

Sex disparity in COVID-19 infection in the Philippines: a biocultural study²³

Disparidad de sexo en la infección por COVID-19 en Filipinas: un estudio biocultural

Disparidade sexual na infecção por COVID-19 nas Filipinas: um estudo biocultural

Disparité entre les sexes dans l'infection au COVID-19 aux Philippines : une étude bioculturelle

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Abstract

Biological sex and socio-cultural factors have been interrelated in epidemiological studies and clinical care. This study aimed to assess sex differences in susceptibility to COVID-19 in the Philippines. COVID-19 numbers of cases until February 28, 2021, were collected from the Philippines' Department of Health (DOH). The student's t-test was used to analyze the data per administrative region and age group. News articles were collected from reputable

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media outlets in the Philippines. Biological and socio-cultural differences were considered. A significant sex difference ($p \leq 0.05$) was observed in the age groups of 30-39, 40-49, and 50-59 years old, which indicates that males in the said age clusters in the Philippines are more susceptible to COVID-19. Sex-specific mechanisms that may disproportionately affect either sex were associated with differences in immune responses, hormones, and underlying medical conditions. Furthermore, gendered lifestyles in the Philippines that involve social gatherings such as cockfighting, gambling, and boxing are dominated by the male population and could directly transmit the disease. Sex disparities linked to the susceptibility of COVID-19 emphasize the importance of gender-based research for risk-reduction strategies and effective public health measures in the Philippines.

Keywords: Sex disparity; COVID-19; Philippines, Biocultural Anthropology; Human Biology.

Resumen

Los factores biológicos sexuales y socioculturales se han interrelacionado en los estudios epidemiológicos y la atención clínica. Este estudio tuvo como objetivo evaluar las diferencias sexuales en la susceptibilidad al COVID-19 en Filipinas. Los números de casos de COVID-19 hasta el 28 de febrero de 2021 se recopilaron del Departamento de Salud de Filipinas (DOH). Se utilizó la prueba t de Student para analizar los datos por región administrativa y grupo de edad. Se recopilaron artículos de noticias de medios de comunicación de renombre en Filipinas. Se consideraron diferencias biológicas y socioculturales, observándose una diferencia de sexo significativa ($p \leq 0.05$) en los grupos de edad de 30-39, 40-49 y 50-59 años, lo que indica que los varones en dichos grupos de edad en Filipinas son más susceptibles al COVID-19. Los mecanismos específicos del sexo que pueden afectar de manera desproporcionada a cualquiera de los sexos se asociaron con diferencias en las respuestas inmunitarias, las hormonas y las afecciones médicas subyacentes. Además, los estilos de vida de género en Filipinas que involucran reuniones sociales como peleas de gallos, juegos de azar y boxeo están dominados por la población masculina y podrían transmitir directamente la enfermedad. Las disparidades de sexo vinculadas a la

susceptibilidad al COVID-19 enfatizan la importancia de la investigación basada en el género para las estrategias de reducción de riesgos y las medidas efectivas de salud pública en Filipinas.

Palabra clave: Disparidad de sexo; COVID-19; Filipinas, Antropología Biocultural; Biología humana.

Résumé

Le sexe biologique et les facteurs socioculturels ont été mis en relation dans les études épidémiologiques et les soins cliniques. Cette étude visait à évaluer les différences entre les sexes dans la susceptibilité au COVID-19 aux Philippines. Les chiffres des cas de COVID-19 jusqu'au 28 février 2021 ont été recueillis auprès du ministère de la Santé des Philippines (DOH). Le test t de l'étudiant a été utilisé pour analyser les données par région administrative et par groupe d'âge. Les articles de presse ont été recueillis auprès d'organes de presse réputés aux Philippines. Les différences biologiques et socioculturelles ont été prises en compte. Une différence significative entre les sexes ($p \leq 0,05$) a été observée dans les groupes d'âge de 30-39 ans, 40-49 ans et 50-59 ans, ce qui indique que les hommes dans lesdits groupes d'âge aux Philippines sont plus sensibles au COVID-19. Les mécanismes spécifiques au sexe qui peuvent affecter de manière disproportionnée l'un ou l'autre sexe ont été associés à des différences dans les réponses immunitaires, les hormones et les conditions médicales sous-jacentes. En outre, aux Philippines, les modes de vie sexués qui impliquent des rassemblements sociaux tels que les combats de coqs, les jeux d'argent et la boxe sont dominés par la population masculine et pourraient transmettre directement la maladie. Les disparités entre les sexes liées à la susceptibilité du COVID-19 soulignent l'importance de la recherche sexospécifique pour les stratégies de réduction des risques et les mesures de santé publique efficaces aux Philippines.

