 (32.9)	1.000	1.000
Ever alcoholic	51 (14.5)	35 (9.9)	16 (4.5)	0.948 [0.854, 1.053]	1.002 [0.909, 1.104]
Immunized VPD > 1					
No	219 (62.2)	103 (29.3)	116 (32.9)	1.000	1.000
Yes	133 (37.8)	117 (33.2)	16 (4.4)	0.732 [0.686, 0.782]*	0.795 [0.733, 0.862]*
History VPD > 1					
No	238 (67.6)	181 (51.4)	57 (16.2)	1.000	1.000
Yes	114 (32.4)	39 (11.1)	75 (21.3)	1.338 [1.249, 1.432]*	1.208 [1.113, 1.310]*
Blood type					
A	82 (23.3)	58 (16.5)	24 (6.8)	1.000	1.000
B	68 (19.3)	42 (11.9)	26 (7.4)	1.069 [0.955, 1.197]	1.047 [0.958, 1.146]
O	181 (51.4)	106 (30.1)	75 (21.3)	1.094 [0.998, 1.199]	1.028 [0.958, 1.103]
AB	21 (5.9)	14 (3.9)	7 (1.9)	1.031 [0.871, 1.222]	0.967 [0.837, 1.117]
Travel history					
No	349 (99.1)	220 (62.5)	129 (36.6)	1.000	1.000
Yes	3 (0.9)	0 (0.0)	3 (0.9)	1.460 [1.407, 1.515]*	1.369 [1.083, 1.173]*

*Significant at 5% level of significance.

**Vocational education refers to the short-course for semi-skilled or skilled technical-vocational programs and certifications offered by the Technical Education and Skills Development Authority (TESDA).

***As per the International Labor Organization, Blue-collar workers are those whose jobs are mostly unskilled, semi-skilled or skilled manual work in various trades, equipment operation, and maintenance. White-collar workers are those whose jobs involve non-manual office, clerical, sales, semi-technical, professional, or supervisory activities[13].

DISCUSSION

This is the first multicenter study in the country to address relevant gaps in the literature by elucidating the systemic inequities and circumstances that contextualize the differential risks in sociodemographic, lifestyle, and obstetric-gynecologic factors between pregnant and non-pregnant women during the early pandemic when vaccines were still unavailable. Further research with consideration of the temporal interaction of the disease with pregnancy is suggested in view of the cumulative nature of this cohort study. This study found that risk factors for unvaccinated women include pregnancy, white-collar jobs, overseas travel, and VPD history. Protective factors, on the other hand, include graduate school education, immunization against VPD, and contraception practice.

Population profile in this present study reveal that pregnant women were younger, single, unemployed or hold unstable jobs, or make lesser monthly income. Before the pandemic, there were already fewer women in the Philippine labor force in 2015[14]. Filipinas

also had a higher incidence of vulnerable employment like self-employment and unpaid home duties, often associated with insufficient income and unsafe working conditions. Prevailing conservative gender roles also translate to women usually being housemakers, even as the Philippines ranks first in gender equality among Asian countries in 2022[4,15]. This cultural practice relegates women from the job market, causing insecure, lower-income employment with lesser bargaining power in most national economies[4]. Pregnancy compounds these intersecting inequities due to behavioral tendencies to take lesser risks even in decisions that may benefit their physical or financial wellbeing[16,17].

