Comparison of Sex Specific Data among Hospitalized Covid-19 Patients

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Introduction

It is critical to identify factors that contribute to disease severity among patients diagnosed with COVID-19 to properly identify and treat infected patients. A systematic review of sex specific COVID-19 clinical outcomes demonstrated that female patients have lower rates of severe infection and mortality, raising the question of whether male sex is an independant risk factor for disease severity. Despite no difference in disease prevalence between sexes, men have consistently had higher rates of severe infection and mortality, with male mortality rates ranging from 2-4 times the rates of female mortality. Interestingly, this data is consistent with the SARS outbreak. There have been several proposals as to why this is the case ranging from differences in biological factors, behavioral factors, and rates of comorbidities. First, the X chromosome is known to contain many immune genes, giving females a potential disease fighting advantage. Also, men are thought to have more ACE2 receptors, the receptor the virus binds to gain entry into cells. Behaviorally, men are more likely to engage in risky behaviors and are more likely to smoke, which is a known risk factor for many comorbidities.

Aim of Study

This study investigates the correlation between biological sex and predisposing conditions as well as COVID-19 disease severity among 689 patients hospitalized within the St. Luke's Hospital Network in Eastern PA/Western NJ to identify if the trend of decreased severity in females holds true.

Methodology

Participants were 689 COVID-19 positive patients hospitalized within the St. Luke's University Hospital network. Data was extracted from patients electronic medical records both during their admission and after discharge. Mean age of participants is 64.0 years (+/- 16.7). Male patients comprised 54.1% of the sample while 45.9% were female. 57.9% of patients identified as Caucasian, 17.3% as African-American, 2.2% as Asian, less than 1% as Native-American, and 19.2% reported their race as "Other". The sample consisted of 30.2% of patients who reported their ethnicity as Hispanic or Latino, 66.0% who reported as Not Hispanic or Latino, and the remaining 3.8% were unknown or other. The average BMI of participants was 31.6 (+/- 7.8), where 54.1% of patients had a BMI of 30.0 or higher, 26.3% had a BMI between 25-29.9, 18.6% of patients had a BMI between 18.6-24.9, and 1.0% of patients had a BMI <18.5. 62.7% of patients never smoked tobacco, whereas 32.7% report quitting tobacco use and 4.2% are active tobacco users. Chi squared test of independence was performed to examine the relation between known COVID-19 risk factors and COVID-19 infected female patients (n=316) compared to male patients (n=373).

Results

Table 1. Risk Factors & Chi Square Analysis

Risk Factor		Female	Male	Total	P Value
		Patient Sex			
		%	%	%	
BMI	Normal	21.5%	18.0%	19.6%	0.241
	Overweight/Obese	78.5%	82.0%	80.4%	
Smoking Exposure	Exposure	32.3%	41.6%	37.3%	0.012
	Never	67.7%	58.4%	62.7%	
Diabetes	No	60.8%	56.3%	58.3%	0.445
	Yes	39.2%	43.7%	41.7%	
HTN	No	40.2%	42.1%	41.2%	0.613
	Yes	59.8%	57.9%	58.8%	
HF	No	86.1%	86.6%	86.4%	0.843
	Yes	13.9%	13.4%	13.6%	
CAD	No	85.4%	82.6%	83.9%	0.307
	Yes	14.6%	17.4%	16.1%	
COPD	No	88.6%	93.0%	91.0%	0.043
	Yes	11.4%	7.0%	9.0%	
Asthma	No	82.3%	91.7%	87.4%	<0.001
	Yes	17.7%	8.3%	12.6%	
Immunosuppression	No	94.3%	94.4%	94.3%	0.970
	Yes	5.7%	5.6%	5.7%	
Malignancy	No	91.1%	89.5%	90.3%	0.481
	Yes	8.9%	10.5%	9.7%	
CKD	No	81.0%	79.9%	80.4%	0.712
	Yes	19.0%	20.1%	19.6%	
Intubation	No	88.3%	83.4%	85.6%	0.067
	Yes	11.7%	16.6%	14.4%	
Mortality	Expired	16.8%	15.3%	16.0%	0.595
	Survived	83.2%	84.7%	84.0%	

Table 2. Demographic Data

		Female	Male	Total
		Patient Sex		
Age	Over 50	81.0%	77.2%	79.0%
	49 and Under	19.0%	22.8%	21.0%
Race	American Indian or Alaska Native	0.3%	0.3%	0.3%
	Asian or Asian American	2.2%	2.1%	2.2%
	Black or African American	16.5%	18.0%	17.3%
	White or Caucasian	63.3%	53.6%	58.1%
	Other Race	14.9%	22.8%	19.2%
	Unknown/Declined	2.8%	3.2%	3.0%
Ethnicity	Hispanic or Latino	25.3%	34.3%	30.2%
	Not Hispanic or Latino or Spanish	71.2%	61.7%	66.0%
	Not Reported/Declined to Answer	1.9%	1.9%	1.9%
	Other/Unknown	1.6%	2.1%	1.9%
BMI	Underweight	1.9%	0.3%	1.0%
	Normal	19.6%	17.7%	18.6%
	Overweight	22.2%	29.8%	26.3%
	Obese	56.3%	52.3%	54.1%
Tobacco Use	Never	67.7%	58.4%	62.7%
	Quit	28.5%	36.2%	32.7%
	Current	3.2%	5.1%	4.2%
	Unknown	0.6%	0.3%	0.4%

Analysis of Results

Risk factors stratified by biological sex showed that female patients were more likely to have COPD (p < 0.05) and asthma (p < 0.001), and less likely to have smoke exposure (p < 0.05). There was no statistically significant difference in any other predisposing risk factor - BMI, diabetes, hypertension, heart failure, coronary artery disease, COPD, immunosuppression, malignancy, chronic kidney disease - between sexes. There was no statistically significant difference in disease severity between the sexes with respect to intubation rate (p = 0.07) and mortality (p = 0.59).

Discussion

The results of this study are important to show that the trend of increased severity among males may not be ubiquitous and care should be taken when considering male sex as an independent risk factor for disease severity. There are many limitations to this study. This is a preliminary study done with a small sample size of the first 689 COVID patients in the network, when ongoing treatment protocol modifications were being made with room for provider treatment bias and poor understanding of disease process. There is also an overrepresentation of obesity within the sample, which is a known risk factor for disease severity. Smoking status was evaluated via self report which is unreliable and may introduce bias. Standardized reporting of pack-years would be a better way to evaluate and compare smoke exposure across disease severity. The methods used to determine disease severity (intubation, mortality) are a proxy for disease severity and do not represent all forms of severe disease. In future studies, factors such as admission to ICU, use of pressors, need for administration of Actemra, Ramdesivir, Convalescent Plasma, and anticoagulation will allow for a more complete investigation of disease severity. Other contributing factors to disease severity include race and ethnicity, neither of which were evaluated in this study. Finally, insurance and health systems in the US are different than in the rest of the world. Patients in this study population are either uninsured and likely waited until disease was very severe before seeking care, or have private insurance and were seeking care early in disease progression, whereas in countries with universal healthcare, patients could seek care at any point in disease progression. this may contribute to disparities when comparing this data to international data.

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