

# The assessment of the risk of COVID-19 infection and its course in the medical staff of a COVID-only and a non-COVID hospital

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## Conflict of interest

None declared

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## Abstract

**Background.** Medical workers are a group that is particularly vulnerable to infection during the coronavirus disease 2019 (COVID-19) pandemic.

**Objectives.** The study aimed to assess the risk of COVID-19 infection and its course in the medical staff of a COVID-only and a non-COVID hospital.

**Materials and methods.** The observational study included 732 participants who were medical workers. The study was conducted between June 2020 and December 2020, before widespread COVID-19 immunization was introduced.

**Results.** Of the 732 employees of the hospitals, 377 had a history of COVID-19. The risk of disease was twice as high in the medical staff of the COVID-only hospital compared to the medical staff of the non-COVID hospital (odds ratio (OR) = 2.0;  $p < 0.001$ ). Among medical personnel, 20.6% of the participants were asymptomatic and 6.4% required hospitalization. For the non-COVID hospital, the employees who were most frequently infected with COVID-19 were nurses/paramedics/medical caretakers. The factor influencing the risk of infection was body mass index (BMI; OR = 1.05;  $p = 0.004$ ). The risk of COVID-19 infection was lower in the influenza vaccine group (OR = 2.23,  $p < 0.001$ ).

**Conclusions.** The study results indicate that employees of the hospital treating only COVID patients have a higher risk of infection. Previous observations on factors predisposing to COVID-19 infection like gender and BMI were confirmed. However, the observations carried out on the studied population did not confirm the influence of other factors, such as the coexistence of chronic diseases (apart from diabetes) on the risk of developing COVID-19. In addition, we noticed that seasonal influenza vaccination has a beneficial effect in patients with COVID-19 infection.

**Key words:** epidemiology, medical staff, COVID-19, risk of infection

## Background

Since the turn of 2019 and 2020, we are struggling with the coronavirus disease 2019 (COVID-19) pandemic. Due to the high transmission rate of the virus, millions of people worldwide contracted COVID-19 within a short period. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection shows a broad spectrum of clinical presentation. In approx. 20% of patients, the disease leads to respiratory failure or damage to other organs. In symptomatic cases, the course of the disease depends on many factors, including age, gender and comorbidities.<sup>1,2</sup> By identifying and assessing risk factors and implementing appropriate strategies, the risk of complications can be reduced. Age-related changes in innate and acquired immunity against COVID-19 infection have not yet been studied in detail, and the impairment and dysregulation of both kinds of immunity in older age can be inferred from examples of other viral infections, including flu. Kim et al. have noted an impaired interferon (IFN) type 1 response in the elderly, which is responsible for the increased replication of flu virus in cell culture.<sup>3</sup> In addition, several common nonstructural proteins of SARS-CoV-2 suppress IFN type 1 responses, and such suppression leads to a poor response of CD8<sup>+</sup> cell and T cell to viral infection.<sup>4,5</sup>

Obesity is another risk factor for severe SARS-CoV-2 course, and this correlation is mainly attributed to impaired innate and acquired immunity among the overweight.<sup>6</sup> In adipose tissue, the expression of ACE2 receptors is higher than in the lung. Adipose tissue performs immune functions by maintaining chronic low-grade inflammation. Macrophages in the tissue can, under favorable conditions, activate a systemic acute inflammatory response, with the synthesis of pro-inflammatory cytokines: interleukin 6 (IL-6), tumor necrosis factor alpha (TNF- $\alpha$ ) and others. In the case of COVID-19 infection, it is thought that this process may contribute to the development of the so-called cytokine storm. Adipocytes in adipose tissue release adiponectin and leptin, which are among the risk markers for cardiovascular disease (CVD) and are also associated with inflammation.<sup>6</sup>

Diabetes in COVID-19 patients has been found to increase the risk of hospitalization, severe complications and death in the course of the disease.<sup>7</sup> It is known that diabetes is associated with impaired innate as well as acquired immunity, which is due to impaired phagocytosis and function of macrophages and neutrophils, T cell function and clearance of viral particles. In addition, diabetic patients suffer from chronic inflammation with increased levels of pro-inflammatory cytokines such as IL-1, IL-6 and TNF- $\alpha$ .