Multivariable analysis and risk determination found that COVID-19-positive women may more likely present as pregnant, white-collar workers, have had at least one VPD infection, or have traveled outside the country during the pandemic. Pregnancy, as a risk factor, supports other studies' findings which have variously been attributed to a more vulnerable immune constitution during gestation[5]. COVID-19-positive women had higher rates of ICU admission, intubation, ICU hospitalization, and preterm birth than their non-pregnant counterparts, according to cohort studies conducted in the United States[18]. Moreover, pregnant women with COVID-19 are more likely to be hospitalized and given moderate ventilation[19]. On the other hand, white-collar workers being at higher risk may be explained by the general nature of their occupations in healthcare, essential bureaucracy as part of a skeleton workforce, and similar jobs that result in increased interaction with suspect cases of the disease. Healthcare workers are at high risk of contracting COVID-19 due to contact with patients with the disease, with nurses and nonemergency wards personnel being the most commonly infected albeit mostly asymptomatic[20]. For this reason, it is also rational, as other studies found to varying significance, to expect international travel as a risk factor for COVID-19 infection and its consequent spread[21,22]. Returning travelers and pilgrims have been found to trigger COVID-19 outbreaks in various countries[23]. Having a history of VPD infection as a risk is a novel finding that warrants further research. The researchers hypothesize that the social and environmental influences that led to a prior VPD infection may have been the same conditions that caused COVID-19 transmission, especially among the densely populated shanty towns of Manila City with poor sanitation systems and ventilation.

In the same vein, immunization for at least one VPD appears to be protective against COVID-19, which likewise requires further immunologic and socio-behavioral investigations. Furthermore, graduate-level education also lowers infection risk, suggesting a positive effect of higher education in forming informed decisions among individuals. Higher educated people are more likely to follow protective measures against COVID-19 such as using disinfectants

and wearing masks in contrast to lower educated people, who are less likely to adapt social distancing, increase hand washing and disinfection, and avoid gatherings, meetings, and personal contact[24]. Subsequently, contraception also lowers the risk of COVID-19 presumably due to the positive health outcomes inherent in the behavior that could have translated into COVID-19-safe practices. People who practice safe sex through contraceptives consider COVID-19 exposure as part of the risky sexual behavior which they are conditioned to refrain from[25]. Furthermore, some studies suggest that higher or physiologic estrogen levels, especially during consumption of combined hormonal contraceptives (CHCs) confer a humoral immune-reactive response by inducing higher antibody levels[26,27].

While this study provides information about the risk and protective factors in women in the Philippines, the limitations of this study pose restrictions to the external validity of the results. First, since data collection was performed during the early pandemic, the population are yet to be vaccinated. Second, genomic surveillance is not routinely done by the Department of Health and therefore unavailable for analysis. Because of this, this study only focuses on identifying predisposing factors of COVID-19 infection regardless of variants. Second, the longitudinal progression of the disease associated with the stage of pregnancy was not addressed since the study is time-limited. Lastly, there is no baseline characterization of the local population yet as of conducting this study. Because of this, the external validity of this study only includes unvaccinated women in the Philippines exposed to dominant variants at the time of data collection.

CONCLUSION

Pregnancy is a significant risk factor for COVID-19 infection among women, as is being a white-collar worker, being infected by at least one VPD, and traveling outside the country during the pandemic. On the other hand, protective factors include graduate-level education, practicing contraception, and being immunized for at least one VPD.

Our findings are useful in providing baseline findings on the characteristics that exacerbate and relieve the susceptibility of unvaccinated Filipinas to COVID-19. This will inform the development of public health response and vaccination efforts with consideration to vulnerable populations, including pregnant women. Further investigations as to the clinical manifestations, maternal and neonatal outcomes, and the possibility of vertical transmission of COVID-19 are recommended.

COMPETING INTERESTS

The authors declare no potential conflicts of interest regarding the research, authorship, and publication of this article.

AUTHOR CONTRIBUTIONS

EFL-C is the principal investigator and first author of this study who gave instrumental contributions to the concept, research design and methodology including the implementation and management of this study. FMH, ESB, METV-U, MSFSC, MUL and PJBR-U assisted in specific components of the study. LCC-C, EIV, CASC, LBHE, CUA, MLDA, CPCM, PNVS, CDQ, JBB, VDdG, RBC, ARD, and ALR implemented the research methodology and provided practical insights and discussion which were considered in the study. ESB, JFF and EFLC conducted statistical data analyses and interpretation. JFF and EFL-C drafted the article and visualization and provided contextual interpretations into the study findings. All have critically revised and approved the final version of the manuscript.