Mots clés: Disparité sexuelle ; COVID-19 ; Philippines, Anthropologie bioculturelle ; Biologie humaine.

Resumo

O sexo biológico e os factores socioculturais têm estado inter-relacionados em estudos epidemiológicos e cuidados clínicos. Este estudo visou avaliar as diferenças sexuais na susceptibilidade à COVID-19 nas Filipinas. Os números de casos da COVID-19 até 28 de Fevereiro de 2021 foram recolhidos no Departamento de Saúde das Filipinas (DOH). O teste t do estudante foi utilizado para analisar os dados por região administrativa e faixa etária. Foram recolhidos artigos noticiosos em meios de comunicação social de renome nas Filipinas. Foram consideradas as diferenças biológicas e socioculturais. Foi observada uma diferença de sexo significativa ($p \leq 0,05$) nos grupos etários de 30-39, 40-49, e 50-59 anos, o que indica que os machos nos referidos grupos etários nas Filipinas são mais susceptíveis à COVID-19. Mecanismos específicos do sexo que podem afectar desproporcionadamente qualquer dos sexos foram associados a diferenças nas respostas imunitárias, hormonas, e condições médicas subjacentes. Além disso, os estilos de vida de género nas Filipinas que envolvem encontros sociais como a luta de galos, o jogo, e o boxe são dominados pela população masculina e podem transmitir directamente a doença. As disparidades sexuais ligadas à susceptibilidade da COVID-19 enfatizam a importância da investigação baseada no género para estratégias de redução de risco e medidas de saúde pública eficazes nas Filipinas.

Palavras-chave: Disparidades sexuais; COVID-19; Filipinas, Antropologia Biocultural; Biologia Humana.

Introduction

The ongoing Novel Coronavirus Disease (COVID-19) outbreak is believed to have started in Wuhan City, China (World Health Organization [WHO], 2020a). It has spread rapidly and poses a global health emergency, with more than 113 million confirmed cases received by the World Health Organization from national authorities as of February 28, 2021 (WHO, 2021a). The first case of COVID-19 in the Philippines was reported on January 30, 2020, and the country has over 574 thousand cases as of February 28, 2021 (Department of Health [DOH], 2020; WHO, 2021b).

Sex differences in susceptibility to COVID-19 have been observed in recent studies. In a meta-analysis of initial reports in COVID-19 patients in China, males accounted for 60% (95% CI [0.54,0.65]) of COVID-19 patients (Li et al., 2020). A similar observation was seen in Europe, which has consistently been two-fold greater for men than women (Gebhard et al., 2020). Meanwhile, there were more confirmed cases in females (62.3%) than males (37.7%) in an initial report in Korea (Korean Society of Infectious Diseases et al., 2020).

The COVID-19 Sex-Disaggregated Data Tracker, the largest worldwide database of its kind, and a partnership of Global Health 5050 (housed at University College London), the African Population and Health Research Center (APHRC), and the International Center for Research on Women (ICRW), has presented the vulnerability of males over females in hospitalizations (26 countries), overall deaths (106 countries) and specifically attributed deaths of confirmed cases from COVID (93 countries), however with the data presented in view on a global scale, there is an equal prevalence (in both male and female) in the number of cases (136 countries) (Global Health 5050 et al., 2021). The disparity in COVID-19 outcomes in terms of sex may reflect the different socio-cultural and behavioral activities across societies.

As the virus continues to spread rapidly, it is important to comprehend the underlying processes and highlight those who are more susceptible to COVID-19, to be able to conceptualize and implement effective health measurements. In the Philippines, there is a lack of sex or gender-based COVID-19 research that would provide such knowledge; hence the general aim of this research paper is to determine sex differences concerning susceptibility with COVID-19 in the Philippines. Furthermore, the specific objectives are to determine whether there are significant sex differences based on administrative regions and age groups in contracting the disease; and discuss and highlight the possible biological and behavioral factors that could influence the sex difference in susceptibility to COVID-19.

Relevance of the Study

This study acknowledges the importance of sex-based research for possible sex-specific responsive health approaches. Sex-disaggregated data regarding COVID-19

outcomes lack from around half of the most severely affected countries (Womersley et al., 2020). Of the 186 countries, 127 countries have reported sex-disaggregated COVID-19 data in confirmed cases, 26 countries in hospitalizations, 16 countries in ICU admissions, and 99 countries in deaths. Without sex-disaggregated data regarding pandemic and other clinical threats in response to treatments, management, testing, and access to services would then be incomplete in analysis; sex-disaggregated data must be a standard for better health outcomes across societies (Global Health 5050 et al., 2021). Furthermore, analyzing the biological and behavioral factors involving males and females is crucial in determining the proximate causes of susceptibility in a given population.

