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Departments of ¹Obstetrics and Gynecology, ³Molecular Biology and Biochemistry, ¹³Clinical Epidemiology and ¹⁴Pharmacology and Toxicology, College of Medicine, University of the Philippines Manila, ¹⁰College of Medicine, University of the Philippines Manila, ²Institute of Child Health and Human Development, National Institutes of Health, University of the Philippines Manila, ⁵Department of Obstetrics and Gynecology, Jose R. Reyes Memorial Medical Center, ⁶Department of Obstetrics and Gynecology, Dr. Jose Fabella Memorial Hospital, ⁷Department of Internal Medicine, Ospital Ng Maynila Medical Center, ⁸Department of Obstetrics and Gynecology, Justice Jose Abad Santos General Hospital, ⁹Department of Obstetrics and Gynecology, Sta. Ana Hospital, ¹¹Department of Health Policy and Administration, College of Public Health, University of the Philippines Manila, ¹²Institute of Clinical Epidemiology, National Institutes of Health, University of the Philippines Manila, Manila, ⁴Department of Virology, Research Institute for Tropical Medicine, Muntinlupa, Philippines

Address for correspondence:

Dr. Erelidia Flores Llamas-Clark, Department of Obstetrics and Gynecology, College of Medicine, University of the Philippines Manila, Manila 1000, Philippines. Institute of Child Health and Human Development, National Institutes of Health, University of the Philippines Manila, Manila 1000, Philippines. E-mail: eflamasclark@up.edu.ph

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Risk determination of COVID-19 among unvaccinated nonpregnant women in Metro Manila, Philippines: A multicenter longitudinal cohort study

Erelidia Flores Llamas-Clark^{1,2}, Francisco M. Heralde III³, Mayan U. Lumandas⁴, Maria Esterlita T. Villanueva-Uy², Leilani C. Chavez-Coloma⁵, Eleyne I. Valencia⁵, Cynthia U. Anzures⁶, Maria Lu D. Andal⁶, Carolina Paula C. Martin⁷, Vanessa D. De Guzman⁸, Ryan B. Capitulo⁸, Arlene R. Dominguez⁹, Abygail L. Recio⁹, Jeremiah Francisco Feliciano¹⁰, Paulyn Jean Buenaflor Rosell-Ubial¹¹, Emmanuel S. Baja^{12,13}, Maria Stephanie Fay Samadan Cagayan¹⁴

Abstract:

BACKGROUND: While the COVID-19 pandemic's impact on the general population is well studied, less attention has been given to preexisting socioeconomic, lifestyle, and obstetric-gynecologic factors affecting baseline risks for unvaccinated nonpregnant women in early pandemic days in the Philippines.

MATERIALS AND METHODS: This prospective multicenter cohort study assessed COVID-19 status and used a validated questionnaire to identify potential disease risks. Generalized linear models with a Poisson distribution were employed to examine the relationship between determinants and COVID-19 status, adjusting for confounding factors.

RESULTS: Risk factors include Manila residency, Muslim faith, smoking history, at least one familial comorbidity, and local government hospital admission. Conversely, postgraduate education and contraceptive use seem protective.

CONCLUSION: Sociodemographic and lifestyle factors may be linked to COVID-19 infection in unvaccinated nonpregnant women. Further exploration of sociocultural pressures on women during the pandemic is warranted.

Keywords:

COVID-19 infection, lifestyle, occupations, risk factors, unvaccinated Filipino women

Introduction

Since its emergence in December 2019, the COVID-19 pandemic has reshaped socioeconomic dynamics in countries like the Philippines.^[1,2] Concerns about vulnerability to COVID-19 highlight gender and age disparities in infection rates and severity.^[3] While older males face higher risk, females contend with

existing social pressures exacerbating their vulnerabilities, including health-care access, testing underutilization, caregiving roles, and even pregnancy.^[3,4] Such issues are made apparent, especially in population-dense and socioeconomically heterogeneous urban areas such as Metro Manila, where the first confirmed case was located and continues to log the highest crude infection and death counts among the regions of the country.^[5,6]

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Understanding these factors within local contexts is crucial for tailored preventive measures in a country with unique socioeconomic dynamics. With limited local research, some resources could be misdirected, hindering mitigation of the impact of socioeconomic, lifestyle, and obstetric factors.