Previous data on the association of smoking with the risk of COVID-19 infection and severity of COVID-19 are inconclusive. Virus entry into host cells occurs via ACE2 receptors. The study by Leung et al. showed an increased ACE2 receptor expression on airway cells of active tobacco smokers, which could explain the increased risk

and more severe course of SARS-CoV-2 in this subgroup.<sup>8</sup> In a cross-sectional study, Jackson et al. demonstrated a nearly 2 times higher incidence of COVID-19 among active smokers compared to non-smokers, regardless of gender, age and comorbidities.<sup>9</sup> Another meta-analysis showed not only an increased risk of severe COVID-19 in active smokers, but also a higher risk of severity and death during hospitalization and the need for mechanical ventilation in former smokers.<sup>10,11</sup> On the other hand, the attention is paid to the so-called smoker's paradox and the anti-inflammatory effect of nicotine.<sup>12</sup> Some observational studies have shown a lower number of active smokers among COVID-19 patients; moreover, no adverse effect of smoking on the disease course was observed.<sup>13</sup> A meta-analysis of 32 studies found that active smokers have a lower risk of COVID-19 infection compared to non-smokers.<sup>14</sup>

The literature also highlights the increased risk of COVID-19 infection among healthcare professionals. A meta-analysis of 49 studies showed that seroconversion to anti-SARS-CoV-2 IgG<sup>+</sup> in the study group affects 8.7% of the population. Risk factors for seropositivity were: male sex, black race, Asian and Hispanic origin, working in a unit dedicated to COVID-19 patients, working in direct contact with patients, and using inappropriate personal protective equipment.<sup>15</sup>

The medical staff has been the group working on the front line in the fight against the virus. When the COVID-19 pandemic began, 2 types of hospitals were established in our country. Some admitted only patients with COVID-19 infection (dedicated COVID hospitals), while other treated only patients with negative results for COVID-19 infection (non-COVID hospitals).

## Objectives

The purpose of this study was to assess the risk of COVID-19 infection among medical staff from 2 hospitals: a dedicated COVID-19 hospital and a non-COVID facility.

## Materials and methods

### Study design

The study group consisted of medical staff from 2 hospitals: a dedicated COVID-19 hospital and a non-COVID-19 hospital. After obtaining individuals' informed consent to participate in the study, the following data were obtained from all participants: age, height, body weight, type of work performed in the case of medical staff (doctor, nurse, paramedic, medical attendant, orderly, hospital cleaner, physiotherapist, laboratory worker, technician, pharmacist), housing conditions (number of people living in a shared household), physical activity (defined as regular physical activity of moderate intensity at least 2 times a week for at least

30 min), history of flu vaccination during the year preceding the survey, comorbidities, and smoking. In addition, the following information regarding the course of SARS-CoV-2 infection was obtained: COVID-19 infection confirmation method (positive polymerase chain reaction (PCR) test based on nasopharyngeal swab, positive antigen test of the nasopharyngeal swab, or positive results of antibodies against SARS-CoV-2), symptoms of SARS-CoV-2 infection, and the severity of the course of the disease.

The participant with past COVID-19 infection was defined as a person who: 1) had a history of positive PCR and/or antigen test results based on a nasopharyngeal swab, and/or 2) was tested positive for immunoglobulin G (IgG) and/or IgM anti-SARS-CoV-2 antibodies (semi-quantitative or quantitative research) at the time of the current study (tested before COVID-19 vaccination).

Other participants who did not meet the above conditions were considered as those with no past COVID-19 infection.

## Laboratory tests

Anti-SARS-CoV-2 antibodies were detected using enzyme-linked immunosorbent assay (ELISA). This assay uses semi-quantitative or quantitative method of detecting antibodies present in human serum following COVID-19 infection and arising from the vaccines based on the S1/RBD subunit of coronavirus.