It is of utmost importance to analyze sex differences in susceptibility to COVID-19. It will provide new information that can be used when conceptualizing and implementing effective pandemic responses and risk-reduction strategies. This study would highlight those who are more susceptible to COVID-19. Given the lack of sex or gender-based COVID-19 research in the Philippines, the findings of this research may benefit future research regarding COVID-19 outcomes about sex and comprehend the possible factors that may influence these. Moreover, this study could also be useful for epidemiology and public health studies in the future.

Material and Methods

Quantitative and qualitative findings were utilized to provide a more in-depth and detailed analysis. A joint display connecting the findings of quantitative data to the results of the qualitative data permits a more accomplished and synergistic utilization of data than to have separate analyses (Schoonenboom & Johnson, 2017).

This research applied quantitative methods to determine sex differences in susceptibility to COVID-19 through statistical analysis. The scope of this research is nationwide, covering all the 17 regions in the Philippines. The data included in this research was collected from the Philippine government's Department of Health's COVID-19 Case Information until February 28, 2021, which contains the sex, age, and region of residence per COVID-19 case recorded in the country. Data include the total number of cases per

administrative division in each region divided amongst the male and female population and the total number of cases per age group divided amongst the male and female population. The age groups presented in this research are based on the World Health Organization global case-based surveillance system (WHO, 2020b). The number of COVID-19 cases was then organized and tabulated according to administrative division and age groups using the "COUNTIFS" function of Microsoft Excel. Data were analyzed statistically by conducting a student's t-test to determine significant sex differences in the number of COVID-19 cases based on the 17 regions and age groups in the Philippines.

Qualitative methods were also applied to understand how biological and behavioral factors may interact and influence sex differences in COVID-19 outcomes. Several news articles from reputable media outlets in the Philippines were also gathered to highlight probable behavioral factors (i.e., noncompliance to health protocols) that may have influenced sex differences in susceptibility to COVID-19 of Filipinos.

Results and Discussion

Underlying factors such as differences in immune responses, hormones, socio-cultural and behavioral aspects may influence the sex difference in susceptibility in COVID-19. In the case of the Philippines, men could be more susceptible to COVID-19 due to these factors.

Table 1 shows the number of COVID-19 cases per region between male and female populations and their respective p-values. No significant sex difference with the number of COVID-19 cases based on regions in the Philippines was observed. However, out of the 17 regions, 15 regions recorded more cases in the male population than in females.

Table 1

Number of COVID-19 Cases per Region

Region	Males	Females	P-value
National Capital Region	118293	104486	0.65
Region IV-A: CALABARZON	54234	45052	0.61

Region VII: Central Visayas	35449	30631	0.85
Region III: Central Luzon	22784	19033	0.74
Region VI: Western Visayas	19097	18598	0.96
Region VIII: Eastern Visayas	9673	9165	0.92
Region X: Northern Mindanao	9431	7861	0.67
Region XI: Davao Region	17602	16631	0.94
Region IX: Zamboanga Peninsula	6276	5458	0.85
Region V: Bicol Region	3352	2683	0.68
Region I: Ilocos Region	5649	4297	0.71
Cordillera Administrative Region	10651	9723	0.90
Region II: Cagayan Valley	5185	5016	0.96
Region XII: SOCCSKSARGEN	4045	4082	0.99
CARAGA	5108	5099	1.00
Region IV-B: MIMAROPA	2022	1426	0.49
Bangsamoro Autonomous Region in Muslim Mindanao	2214	2219	1.00
Total	331065	291460	-

Table 2 shows the number of COVID-19 cases per sex and further layered per age group, as well as their respective student's t-test p-values and the percentage of COVID-19 cases for males and females combined. Significant sex difference was observed among the age groups of 30 to 39 ($p = 0.003335$), 40 to 49 ($p < .00001$), and 50 to 59 ($p = 0.017828$), also known as the working-age group (Galvez, 2020). Furthermore, there are more COVID-19 cases recorded for the male population from the age groups of 0 to 9 up to 60 to 69.