Objectives

This subgroup analysis is a part of the Philippines' first multicenter study investigating these influences on COVID-19 risks for unvaccinated nonpregnant women in the early pandemic days. This study aimed to determine the risk and protective factors associated with COVID-19 among unvaccinated nonpregnant women in five research hospitals in Manila City. In particular, the sociodemographic and lifestyle factors that predispose these unvaccinated nonpregnant women to the viral infection were explored.

Materials and Methods

Study design and setting

The methodological framework of this present subgroup analysis was based on a more extensive study to determine the risk factors of COVID-19 vertical transmission among pregnant and nonpregnant women in Metro Manila; more details can be found elsewhere.^[7,8]

Target population and eligibility criteria

The study was done from November 30, 2020, to February 28, 2022, and included two hospitals under the Department of Health (DOH) and three hospitals operated by the Manila City government. The study population comprised unvaccinated women, pregnant or nonpregnant, seeking medical attention in these hospitals. Excluded were minors under 18-year-old, individuals with reproductive tract issues visible on ultrasound that could impact disease progression, those unable to commit to the study's duration, and those not delivering at the specified hospitals. Incidental findings were appropriately addressed. Eligible participants joined the study after a thorough explanation and upon giving informed consent.

Sampling and data collection

After enrollment in the longitudinal cohort study, participants' COVID-19 status was confirmed through collected swab samples. In addition, the pregnancy status was validated using a pregnancy test and/or pelvic ultrasound. The Research Institute for Tropical Medicine (RITM) conducted sample processing, utilizing reverse transcription-polymerase chain reaction for COVID-19 diagnosis. Moreover, a validated questionnaire adapted from the New South Wales DOH was employed to elicit personal, sociodemographic, lifestyle, obstetric-gynecologic (OB-GYN) history, and

COVID-19-related data.^[7] Out of the initially screened and recruited unvaccinated women cohort ($n = 500$), a final subgroup of 233 nonpregnant women was included for analysis [Figure 1].^[7,9]

Assessment of outcomes and exposures

For this present subgroup analysis, the primary health outcome assessed was the presence or absence of SARS-CoV-2 and the resulting COVID-19 status. The exposures included sociodemographics, lifestyle, OB-GYN, and COVID-19-related factors.

Ethics declaration

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) and RITM Institutional Review provided separate and independent approval of the conduct of this research.

Statistical analysis

Data were aggregated from all respondents, displaying the specified outcome during the study. For nonpregnant women, descriptive statistics summarized sociodemographic, lifestyle, and Ob-Gyn factors by COVID-19 status. Employing a generalized linear model with Poisson distribution, robust variance correction, and log link function, crude prevalence ratios (cPRs) and corresponding 95% confidence intervals were calculated. These models used sociodemographic, lifestyle, and obstetric-gynecologic factors as exposures and COVID-19 status as the outcome. The same generalized linear model was used to determine the adjusted prevalence ratios (aPRs) using the factors in the crude analysis as predictors *a priori*, shedding light on the simultaneous impact of the various factors on COVID-19 susceptibility risk.

Results

Two hundred and thirty-three unvaccinated nonpregnant women were included from the five hospitals throughout the study period. Of them, 120 (51.5%) were COVID-19 positive. All cases were used for bivariable analyses to elicit cPRs and save for variables with missing observations, as shown in Table 1. However, only 111 (47.6%) cases remained for multiple regression models to elicit aPRs after the list-wise omission of missing observations in the included variables of interest. Table 1 shows the women's sociodemographic, lifestyle, and Ob-Gyn characteristics, stratified by their COVID-19 status.

Generally, all factors' proportions were nearly similar for both COVID-19-positive and COVID-19-negative cohorts. The majority of all respondents were admitted to DOH-attached hospitals, which are among the