The samples for the study were collected from medical staff after they provided their written consent to participate in the study. The ELISAs were performed in the laboratory of Euroimmun Polska sp. z o.o. (Wrocław, Poland) on ANALYSER I machines. The method was standard for determining antibodies: anti-SARS-CoV-2 in IgG, IgA and IgM classes and Quantivac IgG tests. Appropriately diluted test serum was placed on a 96-well microplate coated with a specific antigen. The antibodies present in the serum bind to solid-phase antigens. They are detected during the second step, which involves the addition of an immunoglobulin antibody conjugate and an enzyme. The addition of substrate for the enzyme catalyzes a color reaction whose measured intensity is proportional to the number of antibodies.

All reagents were supplied by Euroimmun Polska sp. z o.o. Anti-SARS-CoV-2 antibodies were measured in the IgG, IgA and IgM classes using a semi-quantitative method based on the determination of the ratio coefficient. In addition, anti-IgG-positive sera were further assayed to obtain a quantitative antibody titer result, recorded as BAU/mL international units. For the semi-quantitative method, results above 1.1 were considered positive, while for the quantitative method, the cutoff point was a value of  $\geq 35.2$  BAU/mL.

This study received approval from the institutional ethics committee of Wrocław Medical University, Wrocław, Poland (approval No. KB 634/2020), and adhered to the ethical guidelines of the Declaration of Helsinki.

## Statistical analyses

Analyses were performed using R software package v. 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) and STATISTICA v. 13.1 (TIBCO Software Inc., Palo Alto, USA). Categorical variables were presented as frequencies with percentages, whereas median and interquartile range (IQR) were used to describe continuous variables. Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test. The evaluation of data normality was performed using the Shapiro–Wilk test, and non-normally distributed continuous variables were compared using the Mann–Whitney test. For multiple comparisons, the Kruskal–Wallis test and a post hoc Dunn's test with Benjamini–Hochberg correction were applied. The effect of risk factors on the probability of critical course of SARS-CoV-2 infection was estimated with univariate logistic regression. Outliers were checked with standardized residuals analysis. A p-value of 0.05 was considered statistically significant.

## Results

### Analysis of COVID-19 incidence and SARS-CoV-2 course in a COVID-19 hospital and a non-COVID hospital

#### Risk of disease by workplace – COVID hospital compared to non-COVID hospital

The study group consisted of 732 medical staff, of whom 460 were employees of a non-COVID hospital and 272 were employees of a COVID hospital. The staff included 568 females (78%) and 164 males (22%); the average age of the staff was 47 years. The characteristics of the study group are described in Table 1.

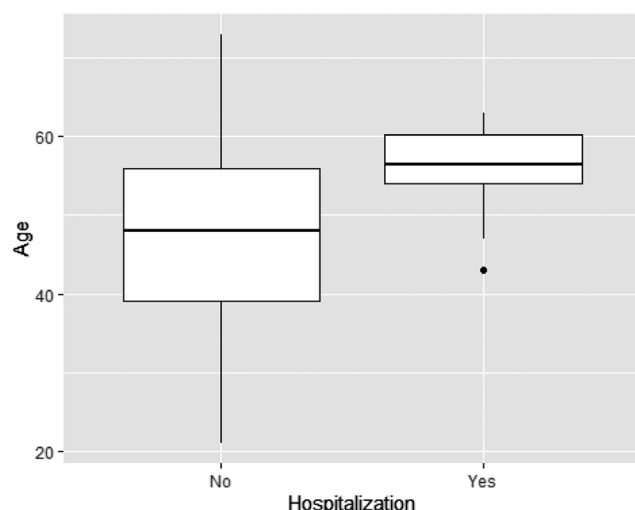
Of 732 hospital workers, 377 had COVID-19 infection in the past. There was a statistically significant relationship ( $\chi^2 = 20.58$ ;  $p < 0.001$ ), indicating that the number of cases depended on the place of work. The risk of disease was twice higher for COVID hospital medical staff than for non-COVID hospital medical staff – 62% and 45%, respectively (odds ratio (OR) = 2.0,  $p < 0.001$ ).