Table 2

Number of COVID-19 Cases per Age Group

Age group	Males	Females	Percentage of cases	P-value
0-9	10156	8813	3.30%	0.23
10-19	16944	16795	5.88%	0.95
20-29	78936	70800	26.08%	0.35
30-39	76461	59393	23.66%	<0.05
40-49	53290	39533	16.17%	<0.05
50-59	37901	33271	12.40%	<0.05
60-69	22254	22084	7.72%	0.94
70-79	9564	10220	3.45%	0.67
80+	3108	4667	1.35%	0.24
Total	308614	265576	-	-

Men and women differ in their immune response, and it could be because of several biological reasons. A well-known fact is that the chromosome structure within the DNA of the female sex biologically constitutes two X in their cells while a male has one X and Y each. The X chromosome contains immune-related genes that contribute to women developing stronger innate and adaptive immune responses (Conti & Younes, 2020; Griffith et al., 2020). Furthermore, the immune-related genes encoded by the X chromosome may cause lower viral load levels, and the presence of two X chromosomes can "emphasize the immune system" of females even if one would be inactive (Conti & Younes, 2020).

Another biological factor is that in the earlier phase of infection (baseline), male patients produced higher levels of pro-inflammatory innate immunity, chemokines, and cytokines (IL8-IL18) due to non-classical monocytes, which could heighten inflammation

because non-classical monocytes are responsible for secreting inflammatory cytokines and chemokines is a type of cytokines responsible for attracting cells to sites of inflammations (Takahashi et al., 2020). Although there is a rapid response of chemokines and cytokines (IL8-IL18) in male patients (at baseline), most of them are generated to focus more on inflammation. They attract more pro-inflammatory cells rather than as an antibody or antiviral response. With this in mind, there is a weaker accumulated antibody response in males as compared to females who generally have better antibody responses to viral infection because they can produce higher levels of antibodies and CD4+ T cells, also known as Helper T cells, given the immune-related genes encoded by the X chromosome (Conti & Younes, 2020; Scully et al., 2020). The Helper T cells have an important role in immunity because they activate B cells that release antibodies to eradicate disease-causing organisms and activate the cytotoxic T cells to kill infected red blood cells such as target cells (Alberts et al., 2002). Antibodies can neutralize the infectivity of organisms such as viruses and bacteria; hence it can prevent the infection of cells in the body as it interferes with the attachment of these organisms to host tissues (Forthal, 2014). Recent findings in a study conducted in France also highlighted that the levels of antibodies reduce faster in men than women, which may influence the susceptibility to COVID-19 (Grover, 2020). Despite men having a higher antibody response than women in the earlier phase, it was emphasized in the research that women have more stable levels of antibodies. In addition, activated CD8 T cells, also known as "killer T cells" (antibody cytokines), are also significantly higher or more robust in females than in male patients in the early phase of the infection, which are responsible for combating pathogens, cancer cells and other invaders, thus, poor T cell response in male patients could be associated to the future progression of the disease (Takahashi et al., 2020). Females having a more vigorous T cell response may have underlying effects in the body with the virus's progression and as the continuous process of retaliation of antibodies occurs.

In addition, the virus uses ACE2 or known as the "SARS-CoV receptor angiotensin-converting enzyme 2," to enter into the host cells to further replicate. Given other recent findings, men have higher ACE2 expression levels than women (Griffith et al., 2020). ACE2 is encoded by the X chromosome (present in both males and females); however, some factors determine how females have lower ACE2 expressions in their lung tissues than males.

Estrogen in females is known to downregulate ACE2 levels, and the lowering of ACE2 levels implies limited spreading of the virus to the lower respiratory tract in the early phase of infection (Bunders&Altfeld, 2020). It has been asserted, however, that during the later stage, there is an induced interferon-stimulated gene (ISG) in the lung tissues, which is a pro-inflammatory antibody, and in response, females produce ACE2 to stop the inflammation of the "cytokine storm", enhance airway ventilation, and prevent Acute Respiratory Distress Syndrome (ARDS), which allows fluid leaks in the lungs.

In contrast, several studies suggest no significant difference in the lung gene expression of ACE2 between males and females in all age groups (Cai, 2020; Li et al., 2020). On the other hand, smoking, which is prevalent among males, increases ACE2 expressions in the lungs (Cai, 2020; Chakladar et al., 2020). It suggests that males are more susceptible to viral infection; however, these can also be rooted in modifiable sex-specific behaviors.