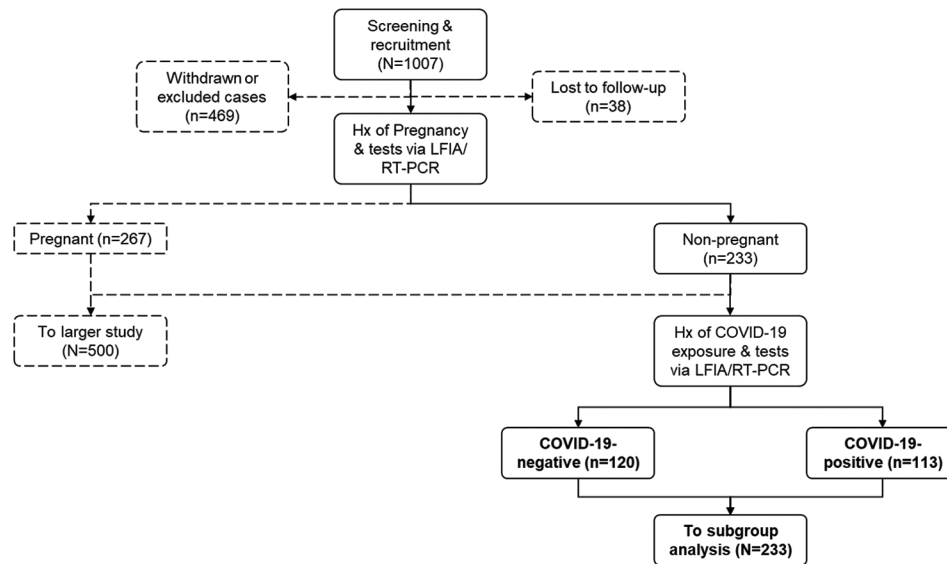


Figure 1: Participant recruitment, screening, selection, and allocation for subgroup analysis. Solid arrows show the flow for this study, while broken lines show the flow for the more extensive study.^[7,9] Hx: History of, LFIA: Lateral flow immunoassay; RT-PCR: Reverse transcription-polymerase chain reaction, N: total sample size, n: subgroup size

health-care institutions with the highest obstetrical and gynecological service capacity in the country. Among other characteristics common to both groups were being relatively middle-aged, with high school- or college-level education, being married, Catholic, neither a smoker nor an alcoholic drinker, having no personal nor familial comorbidity, and having not traveled outside the country during the pandemic. Among the respondents, those who do not use contraception were twice as many compared to those who use them. Furthermore, thrice as many respondents were immunized against at least one vaccine-preventable disease (VPD) or had been infected with at least one VPD compared to those who had not experienced either. Most of the respondents who are COVID-19 positive were Manila City residents, white-collar workers, and were earning USD 88.43 (Php 5000) per month.

Table 2 shows the crude and aPRs of the sociodemographic, lifestyle, and obstetric-gynecologic factors of interest as they relate to the risk of COVID-19 infection. Significant adjusted risks for developing the disease among women include residing in Manila City, being Muslim, being a current or former smoker, having familial history of comorbidities, and admission to Ospital ng Maynila Medical Center (OMMC) and Santa Ana Hospital (SAH). In contrast, significant adjusted protective factors include having postgraduate education and the use of contraception.

Discussion

There is already a growing body of evidence showing an increased risk of negative health outcomes in terms of access to health care, reproductive and

obstetric-gynecologic medical intervention, and various other workplace and home conditions that are uniquely exacerbated among women during the pandemic.^[4] This prospective multicenter cohort study in the Philippines contributes to the baseline determination of factors and conditions that may increase the risks of unvaccinated nonpregnant women contracting COVID-19 with consideration of the local context, including the significance of long-term mitigation for future public health emergencies in the country.

The nonpregnant respondent is from lower- to middle-income strata

We found that the majority of the respondents were between 31 and 48 years of age, living in a household, had high school- or college-level education, married, unemployed or have white-collar work, Catholic, making less than USD 88.43 (Php 5,000) or more than USD 353.73 (Php 20,001) per month, do not use contraception, neither a smoker nor alcoholic drinker, with no personal or familial comorbidities. Most had been immunized from, or infected by, at least one VPD. This group of characteristics is consistent with the socioeconomic and lifestyle characteristics of women in the lower- to middle-income groups in the country.^[10]

Historically, females have been closing the gender gap in education completion. Since 2016, girls have consistently completed basic education at higher rates than men across the socioeconomic strata, such that in 2019, 19.76% of women have finished college versus 15.86% of men.^[7] However, higher education does not necessarily translate to better economic and employment opportunities. In 2019, only 49% of all

Table 1: Characteristics of COVID-19-negative and COVID-19-positive women and their associations