FUNDING

This study was made possible by grants from the Australian Awards and Alumni Engagement Program (Award/Grant Number: N/A), Department of Science and Technology - Philippine Council for Health Research and Development (DOST-PCHRD) (Award/Grant Number: N/A), and the Philippine Obstetrical and Gynecological Society (POGS) (Award/Grant Number: N/A).

ACKNOWLEDGEMENTS

The authors would like to thank the following: Research Institute of Tropical Medicine—Dr Celia Carlos; Manila City Officials headed by former Mayor Francisco 'Isko Moreno' Domagoso; Office of the Mayor Honorable Honey Lacuna-Pangan, the Manila City Councilors headed by Councilor Joel Chua, and Manila City Health Department Staff—Dr Arnold Pangan, Dr Gina Pardilla, and Dr Rosalina R Tan and other public health staff. Our gratitude to the administrators, resident physicians, and medical officers in cooperating in the endeavor. Much appreciation to Ms Kyla Javier and the research staff, as well as the staff of the project site hospitals, and all participants who contributed in this multicenter COVID19 and women study for the Philippines.

PATIENT CONSENT FOR PUBLICATION

Obtained.

DATA AVAILABILITY STATEMENT

Data are available upon reasonable request.

ETHICS APPROVAL

The study was approved by the DOH Single Joint Research Ethics Board (DOH-SJREB Protocol Code 2020-30) and the University of the Philippines Manila Research Ethics Board (UPMREB Code 2020-0320-01-SJREB).

REFERENCES

1. She J, Jiang J, Ye L, Hu L, Bai C, Song Y. 2019 novel coronavirus of pneumonia in Wuhan, China: emerging attack and management strategies. *Clin. Transl. Med.* 2020;9(1). doi:10.1186/s40169-020-00271-z
2. Mahase E. Covid-19: WHO declares pandemic because of "alarming levels" of spread, severity, and inaction. *BMJ*. Published online March 12, 2020:m1036. doi:10.1136/bmj.m1036
3. Connor J, Madhavan S, Mokashi M, et al. Health risks and outcomes that disproportionately affect women during the Covid-19 pandemic: A review. *Soc. Sci. Med*. 2020;266:113364. doi:10.1016/j.socscimed.2020.113364
4. Fortier N. COVID-19, gender inequality, and the responsibility of the state. *Int. J. Wellbeing*. 2020;10(3):77-93. doi:10.5502/ijw.v10i3.1305
5. Phoswa WN, Khaliq OP. Is pregnancy a risk factor of COVID-19? *Eur. J. Obstet. Gynecol. Reprod. Biol*. 2020;252:605-609. doi:10.1016/j.ejogrb.2020.06.058
6. Moore JT, Ricaldi JN, Rose CE, et al. Disparities in incidence of COVID-19 among underrepresented racial/ethnic groups in counties identified as hotspots during June 5–18, 2020 — 22 states, February–June 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(33):1122-1126. doi:10.15585/mmwr.mm6933e1
7. Wacharapluesadee S, Hirunpatrawong P, Petcharat S, et al. Simultaneous detection of omicron and other SARS-CoV-2 variants by multiplex PCR MassARRAY technology. *Sci Rep*. 2023;13(1):2089. doi:10.1038/s41598-023-28715-9
8. Li Y-T, Polotan FG, Sotelo GI, et al. Lineage BA.2 dominated the omicron sars-COV-2 epidemic wave in the Philippines. *Virus Evol*. 2022;8(2):veac078. doi:10.1093/ve/veac078