Hormones, such as estrogen and testosterone, may also be another biological factor that may illustrate the differences in susceptibility to COVID-19 among males and females. Estrogen can boost immune response because its signaling can also promote adaptive T cell response by increasing the accumulation of neutrophil, a type of immune cell; hence it may protect females against the virus (Channappanavar et al., 2017; Pearce, 2020). Men do have estrogen, but it is lower than women (Jewell, 2019). Furthermore, estrogen can also regulate immune responses such that it can lower the expression of ACE2 (Pearce, 2020). On the other hand, testosterone is said to lower adaptive immunity because of the suppressed function of certain types of Helper T cells, which then lowers the antibody responses and production of B cells which are the ones to create antibodies specific to every pathogen encountered by the immune system (Agrawal et al., 2020; Cancer Treatment Centers of America, 2017). When the disease enters the body, males are at increased risk because testosterone lowers immune response, has poor T cell response.

In contrast, estrogen increases immune response in females associated with the higher copy number of immune-related genes (XX chromosome). Besides this, they emphasized that males have lower stress endurance levels than females against different stressors,

including pathogens (Pradhan & Olsson, 2020). However, some studies contradict this and highlight that testosterone can improve the production of "anti-inflammatory cytokines," which help regulate immune responses (Hepworth et al., 2010; Opal & De Palo, 2000).

Table 3 presents the frequency count of media articles about Filipino males and females who could not follow health protocols. More news articles involving males (26) violating various health protocols than females (2). Meanwhile, three news articles have been published wherein both sexes could not follow health protocols, specifically social distancing.

Local government units have implemented health protocols such as wearing face masks in public areas. In Quezon City, several male individuals in Barangay Bahay Toro were reprimanded by those in the QC Department of Public Order and Safety for not wearing face masks (ABS-CBN News, 2020a). Two other male individuals, 40 and 30 years old, were caught not wearing face masks at the checkpoint in Taguig City and Brgy. 46 in Pasay, respectively (Bagaoisan, 2020a, 2020b).

Cockfighting remained prohibited in areas under community quarantine in the Philippines (Geducos, 2020a). Despite this, on July 19, 2020, six men, including a barangay chairman, were arrested after being involved in a cockfighting event in Tondo, Manila, which was under general community quarantine (Merez, 2020; Tiangco, 2020). They were charged for violating the city ordinance for the mandatory use of face masks in all public places and the imposed physical distancing measures. In Cebu City, male individuals were also caught in a cockfight event situated in Sitio Tumoy and Sudlon, Lahug (Geducos, 2020b; Perez, 2020a; Recuenco, 2020a). Meanwhile, in Valenzuela City, 53 individuals were involved in a cockfight, and news photos showed that only male individuals attended the said event (Perez, 2020b). Several more articles of males located in Dapitan City, Batangas, Davao Del Sur, Bulacan, Southern Leyte, Tacloban, Quezon, and Pasig City, who have attended or hosted a cockfighting event, which violated quarantine protocols in the Philippines, were published (ABS-CBN News, 2020b, 2020c, 2020d; Malig, 2020; Marticio, 2020; Recuenco, 2020b, 2020c).

In March 2020, a male individual went to a two-day cockfighting event in Davao City, where he believed he contracted the disease. He was the first COVID-19 patient to be recorded in General Santos City (Tocmo, 2020). A male attendee was said to have had the virus before the cockfighting event, which led to others being infected (Rappler, 2020). The large cockfighting event was then considered as "ground zero" because 26 COVID-19 cases recorded in the Davao region were linked to this cockfighting event. More importantly, COVID-19 cases were recorded in North Cotabato, Maguindanao, Lanao del Norte, Bukidnon, Butuan in General Santos City have been connected to this cockfighting event as well (Tocmo, 2020; Manar, 2020).

In April, four male barangay officials of Barangay 129 in Caloocan City were involved in a cockfighting and gambling event in Manila North Cemetery (ABS-CBN News, 2020e; Calalo, 2020). Furthermore, seven men were arrested in Barangay Putatan, Muntinlupa City, for illegal cockfighting on September 20, while Metro Manila was still under community quarantine (Bagaoisan, 2020c). These news reports show that cockfighting and gambling continue to thrive in the Philippines despite health protocols being imposed, and male individuals dominate these activities (Day, 2018).

Meanwhile, an amateur boxing match was held in Barangay 20, located at Tondo, Manila, in April 2020, and a male individual initiated it despite the imposed community quarantine (ABS-CBN News, 2020f). Around 100 residents were said to have attended while others were playing bingo (Talabong, 2020).