Characteristics	Total (n=233)	COVID-19 negative (n=120)	COVID-19 positive (n=113)
Sociodemographic factors			
Age			
18–30	77 (33.0)	43 (18.5)	34 (14.6)
31–48	105 (45.1)	55 (23.6)	50 (21.5)
>49	51 (21.9)	22 (9.4)	29 (12.4)
Resides in Manila			
No	89 (39.0)	69 (30.3)	20 (8.8)
Yes	139 (60.9)	51 (22.4)	88 (38.6)
Missing	5	0	5
Educational attainment			
Elementary	18 (7.7)	9 (3.9)	9 (3.9)
High school	100 (42.9)	54 (23.2)	46 (19.7)
College	85 (36.5)	33 (14.2)	52 (22.3)
Postgraduate	30 (12.9)	24 (10.3)	6 (2.6)
Type of occupation			
Unemployed/unstable	116 (50.9)	77 (33.8)	39 (17.1)
Blue-collar job	25 (10.9)	8 (3.5)	17 (7.5)
White-collar job	87 (38.2)	34 (14.9)	53 (23.2)
Missing	5	1	4
Marital status			
Single	103 (44.2)	61 (26.2)	42 (18.0)
Married	109 (46.8)	52 (22.3)	57 (24.5)
Cohabiting	15 (6.4)	5 (2.1)	10 (4.3)
Widowed	6 (2.6)	2 (0.9)	4 (1.7)
Religion			
Catholic	196 (86.7)	109 (48.2)	87 (38.5)
Protestant	8 (3.5)	1 (0.4)	7 (3.1)
Muslim	9 (3.9)	4 (1.8)	5 (2.2)
Others	13 (5.8)	6 (2.7)	7 (3.1)
Missing	7	0	7
Socioeconomic status (USD)			
<88.43	96 (41.6)	66 (28.6)	30 (12.9)
88.43–353.72	71 (30.7)	25 (10.8)	46 (19.9)
353.72 and above	64 (27.7)	27 (11.7)	37 (16.0)
Missing	2	2	0
Lifestyle factors			
Use of contraceptive			
No	168 (72.1)	86 (36.9)	82 (35.2)
Yes	65 (27.9)	34 (14.6)	31 (13.3)
Smoking history			
Never	207 (89.2)	109 (46.9)	98 (42.2)
Current or former	25 (10.8)	10 (4.3)	15 (6.5)
Missing	1	1	0
Alcohol use			
Never	170 (73.3)	93 (40.1)	77 (33.2)
Current or former	62 (26.7)	26 (11.2)	36 (15.5)
Missing	1	1	0
Having at least one comorbidity			
No	141 (60.5)	78 (33.5)	63 (27.0)
Yes	92 (39.5)	42 (18.0)	50 (21.5)
Family history of at least one comorbidity			
No	123 (60.3)	68 (33.3)	55 (26.9)
Yes	81 (39.7)	49 (24.0)	32 (15.7)
Missing	29	3	26

Contd...

Table 1: Contd...

Characteristics	Total (n=233)*	COVID-19 negative (n=120)	COVID-19 positive (n=113)
Immunized from at least one VPD			
No	106 (74.1)	58 (40.6)	48 (33.6)
Yes	37 (25.9)	29 (20.3)	8 (5.6)
Unrecalled	90	33	57
History of at least one VPD			
No	160 (70.2)	84 (36.8)	76 (33.3)
Yes	68 (29.8)	31 (13.6)	37 (16.2)
Missing	5	5	0
Travel history			
No	219 (93.9)	119 (51.1)	100 (42.9)
Yes	14 (6.0)	1 (0.4)	13 (5.6)
Obstetric-gynecologic factors			
Admitting hospital			
Dr. Jose Fabella Memorial Hospital (DOH)	78 (33.5)	39 (16.7)	39 (16.7)
Jose R. Reyes Memorial Medical Center (DOH)	78 (33.5)	44 (18.9)	34 (14.6)
Hospital ng Maynila Medical Center (LGU)	26 (11.2)	14 (6.0)	12 (5.2)
Sta. Ana Hospital (LGU)	29 (12.4)	12 (5.2)	17 (7.3)
Justice Jose Abad Santos General Hospital (LGU)	22 (9.4)	11 (4.7)	11 (4.7)
Blood type			
A	43 (20.7)	25 (12.0)	18 (8.7)
B	37 (17.8)	26 (12.5)	11 (5.3)
O	113 (54.3)	60 (28.8)	53 (25.5)
AB	15 (7.2)	6 (2.8)	9 (4.3)
Unrecalled	25	3	22
Gravidity			
Two at most	153 (65.9)	83 (35.8)	70 (30.2)
At least 3	79 (34.1)	36 (15.5)	43 (18.5)
Missing	1	1	0
Parity			
Two at most	161 (69.4)	88 (37.9)	73 (31.5)
At least 3	71 (30.6)	31 (13.4)	40 (17.2)
Missing	1	1	0