9. Morales NJ, Dela Cruz E. Philippines reports record virus cases as Delta variant spreads. *Reuters*. August 23, 2021.
10. Tablizo FA, Lapid CM, Maralit BA, et al. Analysis of SARS-COV-2 genome sequences from the Philippines: Genetic surveillance and transmission dynamics. *medRxiv*. 2020. doi:10.1101/2020.08.22.20180034
11. Llamas-Clark EF, Singson RB, Heralde FM, et al. Risk factors of COVID-19 vertical transmission among pregnant and non-pregnant Filipinos in Metro Manila: a multicentre cohort study protocol. *BMJ Open*. 2022;12(4):e053389. doi:10.1136/bmjopen-2021-053389
12. Petersen MR, Deddens JA. A comparison of two methods for estimating prevalence ratios. *BMC Med. Res. Methodol*. 2008;8(1). doi:10.1186/1471-2288-8-9
13. Heron R & Unger L Glossary of Labour Administration and Related Terms. International Labour Organization. 1999. https://www.ilo.org/wcmsp5/groups/public/---ed_dialogue/---lab_admin/documents/publication/wcms_111331.pdf
14. Albert, JRG, Vizmanos JFV. Do men and women in the Philippines have equal economic opportunities? *Philippine Institute for Development Studies Policy Notes*. 2017;2017(9). https://www.pids.gov.ph/publication/policy-notes/do-men-and-women-in-the-philippines-have-equal-economic-opportunities
15. World Economic Forum. *Global gender gap report 2022*. https://www3.weforum.org/docs/WEF_GGGR_2022.pdf. Published 2022. Accessed July 14, 2022.
16. Mielcarska K, Żelaźniewicz A, Pawłowski B. Risk taking propensity in pregnancy — Longitudinal study. *Pers. Individ. Differ*. 2017;110:7-11. doi:10.1016/j.paid.2017.01.012
17. Lyerly AD, Mitchell LM, Armstrong EM, et al. Risk and the Pregnant Body. *Hastings Center Report*. 2009;39(6):34-42. doi:10.1353/hcr.0.0211
18. Chinn J, Sedighim S, Kirby KA, Hohmann S, Hameed AB, Jolley J, et al. Characteristics and outcomes of women with covid-19 giving birth at US academic centers during the COVID-19 pandemic. *JAMA Netw Open*. 2021;4(8):e2120456. doi:10.1001/jamanetworkopen.2021.20456
19. Qeadan F, Mensah NA, Tingey B, Stanford JB. The risk of clinical complications and death among pregnant women with covid-19 in the cerner covid-19 cohort: A retrospective analysis. BMC Pregnancy and Childbirth. 2021;21(1). doi: 10.1186/s12884-021-03772-y

20. Gómez-Ochoa SA, Franco OH, Rojas LZ, et al. Covid-19 in health-care workers: A living systematic review and meta-analysis of prevalence, risk factors, clinical characteristics, and outcomes. *Am J Epidemiol*. 2020;190(1):161-175. doi:10.1093/aje/kwaa191
21. Burns J, Movsisyan A, Stratil JM, et al. International travel-related control measures to contain the COVID-19 pandemic: a rapid review. *CDSR*. 2021;2021(3). doi:10.1002/14651858.cd013717.pub2
22. Klinger C, Burns J, Movsisyan A, et al. Unintended health and societal consequences of international travel measures during the COVID-19 pandemic: a scoping review. *J. of Travel Med*. 2021;28(7). doi:10.1093/jtm/taab123
23. Wilder-Smith A. COVID-19 in comparison with other emerging viral diseases: Risk of geographic spread via travel. *Trop Dis Travel Med Vaccines*. 2021;7(1). doi:10.1186/s40794-020-00129-9
24. Lüdecke D, von dem Knesebeck O. Protective Behavior in Course of the COVID-19 Outbreak—Survey Results From Germany. *Front Public Heal*. 2020;8. https://www.frontiersin.org/articles/10.3389/fpubh.2020.572561
25. Bowling J, Montanaro E, Gattuso J, Gioia D, Guerrero Ordonez S. "Everything feels risky now": Perceived "risky" sexual behavior during COVID-19 pandemic. *J Health Psychol*. 2021;27(6):1498-1506. doi:10.1177/13591053211004684
26. The gendered impact of coronavirus disease (COVID-19): do estrogens play a role? The Eur. *J. Contracept. Reprod. Health Care*. Published 2020. Accessed October 24, 2022. https://www.tandfonline.com/doi/full/10.1080/13625187.2020.1766017
27. Kaushic C, Roth KL, Anipindi V, Xiu F. Increased prevalence of sexually transmitted viral infections in women: the role of female sex hormones in regulating susceptibility and immune responses. *J. Reprod. Immunol*. 2011;88(2):204-209. doi:10.1016/j.jri.2010.12.004