Female individuals have also been caught violating health protocols, although fewer in numbers. A woman was arrested in Caloocan City after she tried to enter Barangay 156, a place under total lockdown during that time because of the rise in COVID-19 cases in the area, and she was also not wearing a face mask (Marquez, 2020). Another female individual was caught not wearing a face mask while she was doing her laundry outside her house in Parañaque (ABS-CBN News, 2020g)

In July 2020, thousands of residents were stranded in Rizal Memorial Sports Complex because of heavy downpours. They specifically gathered there because of the free transportation program of the government, which would help them return to their home provinces (Roper, 2020). In September, a massive crowd gathered at Manila Bay when it opened to see the dolomite sand placed there for aesthetic purposes (ABS-CBN News, 2020h). There were male and female individuals who attended a party held at the Manila North Cemetery. They were all caught not wearing face masks and not practicing physical distancing (Pascual, 2020).

Table 3

Frequency Count of News Articles during Quarantine

News Outlets, Authors	Location	Event	Sex Group Involved	Frequency
Merez, 2020; Tiangco, 2020; Geducos, 2020b; Perez, 2020a, 2020b; Recuenco, 2020a, 2020b, 2020c; ABS-CBN News, 2020b, 2020c, 2020d, 2020e; Malig, 2020; Marticio, 2020; Tocmo, 2020; Rappler, 2020; Manar, 2020; Calalo, 2020; Bagaoisan, 2020c	Manila City, Cebu City, Valenzuela City, Dapitan City, Batangas City, Davao del Sur, Bulacan, Southern Leyte, Quezon, Davao City, North Cotabato, Maguindanao, Lanao del Norte, Bukidnon, General Santos City, Muntinlupa City	Cockfighting	Males	19
ABS-CBN News, 2020e; Calalo, 2020	Manila City,	Gambling	Males	2
ABS-CBN News, 2020f; Talabong, 2020	Manila City	Boxing	Males	2

ABS-CBN News, 2020a; Bagaoisan, 2020a, 2020b	Quezon City, Taguig City, Pasay City	No face mask	Males	3
Marquez, 2020; ABS-CBN News, 2020g	Caloocan City, Parañaque City	No face mask	Females	2
Ropero, 2020; ABS-CBN News, 2020h; Pascual, 2020	Manila City	Mass gathering	Both	3

Besides biological factors, the behavioral aspect, including high-risk behaviors and lifestyle, should also be considered as to why there is a significant difference in susceptibility to COVID-19 between males and females in certain age groups in the Philippines. Numerous news articles have been published regarding violations of health protocols such as not wearing face masks, holding cockfighting, boxing, and gambling events which leads to mass gatherings despite being under community quarantine, and male individuals are highly involved in these incidents as presented in the results. Health protocols such as physical distancing have been implemented since the beginning of community quarantine in the Philippines on March 17, 2020 (Office of the President of the Philippines, 2020). In order to control the spread of a highly contagious disease such as COVID-19 that is capable of transmitting through close contact from person to person, the implementation of physical distancing has been crucial (Chu et al., 2020; Santa Clara County Public Health Department, 2020). With this in mind, males are more susceptible to COVID-19 than females because of the activities they are involved in (such as cockfighting and gambling), wherein physical distancing is not maintained.

Cockfighting in the Southeast Asian island Bali represented Balinese people's social and cultural structure, which is fundamentally centered on prestige and status and not on monetary gain (Geertz, 2005). On the other hand, an ethnography written on cockfighting in the Philippines discussed that cockfighting or sabong is a "male-oriented activity" and that men perceive it to enhance their status in society; it holds a cultural and symbolic significance (Agcaoili et al., 2019). Documentation of lived experiences in the countryside has shown that

cockfighting is a form of recreational and social activity for husbands but frequently affects household resources; getting used to this activity is believed to be a common coping mechanism in households in the Philippines, especially in the countryside (Cabadsan, 2019). Moreover, cockfighting seemed to be a leisure activity for Filipinos as a form of diversion or escape from life stressors even at the expense of health and money; gambling in cockfighting is sustained through familial influence (usually from the male members of the family) and accessibility of cockpit facilities (Peñalba, 2020).

Men are also more likely to participate in most gambling forms regularly and gamble more frequently (Hing et al., 2015). Addiction to gambling, also known as "ludomania," is more common in men than in women (Halili-Jao, 2017). In addition, men have been observed to take more risks and have lower levels of impulsive coping than females, which made them likely to gamble (Wong et al., 2013). Furthermore, "impulsive copers" tend to be the ones involved in "addictive behaviors" when under emotional distress, and given the COVID-19 situation, it is highly likely that Filipino males engage in gambling despite health protocols being implemented (Cyders & Smith, 2008).