*Unless otherwise specified, all summary statistics are expressed in counts and percentages of the total, *n* (%). VPD: Vaccine-preventable disease, DOH: Department of Health, LGU: Manila City local government unit

eligible women are in the labor force (where the East Asia Pacific general average was 59%), 27% lagging behind men.^[11] Furthermore, the relatively higher frequency of respondents reporting either unemployment or having white-collar occupations reflects the skills disparity, wherein women are unemployed fulfilling family carer obligations, underemployed or in low-skill positions due to economic constraints, or in high occupations due to advanced education.^[11,12] This disparity consequently causes attracting higher salaries for women than men in highly skilled occupations but substantially lower income for women in low-skill jobs.

There is a perception that the Philippines is a very conservative country, with the majority of women being Catholics, following dogmatic teachings of marital sacrament, aversion to contraception, and vices such as smoking or alcohol. However, in the 2017 National Demographic Health Survey, it was found that three in five women are married or cohabiting, 40% of women practice a modern method of contraception, <1 in 20

women smoke a tobacco product, and around 74% do not consume alcoholic beverages.^[13] This information of sociobehavioral responses at the macro level may not reflect the local community context. This view can be an oversimplification without consideration of other factors, such as the fact that 83% of Filipinas seeking contraception have not sought the consultation of a social worker nor health professional, and more idle time, and intersections of education and employment factors increase the propensity of vices among women.^[13,14] The reasonable effectiveness of government social welfare services such as routine immunization against VPDs and the limited reach of contraceptive availability in the local health centers reflect upon the distributions observed in this study.^[15,16] Consequently, women of nuclear and extended family structures with numerous traditional responsibilities are commonly observed in lower- to middle-income families. The opportunities for vices and sedentary lifestyles that lead to comorbidities are generally lower in women than they are in men.^[4,17,18]

Table 2: Crude and adjusted prevalence ratios with 95% confidence intervals for associations between sociodemographics, COVID-19, and cofactors

Characteristics	95% CI	
	cPR	aPR
Sociodemographic factors		
Age		
18–30	1.000	1.000
31–48	1.024 (0.926–1.132)	0.845 (0.781–1.019)
>49	1.088 (0.969–1.222)	0.892 (0.813–1.107)
Resides in Manila		
No	1.000	1.000
Yes	1.333 (1.223–1.453)*	1.119 (1.011–1.239)*
Educational attainment		
Elementary	1.000	1.000
High school	0.973 (0.823–1.151)	0.994 (0.781–1.266)
College	1.075 (0.909–1.270)	0.965 (0.738–1.263)
Postgraduate	0.800 (0.658–0.972)*	0.672 (0.462–0.975)*
Type of occupation		
Unemployed/unstable	1.000	1.000
Blue-collar job	1.257 (1.108–1.427)*	0.968 (0.792–1.182)
White-collar job	1.204 (1.100–1.318)*	1.056 (0.847–1.316)
Marital status		
Single	1.000	1.000
Married	1.082 (0.987–1.185)	0.928 (0.825–1.045)
Cohabiting	1.184 (1.011–1.387)*	0.819 (0.647–1.036)
Widowed	1.184 (0.935–1.499)	1.004 (0.748–1.349)
Religion		
Catholic	1.000	1.000
Protestant	1.299 (1.139–1.481)*	1.320 (0.862–2.023)
Muslim	1.077 (0.870–1.335)	1.240 (1.028–1.495)*
Others	1.066 (0.888–1.279)	1.033 (0.877–1.216)
Socioeconomic status (USD)		
<88.43	1.000	1.000
88.45–353.72	1.256 (1.139–1.384)*	1.131 (0.965–1.326)
353.73 and above	1.202 (1.083–1.335)*	1.199 (0.924–1.555)
Lifestyle factors		
Use of contraceptive		
No	1.000	1.000
Yes	0.992 (0.901–1.093)	0.873 (0.782–0.975)*
Smoking history		
Never	1.000	1.000
Current or former	1.086 (0.955–1.235)	1.302 (1.097–1.545)*
Alcohol use		
Never	1.000	1.000
Current or former	1.088 (0.991–1.194)	1.011 (0.893–1.143)
Having at least one comorbidity		
No	1.000	1.000
Yes	1.067 (0.978–1.164)	1.086 (0.956–1.234)
Family history of at least one comorbidity		
No	1.000	1.000
Yes	0.964 (0.874–1.063)	1.136 (1.010–1.278)*
Immunized from at least one VPD		
No	1.000	1.000
Yes	0.837 (0.737–0.951)*	1.014 (0.884–1.162)
History of at least one VPD		
No	1.000	1.000
Yes	1.047 (0.954–1.149)	1.038 (0.907–1.187)