Supplemental Table 1. Characteristics of respondents included in the study, stratified by pregnancy status.

Characteristics	Total, n=500	Non-pregnant, n=233	Pregnant, n=267
SOCIODEMOGRAPHIC FACTORS			
Admitting hospital			
DJFMH	166 (33.2)	78 (15.6)	88 (17.6)
JRRMMC	168 (33.6)	78 (15.6)	90 (18.0)
OMMC	58 (11.6)	26 (5.2)	32 (6.4)
SAH	59 (11.8)	29 (5.8)	30 (6.0)
JJASGH	49 (9.8)	22 (4.4)	27 (5.4)
Age			
18-30	246 (49.2)	77 (15.4)	169 (33.8)
31-48	202 (40.4)	105 (21.0)	97 (19.4)
>49	52 (10.4)	51 (10.2)	1 (0.2)
Resides in Manila			
No	226 (45.7)	89 (17.9)	137 (27.7)
Yes	269 (54.3)	139 (28.1)	130 (26.3)
Missing	5	5	0
Address type			
Household	494 (98.9)	228 (45.7)	266 (53.3)
Aged care facility	1 (0.2)	1 (0.2)	0 (0.0)
Other residence type	4 (0.8)	3 (0.6)	1 (0.2)
Missing	1	1	0
Educational attainment			
Elementary	33 (6.6)	18 (3.6)	15 (3.0)
High school	234 (46.8)	100 (20.0)	134 (26.8)
College	195 (39.0)	85 (17.0)	110 (22.0)
Graduate school	35 (7.0)	30 (6.0)	5 (1.0)
Vocational**	3 (0.6)	0 (0.0)	3 (0.6)
Type of occupation*			
Unemployed/Unstable	306 (64.3)	116 (24.4)	190 (39.9)
Blue-collar job	42 (8.8)	25 (5.3)	17 (3.6)
White-collar job	128 (26.9)	87 (18.3)	41 (8.6)
Missing	24	5	19
Marital status			
Single	278 (55.6)	103 (20.6)	175 (35.0)
Married	189 (37.8)	109 (21.8)	80 (16.0)
Cohabiting	27 (5.4)	15 (3.0)	12 (2.4)
Widowed	6 (1.2)	6 (1.2)	0 (0.0)
Religion			
Catholic	440 (89.8)	196 (40.0)	244 (49.8)
Protestant	11 (2.2)	8 (1.6)	3 (0.6)
Muslim	15 (3.1)	9 (1.8)	6 (1.2)
Others	24 (4.9)	13 (2.7)	11 (2.2)
Missing	10	7	3
Socioeconomic status			
Less than 90.91 USD (5,000 PHP)	250 (50.3)	96 (19.3)	154 (30.9)
90.91 USD to 363.62 USD (5,000 to 20,000 PHP)	159 (31.9)	71 (14.3)	88 (17.7)
Above 363.62 USD (20,000 PHP)	88 (17.7)	64 (12.9)	23 (4.8)

