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THE INFLUENCE OF OBESITY ON THE EVOLUTION OF SARS-COV2 INFECTION

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ABSTRACT

Aim: The issue of body weight has left a deep mark on the COVID-19 pandemic, where this category of patients has been linked to significant increases in morbidity and mortality due to infection. Conversely, due to the restrictions imposed, the pandemic has worsened the situation of overweight people. Our study conducted over a period of one year and five months aims to assess the prevalence of obesity among patients with SARS-COV2 infection in Constanta County.

Material and method: This retrospective study included a number of 177 patients hospitalized with the diagnosis of SARS-COV2 infection in the Clinical Hospital of Pneumoftiziology Constanta.

Results: 2483 of patients confirmed with SARS-COV2 infection were identified in our Department, out of which 302 had a body mass index over 30 kg/m2. We included a random sample of 95 men and 82 women in a database. The average age was 55 years. The most common comorbidities were hypertension (48%), diabetes (13%), and cardiovascular disease (12%). The most common symptoms were fever (67%), cough (58%), dyspnea (37%), and asthenia (29%). The radiological appearance showed the predominance of the moderate form (49%) and the severe form (22%). Antibiotic treatment was based on third-generation cephalosporins (53%), and the evolution was for improvement with a survival rate of 86%. Only one death was reported in our study.

Conclusion: The body mass index influences the evolution of infected cases. Old age, male gender and associated comorbidities are risk factors for a poorer prognosis and greater complications in patients with SARS-COV2.

Keywords: SARS-COV2, COVID-19, obesity, vaccination.

Introduction.

The COVID-19 pandemic has spread around the world when the prevalence of overweight people is on the rise and organizations' goals of lowering the disease rate by 2025 seem increasingly difficult to achieve. Globally, obesity is the fourth leading cause of death, with the latest estimates showing more than 800 million illnesses, with an annual death toll of about 3.4 million (1). From a pathophysiological point of view, the basic mechanism has been mentioned in numerous publications. Chronic subacute inflammation in obesity leads to altered thrombogenic and immune responses to SARS-COV2 infection. The virus invades the cells that express on their surface ACE2 (cells found in adipose, heart, gastrointestinal, lung tissue), resulting in an intense inflammatory state, mediated by IL-6 and called a "cytokine storm" (2-4). Thus, a higher viral load causes a lower action of phagocytosis by macrophages, delayed antigen presentation and development of antibodies, lower activity of T and B lymphocytes, and reduced interferon production (5). According to the latest recommendations of the European

Association for the Study of Obesity (EASO), vaccination is a priority for this category of patients and research should be intensified for the correct management of the situation (6).

Materials and method.

Study design. We performed a retrospective cohort study conducted at the Clinical Hospital of Pneumoftiziology Constanta, which was classified as a second line hospital for care during the pandemic. All patients included in the study were selected between March 14, 2020 and August 3, 2021.

Patients were divided in two groups: patients with confirmed SARS-COV2 infection and normal weight (control group) and patients with confirmed SARS-COV2 infection and obesity (study group). The selection of patients for the study group was made according to inclusion criteria as age over 17, female and male patients, SARS-COV2 infection confirmed by RT-PCR test, body mass index >30 kg/m2, risk factors present, other comorbidities. Exclusion criteria were age under 17, body mass index <30 kg/m2, unconfirmed SARS-COV2 infection.

Informed consent was signed by each patient.

Data collection. We used a data collection form that included: demographic, clinical, paraclinical values, other comorbidities, smoker/ non-smoker/ ex-smoker quality, treatment administered, the form of illness, and condition at discharge. We also used the hospital`s computerized record system and patient observation sheets.

Statistical method. For the statistical analysis, we used the Excel program from the Microsoft Office package, version 2013. We analyzed quantitative variables (age, length of hospitalization), and qualitative variables (sex, smoking status, risk factors, comorbidities, symptoms, laboratory tests, form disease, radiological appearance, treatment administered, complications, evolution). Body Mass Index (BMI) was calculated using the method described by Chirila et al (7). Comparisons between results were made using the T-test. Statistical P values <0.05 were considered significant.

Results.

We identified a number of 2483 of patients confirmed with SARS-COV2 infection within the Department. Out of these, 302 were with a BMI >30 kg/m2. We conducted research on a random sample so that the study included 177 patients aged 17-88 years, of which 95 men and 82 women were included in a database. The study group consisted of 88 patients, and the control group included 89 patients. Of those with obesity included in the study, 53 had grade I obesity, 25 grade II obesity, 9 grade III obesity, 1 grade IV obesity. The percentage of vaccination in the general group was 22.03% (39 patients), and in the studied group 25% (22 patients). Out of these, 36.36% (8 patients) had persistent acute respiratory failure, requiring additional care in 25% of cases (2 patients). Out of the other 66 unvaccinated patients in the study group, 28.79% (19 patients) showed an unfavorable evolution with aggravation of acute respiratory failure, and 26.32% (5 cases) were transferred to an intensive care unit.