Hospitalized patients were older than those with mild or asymptomatic COVID-19. In the analyzed population, hospitalized patients had a significantly higher median age than those who did not require hospitalization – 57 (54–60) years and 48 (39–56) years, respectively ( $p < 0.001$ ) (Fig. 1). In the univariate model, the chance of being hospitalized was 10% higher with age increasing by 1 year (OR = 1.1,  $p < 0.001$ ). Data on regression, 95% confidence intervals (95% CIs) for ORs, statistical significance for the entire model, and a measure of goodness-of-fit (Nagelkerke pseudo  $R^2$ ) are presented in Table 2.

**Table 1.** Characteristics of medical staff in a COVID hospital and a non-COVID hospital

Variable	n (%)			p-value
	total (n = 732)	COVID hospital (n = 272)	non-COVID hospital (n = 460)	
Age, mean (SD) [years]	47 (12)	47 (11)	46 (12)	0.92*
Gender				
male	164 (22)	51 (19)	113 (25)	0.07**
female	568 (78)	221 (81)	347 (75)	
BMI, mean (SD) [kg/m <sup>2</sup> ]	26 (5)	27 (5)	26 (4)	0.83*
Smoking				
non-smoker	478 (65)	171 (63)	306 (66)	0.65***
former smoker	125 (17)	47 (17)	78 (17)	
passive smoker	20 (3)	7 (3)	13 (3)	
active smoker	109 (15)	47 (17)	63 (14)	
Number of persons in a household				
1	94 (13)	32 (12)	62 (13)	0.30***
2	266 (36)	92 (34)	174 (38)	
>2	372 (51)	148 (54)	224 (49)	
Number of households with children <5 years of age	63 (9)	24 (9)	39 (9)	1**
Number of households with persons >65 years of age	61 (8)	23 (9)	38 (8)	1**
Chronic diseases	240 (33)	96 (35)	144 (31)	0.17**
Renal diseases	6 (1)	2 (1)	4 (1)	1****
Cardiovascular diseases	69 (9)	19 (7)	50 (11)	0.15**
Pulmonary diseases	17 (2)	3 (1)	14 (3)	0.18****
Systemic connective tissue diseases	3 (0.4)	0 (0)	3 (1)	<0.001****
Neurological diseases	12 (2)	6 (2)	6 (1)	0.48**
Hashimoto's thyroiditis	67 (9)	23 (9)	44 (9)	0.83**
Diabetes	15 (2)	4 (1)	11 (2.5)	0.006****

COVID – coronavirus disease; SD – standard deviation; BMI – body mass index; \* Mann–Whitney U test; \*\*  $\chi^2$  test; \*\*\* Kruskal–Wallis test; \*\*\*\* Fisher's exact test.

**Fig. 1.** Relationship between age and the hospitalization due to coronavirus disease 2019 (COVID-19) infection

Among the studied medical staff, 48% of women and 62% of men have been infected with COVID-19 in the past. In 20.6% the course of the disease was asymptomatic, in 73% required only home treatment and in 6.4% required hospitalization. In terms of severity,

there were no statistically significant differences between COVID and non-COVID hospitals.

### Risk of disease according to occupational groups

#### Risk for all hospital staff

A statistically significant relationship between occupational group and risk of infection ( $\chi^2 = 20.05$ ;  $p = 0.0012$ ) was demonstrated for all medical staff. The group of medical staff who were most likely to be infected with COVID-19 were the nurses/paramedics/medical caretakers (60%), orderlies/hospital cleaners (55%) and physiotherapists (53%). Lab workers/technicians/pharmacists were the least likely to be infected (38%).

#### Risk of disease by workplace (COVID compared to non-COVID hospital)

For the medical staff as a whole, the group of employees who were most frequently infected with COVID-19 were nurses/paramedics/medical caretakers (56%) and the group of employees who were least frequently infected were administrative workers (23%). The above relationship was not observed for a COVID-19 hospital. There were no statistically significant correlations in incidence rates between occupational groups ( $p = 0.37$ ) (Table 3).