Missing	3	2	1
LIFESTYLE FACTORS			
Use of contraceptive			
No	338 (77.6)	168 (33.6)	220 (44.0)
Yes	112 (22.4)	65 (13.0)	47 (9.4)
Smoking history			
Never smoker	468 (93.8)	207 (41.5)	261 (52.3)
Ever smoker	31 (6.2)	25 (5.0)	6 (1.2)
Missing	1	1	0
Alcohol use			
Never alcoholic	412 (82.6)	170 (34.1)	242 (48.5)
Ever alcoholic	87 (17.4)	62 (12.4)	25 (5.0)
Missing	1	1	0
Illicit drug use			
No	496 (99.4)	230 (46.1)	266 (53.3)
Yes	3 (0.6)	2 (0.4)	1 (0.2)
Missing	1	1	0
Immunized from at least one VPD			
No	260 (64.4)	106 (26.2)	154 (38.1)
Yes	144 (35.6)	37 (9.2)	107 (26.5)
Missing	96	90	6
History of at least one VPD			
No	344 (69.8)	160 (32.5)	184 (37.3)
Yes	149 (30.2)	68 (13.8)	81 (16.4)
Missing	7	5	2
Blood type			
A	113 (24.1)	43 (9.2)	70 (14.9)
B	88 (18.8)	37 (7.9)	51 (10.9)
O	237 (50.5)	113 (24.1)	124 (26.4)
AB	31 (6.6)	15 (3.2)	16 (3.4)
Unrecalled	31	25	6
Travel history			
No	484 (96.8)	219 (43.8)	265 (53.0)
Yes	16 (3.2)	14 (2.8)	2 (0.4)
OBSTETRIC-GYNECOLOGIC FACTORS			
Gravidity			
Two at most	320 (64.1)	153 (30.7)	167 (33.5)
At least 3	179 (35.9)	79 (15.8)	100 (20.0)
Missing	1	1	0
Parity			
Two at most	376 (75.4)	161 (32.3)	215 (43.1)
At least 3	123 (24.6)	71 (14.2)	52 (10.4)
Missing	1	1	0
COVID-19 EXPOSURE			
Negative	267 (53.4)	120 (24.0)	147 (29.4)
Positive	233 (46.6)	113 (22.6)	120 (24.0)

*Unless otherwise specified, all summary statistics are expressed in counts and percentage of the total, *n (%)*.

**Vocational education refers to the short-course for semi-skilled or skilled technical-vocational programs and certifications offered by the Technical Education and Skills Development Authority (TESDA).

***As per the International Labor Organization, Blue-collar workers are those whose jobs are mostly unskilled, semi-skilled or skilled manual work in various trades, equipment operation, and maintenance. White-collar

workers are those whose jobs involve non-manual office, clerical, sales, semi-technical, professional, or supervisory activities[27].

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In your methods section, say that you used the STROBE cohort reporting guidelines, and cite them as:

von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies.

		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1

Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	#4	Present key elements of study design early in the paper	4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	4
Eligibility criteria	#6b	For matched studies, give matching criteria and number of exposed and unexposed	4
Variables	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one	5

		group. Give information separately for for exposed and unexposed groups if applicable.	
Bias	#9	Describe any efforts to address potential sources of bias	4
Study size	#10	Explain how the study size was arrived at	4
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	5
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	N/A
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, explain how loss to follow-up was addressed	5
Statistical methods	#12e	Describe any sensitivity analyses	N/A
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed	6

		eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	
Participants	#13b	Give reasons for non-participation at each stage	6
Participants	#13c	Consider use of a flow diagram	
N/A			
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	
6			
Descriptive data	#14c	Summarise follow-up time (eg, average and total amount)	
N/A			
Outcome data	#15	Report numbers of outcome events or summary measures over time. Give information separately for exposed and unexposed groups if applicable.	
7-9			

Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
Main results	#16b	Report category boundaries when continuous variables were categorized	7-9
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
N/A			
Other analyses	#17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	#18	Summarise key results with reference to study objectives	9
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	11
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	9-11
Generalisability	#21	Discuss the generalisability (external validity) of the study results	11
Other Information			

Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12