Contd...

Table 2: Contd...

Characteristics	95% CI	
	cPR	aPR
Travel history		
No	1.000	1.000
Yes	1.324 (1.218–1.439)*	1.721 (1.151–2.574)
Obstetric-gynecologic factors		
Admitting hospital		
Dr. Jose Fabella Memorial Hospital (DOH)	1.000	1.000
Jose R. Reyes Memorial Medical Center (DOH)	0.957 (0.861–1.065)	1.154 (0.970–1.372)
Hospital ng Maynila Medical Center (LGU)	0.974 (0.838–1.133)	1.644 (1.366–1.979)*
Sta. Ana Hospital (LGU)	1.057 (0.924–1.210)	1.552 (1.133–2.126)*
Justice Jose Abad Santos General Hospital (LGU)	1.000 (0.854–1.171)	1.172 (0.989–1.389)
Blood type		
A	1.000	1.000
B	0.914 (0.784–1.067)	0.898 (0.770–1.046)
O	1.036 (0.917–1.169)	1.095 (0.924–1.296)
AB	1.128 (0.936–1.359)	0.972 (0.782–1.207)
Gravidity		
Two at most	1.000	1.000
At least 3	1.060 (0.969–1.159)	0.947 (0.709–1.264)
Parity		
Two at most	1.000	1.000
At least 3	1.076 (0.982–1.178)	1.130 (0.836–1.529)

*Significant at 5% level of significance. CI: Confidence interval, cPR: Crude prevalence ratio, aPR: Adjusted prevalence ratio, VPD: Vaccine-preventable disease, DOH: Department of Health, LGU: Manila City local government unit

Associations with COVID-19 among respondents show a sociocultural gradient

Residing in Manila City, being a Muslim, having smoked or with a familial history of at least one comorbidity, and being admitted to LGU hospitals appeared to pose significant risks among nonpregnant unvaccinated respondents. Residing in Manila coincides with the city being a consistent hotspot for relatively shorter outbreaks compared to other international cities, despite more sophisticated lockdown and test-trace-vaccinate strategies.^[6,19,20] Studies to determine sex-disaggregated differences on risks and protective factors among Manila City residents may provide further insights on this finding. Belonging to particular faiths is a novel finding which could not be simply explained by individual or collective religious activities, as everyone is equally affected by movement restriction and quarantine policies.^[21] For instance, crude risks show Protestantism posing significant risks, which might also be due to the heterogeneity of people of Protestant faith living in Metro Manila. Meanwhile, adjusted estimates show Muslims to be at significant risk, which could be compounded by the fact that Muslim communities have historically lived close together as a community in Manila City, in such a manner that an initial outbreak could easily lead to substantial infected individuals despite an abundance of caution.^[21,22] While both findings could be related to religion being a function of social cohesion and support, this complexity could also be explored further with intersectionality studies. Meanwhile, smoking is

an established risk for severe COVID-19, with one of the potential underlying pathophysiologies being the contributing pro-inflammatory effect of smoking on pulmonary tissues.^[23] A family history of at least one comorbidity such as obstructive pulmonary diseases, cardiovascular conditions, obesity, and hypertension may also increase susceptibility to the virus.^[24] Further characterization through sex-disaggregated analyses is recommended to elucidate specific hereditary risks among women. Finally, admission to two local government hospitals apparently increases the risk for infection after adjusting with other factors. We hypothesize this finding to be a proxy for complex interacting latent factors such as the spatial distribution of infections around the vicinity of research sites, the proportionality of enrolled COVID-19-positive respondents in each hospital, and the temporal nature of infectivity during the study. Furthermore, the designations of OMMC and SAH as COVID-19 and tertiary referral centers, respectively, increased the propensity of admissions of infected individuals in the said hospitals.^[24]