**Table 2.** Data on regression, confidence intervals for odds ratios, statistical significance for the entire model, and a measure of goodness-of-fit (Nagelkerke pseudo R<sup>2</sup>)

Variable	Model	Estimate	SE	p-value	OR	95% CI	Nagelkerke pseudo R <sup>2</sup>
Age	univariate	0.095	0.03	<0.001	1.10	[1.05; 1.16]	0.12
	multivariate	0.09	0.03	0.001	1.09	[1.04; 1.16]	0.14
Male sex	univariate	–1.26	0.75	0.092	0.28	[0.04; 0.99]	0.03
	multivariate	–0.98	0.77	0.200	0.37	[0.06; 1.37]	0.14

SE – standard error; OR – odds ratio; 95% CI – 95% confidence interval.

**Table 3.** Risk of disease by workplace (COVID-19 hospital compared to non-COVID hospital)

Variable		Workplace						p-value
		administrative workers n (%)	nurses/paramedics/ medical caretakers n (%)	orderlies/ hospital cleaners n (%)	physio- therapists n (%)	lab workers/ technicians/ pharmacists n (%)	treating physicians n (%)	
Non-COVID hospital	COVID-19-positive	7 (23)	86 (56)	6 (46)	7 (44)	31 (38)	73 (43)	0.009*
	COVID-19-negative	24 (77)	68 (44)	7 (54)	9 (56)	50 (62)	98 (57)	
COVID hospital	COVID-19-positive	25 (69)	104 (64)	10 (67)	3 (100)	4 (36)	21 (55)	0.370*
	COVID-19-negative	11 (31)	59 (36)	5 (33)	0 (0)	7 (64)	17 (45)	

COVID-19 – coronavirus disease 2019; \*  $\chi^2$  test.

## Effect of analyzed factors on risk of infection and on COVID-19 infection and the severity of the course of the disease

### BMI and physical activity and the risk of infection and the severity of the course of the disease

For medical staff, the risk of COVID-19 infection was 5% greater with an increase in body mass index (BMI) by 1 unit (OR = 1.05,  $p = 0.004$ ), whereas the risk of COVID-19

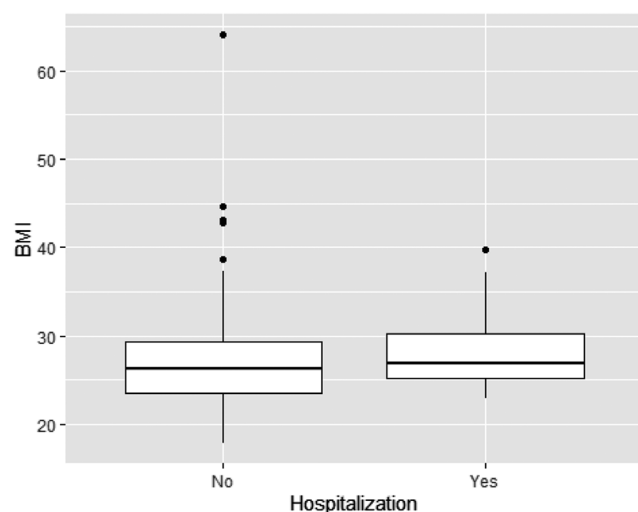
infection was 85% greater for those who were overweight or obese compared to those who were underweight or of normal weight (OR = 1.85,  $p < 0.001$ ). In addition, there was a statistically significant correlation between the severity of infection (no symptoms, home treatment, hospitalization) and BMI ( $\chi^2 = 17.028$ ,  $p < 0.001$ ). Among hospitalized patients, a significantly higher median BMI was noted compared to non-hospitalized patients – 26.8 (IQR 25.3–30.3) kg/m<sup>2</sup> and 26.2 (IQR 23.5–29.4) kg/m<sup>2</sup>, respectively ( $p = 0.043$ ) (Fig. 2).

There was no correlation between the physical activity declared by the persons and the risk of infection and the severity of the course of the disease.

### Impact of comorbidities and smoking on COVID-19 incidence and the course of the disease

Among the medical staff surveyed, diabetes was present in a small group of 15 people (2%). The study results did not show that diabetic patients developed COVID-19 more frequently than those in the general population (Table 1). The influence of diabetes on the risk of hospitalization was observed in the group of COVID-19-positive patients. The history of diabetes was more than 5 times more frequent (OR = 5.5;  $p = 0.049$ ) among hospitalized patients compared to non-hospitalized patients (8.3% and 1.6%, respectively).