A significant sex difference in the number of COVID-19 cases is observed among the working-age groups of 30 to 39, 40 to 49, and 50 to 59. It has been highlighted that 25 to 40 years are considered the "most productive periods" as one can work efficiently and contribute to the economy (Palabrica, 2019). Concerning this, it has been reported that the majority of the COVID-19 cases have shifted towards the working-age group of 20 years old until 59 years old as community restrictions were eased (Galvez, 2020). Those belonging to this age group have increased exposure and socialization with other individuals. They had to frequently go out of their homes to work, which may have increased their chances of contracting the disease. With this in mind, it is important to note that six in every ten of the estimated 40.6 million employed Filipinos back in July 2018 were males, which may explain why there is a greater number of COVID-19 cases recorded for the male population as observed in 15 out of 17 regions in the country as well as the age groups 0 to 9 until 60 to 69 (Philippine Statistics Authority [PSA], 2019). Furthermore, the largest groups of employed individuals consist of the age groups 25 to 34 years old (26.9%), 35 to 44 years old (23.2%),

and 45 to 54 years old (18.8%), which could explain why the working-age group contains the bulk of COVID-19 cases in the Philippines (30 to 39 years old - 23.87%, 40 to 49 years old - 16.25%, and 50 to 59 years old - 12.39%) and the significant sex difference in three age groups.

Another factor that may have an important role in the sex difference in susceptibility to COVID-19 is the lifestyle practiced by males and females in general. In comparison to women, men have lower rates in terms of practicing hand hygiene, physical distancing, and wearing face masks; fewer men have been reported to avoid large public gatherings or close physical contact compared to women, which can also be observed in the Philippines, given the numerous instances community quarantine regulations have been violated by male individuals as reported on the news (Griffith et al., 2020). Furthermore, high-risk behaviors such as smoking are more prevalent in males than females. From a global perspective, 35% of men smoke, which is significantly higher than women, which is only at 6% (Ritchie & Roser, 2019). Smoking harms the lungs' health and delays immune responses against pathogens such as viruses (Gao et al., 2017; Qiu et al., 2017). In the Philippines, the prevalence of using tobacco among adults is 23.8% (41.9% among men while 5.8% among women) (PSA & DOH, 2017). Smoking behavior has been linked to ACE2 expression levels and susceptibility to the disease because ACE2 plays a vital role in how SARS-CoV-2 can enter the cells. SARS-CoV-2 can bind with ACE2, a protein found on various cell types in organs such as the kidney, heart, gastrointestinal tract, and others (Agrawal et al., 2020). From this, SARS-CoV-2 can enter into the cells, allowing the cell to be infected and cause COVID-19 (Sriram et al., 2020).

Being physically inactive may also be a factor that influences the difference in susceptibility to COVID-19 between males and females. Exercise has an important role in the normal functioning of the immune system, which may minimize the impact of a virus because immune cells are mobilized during exercise. Those that can recognize and kill cells infected by a virus are also included (Simpson, 2020). Given the lack of physical activity and prolonged confinement because of the community quarantine imposed in the Philippines, this may result in negative effects in the immune system and higher susceptibility to COVID-19

in a particular gender group, as presented in the results. One negative effect would be that cortisol is elevated when you lack exercise, which can inhibit certain critical functions in the immune system, such as reducing the ability of T cells to multiply. Concerning this, the proportion of Filipino adults older than 20 years old who are physically inactive is 92.6% for transport-related activities and leisure-related activities (Philippine Academy of Family Physicians, 2009). Furthermore, more males (90.1%) are inactive than females (72.4%) in non-occupational related activities.

Lifestyle diseases, commonly known as non-communicable diseases (NCDs), are lifestyle-related and behavioral and may also be a factor that influences the difference in susceptibility for COVID-19 (DOH, 2018). High-risk behaviors such as smoking and physical inactivity, which are also prevalent in males (as previously mentioned), are linked to non-communicable diseases. Non-communicable diseases had been in the top three leading causes of mortality and morbidity over infectious diseases starting from the 1960s (Ladrero & Española, 2017). The following lifestyle diseases to be discussed are common in the Philippines, which may illustrate the sex difference in susceptibility of COVID-19 because those with pre-existing health conditions, such as hypertension and diabetes, have a weaker immune response towards a viral infection (Li et al., 2020; International Diabetes Federation [IDF], 2021).