In contrast, postgraduate degree holders and those practicing contraception appear to be protected from viral infection. We posit that such factors reflect a positive reinforcement of protective and health-seeking behaviors among those with some level of formal education, ultimately creating a good correlation with comprehension and conformity with minimum public health standards in the country.^[19] However, this finding

may also be influenced by the nature of work and monthly income, despite both being nonsignificant risk factors after adjustment. Notwithstanding the level of education, crude estimates also suggest that monthly earners of at least USD 88.43 (Php 5000) were more exposed to viral infection simply due to the nature of the distribution of incomes. We expected an increase in lay-off rates and loss of income sources, as shown by the near-proportional distribution of cases across the three income tertiles, wherein at least 46% of the samples have incomes less than USD 88.43. However, for those still with work, a daily minimum wage of USD 9.49 (Php 537) translates to an average of USD 189.95 (Php 10,740), which falls well within the middle-income group.^[25] Such jobs, which are deemed low paying, have higher propensities of face-to-face contact.^[25,26] The same can be said for jobs with salary grades falling within the highest income group, which belong to higher salary grades and are commonly attributed to jobs with advanced skills such as health care.^[27]

Limitations and future prospects

While this study identified risk and protective factors in unvaccinated women respondents, several limitations warrant consideration. First, despite our efforts to achieve representative samples and mitigate biases, the limited ability to randomly select cases and the relatively small sample size ($n = 233$) may limit generalizability, particularly across different races or ethnicities. Second, the dynamic nature of the pandemic posed challenges in terms of our financial and workforce capacities, which constrained data collection, analysis, and depth of our study. Third, due to a predefined study duration, we encountered restrictions in investigating the longitudinal disease progression among our respondents. In addition, the absence of routine genomic surveillance by the DOH limited our ability to isolate the intra- and inter-variant effects of the virus, which could have provided valuable insights into disease dynamics. In light of these limitations, it is recommended that further research on the longitudinal progression of COVID-19 in women, especially within the context of ongoing mass vaccination efforts, be continued to address these challenges and enhance the comprehensiveness and applicability of our findings.

Conclusion and Recommendations

Residing in Manila City, religious affiliation, a history of smoking and at least one familial comorbidity, and admission to local government hospitals increase susceptibility to COVID-19 infection. Conversely, postgraduate education and contraceptive use offer viral infection protection.

The baseline data from this study will guide ongoing research on health-care access and social welfare services.

It also offers policy insights for safe access to obstetric and gynecological care during public health emergencies. Further exploration of how institutional and personal intersectional pressures affect women's risks is advised.

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Authorship contributions

Erlidia F. Llamas-Clark, MD, PhD – Involved in conceptualization, methodology, investigation, resource acquisition and distribution, supervision of the project, project administration, data curation and validation and funding acquisition and management, writing of the original draft, review, and editing.

Francisco M. Heralde III, MSc, PhD – Involved in methodology development and validation, investigation, project administration, data curation, review and editing of the manuscript.

Mayan U. Lumandas, MD, MSc – Involved in methodology development and validation, investigation, project administration, formal analysis, review and editing of the manuscript.

Maria Esterlita T. Villanueva-Uy, MD, MPH – Involved in methodology, investigation, project administration, and review and editing of the manuscript.

Leilani C. Chavez-Coloma, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Eleyne I. Valencia, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Cynthia U. Anzures, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Maria Lu D. Andal, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Carolina Paula C. Martin, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Vanessa D. de Guzman, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Ryan B. Capitulo, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Arlene R. Dominguez, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Abygail L. Recio, MD – Involved in investigation, project administration, and review and editing of the manuscript.

Jeremiah F. Feliciano, BSc – Involved in software management, validation, statistical analysis, data curation, writing of the original draft, review and editing of the manuscript.

Emmanuel S. Baja, MSc, ScD – Involved in methodology, investigation, statistical analysis, data curation and validation, project administration, review and editing of the manuscript.

Ma. Stephanie Fay S. Cagayan, MD, PhD – Involved in methodology, investigation, validation, project administration, review and editing of the manuscript.

All have critically appraised and approved the final version of the manuscript. All authors attest to the honesty and integrity of the content of this manuscript.

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Conflicts of interest

There are no conflicts of interest.

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