We took into account the coexistence of chronic diseases in general and we divided these conditions into cardiovascular, pulmonary and renal disease, systemic connective tissue disease, neurological disease, and Hashimoto's thyroiditis. Participants with chronic diseases were not shown

**Fig. 2.** Box plot of the correlation of body mass index (BMI) and coronavirus disease 2019 (COVID-19) infection. The horizontal line marks the median, the box marks the interquartile range (IQR; Q1–Q3), and the whiskers mark the range of outliers. Empty bubbles are outliers



to be more likely to have COVID-19 than those without these diseases. Among the medical staff in the study group, only 3 persons had systemic connective tissue disease, and all of them had COVID-19, but because of the very small group size, we were unable to draw firm conclusions.

Smoking did not have a significant impact on the incidence of COVID-19 ( $p = 0.58$ ).

#### Association of flu vaccination with COVID-19 infection rates and SARS-CoV-2 course severity

Data on past flu vaccination was available for only a subset of the non-COVID hospital staff. The percentage of those who were vaccinated against flu and became infected was significantly lower than of those who were not vaccinated and became infected ( $\chi^2 = 17.401$ ;

$p < 0.001$ ). The chance of COVID-19 infection was more than twice as high among those not vaccinated against flu (OR = 2.23,  $p < 0.001$ ). The analysis of the severity of infection is difficult because only 5 participants out of 460 analyzed with data concerning flu vaccination were hospitalized (among them 3 were not vaccinated against flu).

#### The correlation of COVID-19 incidence and number of people living in a shared household

There was no statistical relationship between the number of people living in the same household and the frequency of COVID-19 infection and severity. The number of infections and their severity was similar regardless of living with children under 5 and with persons over 65 in the same household (Table 1,4).

**Table 4.** COVID-19 infections among medical staff at a COVID hospital and a non-COVID hospital

Variable	n (%)			p-value
	total (n = 732)	COVID-19-positive (n = 377)	COVID-19-negative (n = 355)	
Age, mean (SD) [years]	47 (12)	47 (12)	47 (12)	0.73*
Sex				
male	164 (22)	103 (62.8)	61 (37.2)	0.001**
female	568 (78)	272 (48)	296 (52)	
BMI, mean (SD)	26 (5)	26.7	25.5	<0.001*
BMI				
underweight	11 (2)	3 (1)	8 (2)	0.001***
normal weight	333 (45)	147 (39)	186 (52)	
overweight	260 (35)	155 (41)	105 (30)	
obesity	128 (18)	72 (19)	56 (16)	
Smoking				
non-smoker	478 (65)	240 (64)	238 (67)	0.05***
former smoker	126 (17)	77 (20)	49 (14)	
passive smoker	19 (3)	12 (3)	7 (2)	
active smoker	109 (15)	48 (13)	61 (17)	
Number of persons in a household				
1	96 (13)	44 (12)	52 (15)	0.47***
2	267 (36)	142 (38)	125 (35)	
>2	369 (51)	191 (51)	178 (50)	
Number of households with children <5 years of age	63 (9)	29 (8)	34 (10)	0.52**
Number of households with persons >65 years of age	61 (8)	33 (9)	28 (8)	0.79**
Chronic diseases	240 (33)	124 (33)	116 (33)	1**
Renal diseases	6 (1)	3 (1)	3 (1)	1****
Cardiovascular diseases	69 (9)	35 (9)	34 (10)	0.87**
Pulmonary diseases	17 (2)	6 (1)	11 (3)	0.16**
Systemic connective tissue diseases	3 (1)	3 (1)	0 (0)	<0.001****
Neurological diseases	12 (2)	6 (2)	6 (2)	1**
Hashimoto's thyroiditis	67 (9)	39 (10)	28 (8)	0.3**
Diabetes	15 (2)	8 (2)	7 (2)	1**
Flu vaccination (460)	235 (51)	83 (40)	152 (59)	<0.001**
Physical activity	323 (44)	159 (42)	164 (46)	0.34**

COVID-19 – coronavirus disease 2019; SD – standard deviation; BMI – body mass index; \*Mann–Whitney U test; \*\* $\chi^2$  test; \*\*\* Kruskal–Wallis test; \*\*\*\* Fisher's exact test.