First, heart disease individuals often have underlying conditions such as hypertension, which weakens their body's defense systems towards a viral infection; hence, they may be more susceptible to COVID-19 (Li et al., 2020). For illustrating this, the high prevalence of hypertension among COVID-19 patients is presented in several studies. Of the 191, 58% of COVID-19 Chinese patients in the study had morbidity, with hypertension being the most common (30%) (Zhou et al., 2020). A similar study found that 49% of COVID-19 Italian patients out of the 1,043 had hypertension (Grasselli et al., 2020). Another study has shown that the most common comorbidity was hypertension, with 56.6% among the 5,700 COVID-19 American patients included (Richardson et al., 2020).

On the other hand, hypertension in the Philippines for 2020 was 38.6% and the highest among other cardiovascular diseases (Sison et al., 2020). Mean blood pressure was

significantly higher in males with 27.5% prevalence than females with 20.8% in the year 2015; large increases were observed between the age of 30 (16.7%) and 40 (28.3%) years (Department of Science and Technology - Food and Nutrition Research Institute, 2016). Furthermore, the number of deaths recorded for 2019 was 58,233 or 16.4 percent of the total registered deaths among males and 39,242 or 14.8 percent of the total deaths among females due to (ischaemic) heart diseases (PSA, 2021). It has been emphasized that the main cause of heart disease is unhealthy lifestyles such as smoking, drinking, and poor dietary choices (Junio, 2019). Such high-risk behaviors are also prevalent among men, as recorded in a previous study wherein the frequency of smoking (8.8% vs. 0%) and drinking (8.8% vs. 0.2%) were significantly higher among adult male COVID-19 patients from Wuhan Infectious Disease Hospital (Liu et al., 2020).

Secondly, individuals with diabetes are known to be prone to acquiring (rare) infections and susceptible to certain complications when infected with pathogens; hence the prevalence of diabetes in COVID-19 patients as presented in several studies may expound as to why there is a sex difference in susceptibility to COVID-19 (Knapp, 2013). Second to cardiovascular diseases, diabetes with a 7.3% case fatality rate (CFR) was among the prevalent pre-existing comorbid conditions found in COVID-19 Chinese patients (Wu & McGoogan, 2020). Diabetes among the COVID-19 Italian patients was prevalent, with a case fatality rate of 35.5%, preceded by ischemic heart disease (Onder et al., 2020). A high prevalence of diabetes was also presented among the 5700 American patients with 33.8%, alongside hypertension (56.6%) and obesity (41.7%) (Richardson et al., 2020).

In the IDF Diabetes Atlas 9th Edition (2019), it was recorded that approximately 463 million adults (20-79 years) had diabetes, and 79% of adults were living in low- and middle-income countries, including the Philippines, which may explain as to why there is a significant sex difference in the number of COVID-19 cases in the age groups of 30 to 39, 40 and 50 to 59 (IDF, 2019). Furthermore, the number of deaths attributable to high blood glucose was higher in male populations than in female populations within the age groups of 30-69 and 70+ (WHO, 2016).

Conclusion

This research aimed to determine sex differences in susceptibility to COVID-19 and elaborate on the possible biological and behavioral factors that may influence the sex difference in susceptibility to COVID-19. The data analyzed in this study is limited to the available COVID-19 case information provided by the local health department to the public. It has been evident through several studies that there is a different response of both sexes towards viral infections, which may influence who is more susceptible to the disease. The underlying factors which may have influenced the sex difference in susceptibility to COVID-19 in the country are linked to several immune responses, hormones, socio-cultural and behavioral aspects as presented in the discussion. Upon analyzing the Department of Health data until February 28, 2021, our results have shown that there is no significant sex difference in the number of COVID-19 cases based on regions for males and females. However, a significant sex difference occurs in the age groups of 30-39, 40-49, and 50-59 years old, also known as the working group in the Philippines, which suggests susceptibility of the male population. COVID-19 cases are associated with certain comorbidities. Such diseases as hypertension and diabetes are lifestyle diseases linked to how people live (Centers for Disease Control and Prevention, 2020). These diseases are associated with negative lifestyles, for instance: smoking and physical inactivity. Other factors may also be linked to socio-cultural activities that involve social gatherings dominated by the male population, such as cockfighting, gambling, and boxing amid the pandemic.

Moreover, the sex difference in susceptibility to COVID-19 may also be linked to biological aspects such as the difference in immune response between the male and female populations. Such factors involve the X-linked immune-related genes and hormonal factors, which are then associated with the innate and adaptive immune system emphasized in the female population in response to viral infections. In conclusion, analyzing the sex-specific mechanisms may provide a better clinical insight into the impact of viral infections on both males and females. With that, it would yield more effective public health strategies in the Philippines, specifically in containing and serving gender-sensitive treatments and recommendations.

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