## Discussion

In the presented study, we showed the relationship between BMI, age and coexistence of diabetes mellitus with the risk of hospitalization due to COVID-19 in the population of medical professionals. We have shown that previous influenza vaccination is a factor that may influence the risk of COVID-19 infection. Other analyzed risk factors, including comorbidities other than diabetes, smoking and socioeconomic factors, did not affect the risk of COVID-19 infection and the course of the disease.

By analyzing the risk of COVID-19 infection among medical staff, it was shown that the risk of COVID-19 infection is 2 times higher among employees of a COVID hospital. The greatest risk of infection was for staff in direct contact with patients, namely nurses/paramedics/medical caretakers, orderlies, hospital cleaners, and physiotherapists. The staff who was not in direct contact with the patient (laboratory technicians, pharmacists) got infected least frequently. In the analysis of incidence patterns in a COVID hospital compared to a non-COVID hospital, this incidence profile was only retained for the non-COVID hospital. The COVID hospital workers showed no significant differences between occupational groups, which can be explained by the high risk of exposure to COVID-19, despite the personal protection methods used. This indicates that the employees of COVID hospitals have a higher risk of contracting the disease without even having direct contact with the patients. It may be related to the exposure to infection from other hospital employees. The presented analysis concerned data obtained before the introduction of universal vaccination against COVID-19, which is also important for the frequency and severity of cases among medical personnel. Because of this, medical staff members require prophylactic methods (vaccination), appropriate personal protective equipment and early diagnosis of possible infection.

Similar to other publications, among our study group, men were more likely to contract COVID-19, which confirms that it is one of the most important non-modifiable risk factors.<sup>16–18</sup> The reason for this tendency has not yet been fully examined. It is suspected that this may be related to the distribution of sex-specific hormones and their effects on specific receptors. As demonstrated by another authors, estradiol, which is present at high levels in women, causes an increase in expression and activity of ADAM17.<sup>19,20</sup> The ADAM17 protein is more highly expressed in the lung and liver, which is associated with the excretion of surface proteins such as ACE2. The ADAM17 activity increased by estradiol results in increased ACE2 solubility in women, which ultimately may be one of the reasons for the reduced incidence of COVID-19 in women compared with men.<sup>20,21</sup> Men were more likely to require intensified treatment, including hospitalization, which is consistent with the literature.<sup>22</sup>

No relationship between COVID-19 incidence and severity of the infection and the number of people living

in the same household was found. We also did not observe such an association when considering children under 5 and elderly people in the household, although infections were more likely if people over 65 lived in the household, which may be due to the small number of such households in our analysis. A meta-analysis conducted by Madewell et al. demonstrated a higher prevalence of COVID-19 infection in households with the elderly than with children.<sup>23</sup>

Another risk factor for more severe SARS-CoV-2 infection is age. Hospitalized patients were on average 9 years older than those with mild or asymptomatic SARS-CoV-2 course. Age-related decline and dysregulation of immune function, i.e., immunosenescence and inflammaging, play a major role in contributing to the increased susceptibility to severe sequelae of SARS-CoV-2 in older age.<sup>24,25</sup>

The epidemiology of COVID-19 incidence based on analyses of large populations shows a clear association with body weight, especially with obesity.<sup>26,27</sup>

In a study conducted in a group of medical staff employed at both COVID and non-COVID hospitals, BMI values were higher for those who had an infection compared to those who were not infected. Consistent with our studies, Popkin et al. found an increased number of COVID-19-positive individuals among obese ones; in addition, individuals with obesity were more likely to be hospitalized.<sup>28</sup> Overweight and obesity were risk factors for hospitalization, mechanical ventilation and death.<sup>29</sup>

Based on a prospective study, Gao et al. confirmed the relationship of BMI with hospitalization and death due to SARS-CoV-2; the relationship was J-shaped and meant a worse prognosis for people with malnutrition.<sup>30</sup> In our study group, only 11 persons had below-normal BMI, and 3 of them had an infection. Determining the cutoff line for BMI at which the risk of COVID-19 infection and/or severity increases is an interesting and important challenge for further research on the epidemiology of COVID-19.

Physical activity is related to weight reduction and redistribution of body fat. It also reduces the risk of metabolic and CVD and depression, and stimulates the immune system. Nevertheless, the studies on the effect of physical activity on the risk of COVID-19 infection and the severity of the course of infection are limited and remain inconclusive, which may be related to the methodology used.<sup>31–33</sup> In the study group, no correlation between the declared level of physical activity and the risk of COVID-19 infection or severity of SARS-CoV-2 was found.

Although diabetic patients are exposed to a higher incidence of various infections, we have not shown that they have an increased frequency of COVID-19 infection and the results of our study confirm the previous observations. However, people with diabetes have a more severe course of SARS-CoV-2 infection. Pro-inflammatory activation of vascular endothelial cells and pro-thrombotic state, co-occurring with diabetes, may be responsible for this. These processes may influence both an increased inflammatory response in the form of a “cytokine storm” in COVID-19

as well as more frequent thromboembolic complications. Hypertension, CVD<sup>7</sup> and chronic obstructive pulmonary disease (COPD) increased the risk of severe COVID-19<sup>34</sup>; however, we did not confirm this observations in our study. In the present study, COVID-19 patients with coexisting diabetes were more likely to require hospitalization, which is consistent with the literature data.<sup>7,35</sup>

The foregoing findings do not allow firm conclusions to be drawn regarding the association between smoking and COVID-19 infection. The results of our study did not show a link between smoking and the risk of developing a disease. The study population was dominated by non-smokers.

The idea of a possible effect of seasonal flu virus vaccination on reducing the risk of COVID-19 infection or a milder course of SARS-CoV-2 was based on the potential role of the nonspecific immune response. We have shown that the risk of contracting COVID-19 is more than twice as high in persons not vaccinated against flu. Our observations confirm the results of the studies published so far. A retrospective analysis of a medical record database showed a beneficial effect of past flu vaccination on the risk of COVID-19 infection in a population older than 65.<sup>36</sup> Also, Candelli et al. indicated the benefits of flu vaccination in the population over 65. In a retrospective analysis of COVID-19 patients, these authors showed a lower risk of death over a 60-day period among those vaccinated.<sup>37</sup> On the other hand, a study conducted on a group of 3500 medical staff showed neither positive nor negative association between COVID-19 infection and flu vaccination during the preceding 5 flu seasons.<sup>38</sup> A broader aspect of the impact of flu vaccination on the course of COVID-19 infection includes mainly, in addition to the nonspecific immune response, a reduction in the risk of co-infection. Flu virus causes increased expression of ACE2 receptors on airway cells, which could potentially worsen SARS-CoV-2 course.

## Limitations of the study

Our observations did not confirm previous data on the association of certain chronic diseases and smoking with the risk of developing COVID-19. However, the presented results should be interpreted with caution, because only 24 people of those who experienced COVID-19 required hospitalization.


## Conclusions

The results of our study showed that the incidence of COVID-19 infection was 2 times higher among COVID hospital medical staff. The highest risk of infection for a non-COVID hospital was for staff who had direct contact with patients, whereas for a COVID hospital, the risk of infection was the same among all hospital staff. Based

on the literature and our study, it appears that gender may influence the pathogenetic mechanisms of COVID-19, the risk of infection and severity of disease, and thus the sequelae. Our study confirmed that BMI value is important for infection risk and severity of COVID-19. In addition, we have shown that while diabetes does not increase the risk of developing SARS-CoV-2, it significantly affects the risk of hospitalization among people infected with COVID-19. We have also confirmed the importance of flu vaccination, i.e., the chance of the infection was more than twice as high among non-vaccinated individuals. The COVID-19 pandemic remains a global problem, despite the tremendous progress that has been made in a short period of time in the diagnosis and prevention of the disease.

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