Table I: Characterization of groups by age group, sex and smoking status

AGE	COVID-19	COVID-19 & OBESITY	P VALUE
	54.39±18.63 (88-2)	55.74±14.45 (88-22)	0.29
<25	5 (7%)	3 (3%)	0.12
25-45	14 (19%)	18 (17%)	0.43
45-60	28 (37%)	38 (37%)	0.29
>60	28 (37%)	44 (43%)	0.01
SEX			0.33
M	37 (49%)	59 (57%)	0.03
F	38 (51%)	44 (43%)	0.005
SMOKING STATUS			0.21
YES	10 (13%)	9 (9%)	0.69
NO	61 (81%)	75(73%)	3.89
EX-SMOKING	4 (5%)	18(17%)	0.66
Duration of illness			
Days	10.07±5.59 (24-0)	9.14±5 (20-1)	0.16

In our study, obesity was associated with an increased risk of adverse outcomes in patients under 65 years. This was not the case for those aged 65 or over, as the percentage of obesity in this category was low (14.29%). Regarding sex, we detected a slight predominance of men

in the study group (57%). In contrast to a study conducted in China, which found that patients with a history of smoking had a higher risk of disease progression than non-smokers (8), our study showed a higher percentage of non-smokers (73%). The average length of hospitalization was 9 days.

Table II: Characterization of groups according to associated comorbidities

Associated medical conditions	COVID-19	COVID-19 &OBESITY	P VALUE
Hypertension	22(29%)	49 (48%)	0.15
Cardiovascular diseases	4(5%)	12 (12%)	0.71
Diabetes	6 (8%)	13 (13%)	0.8
Thyroid diseases	3 (4%)	13 (13%)	0.71
GI diseases	4 (5%)	3 (3%)	0.0009
Rheumatic diseases	3 (4%)	2 (2%)	0.07
Neurological diseases	4 (5%)	5 (5%)	0.28
Urogenital diseases	2 (3%)	6 (6%)	0.73
Other pulmonary diseases	7 (9%)	11 (11%)	0.42
Liver diseases	3 (4%)	3 (3%)	0.69

In contrast to Anderson M`s New York study, which found that patients with a BMI greater than 35 kg/m2 were more likely to have chronic obstructive pulmonary disease, asthma or cardiopulmonary disease (9), we found in our study that regardless of the degree of obesity, patients had the most common essential hypertension (48%), diabetes (13%), thyroid disease (13%) and cardiovascular disease (12%), similar to Garg S`s article, according to which almost 90% of the hospitalized cases in the USA presented these comorbidities (10). Significant differences were only in the case of gastrointestinal disorders (P=0.0009).

The most common symptoms were: fever (67%), cough (58%), dyspnea (37%), and asthenia (29%), compared to other studies, including one conducted in Turkey according to which the most common symptoms in addition to coughing and fever, there were fatigue, agitation and myalgia (11). In addition, we found significant differences (P <0.05) in cough, dyspnea, myalgia, anosmia, ageuzia, asthenia and arthralgia.

Table III: Characterization of groups according to symptomatology

Clinical presentation	COVID-19	COVID19 & OBESITY	P VALUE
Fever	22 (33%)	45 (67%)	0.47
Chills	13 (17%)	28 (27%)	0.19
Myalgia	17 (23%)	25 (24%)	0.01
Cough	44 (59%)	60 (58%)	0.01
Diarrhea	9 (12%)	14 (14%)	0.84
Dyspnea	27 (36%)	38 (37%)	0.04
Anosmia	16 (21%)	19 (18%)	0.03
Ageusia	12 (16%)	14 (14%)	0.05
Vomiting	9 (12%)	8 (8%)	0.38
Headache	19 (25%)	28 (27%)	0.37
Thoracalgia	6 (8%)	14 (14%)	0.84
Asthenia	19 (25%)	30 (29%)	0.007
Sweating	4 (5%)	17 (17%)	0.57
Vertigo	3 (4%)	7 (7%)	0.75
Arthralgia	3 (4%)	8 (8%)	0.01
Rhinorrhea	1 (1%)	5 (5%)	0.17

Table IV: Characterization of groups according to laboratory data

Biological tests	COVID-19	COVID-19 & OBESITY	**P VALUE**
Hb	13.81±1.32	14.21±1.66	**0.04**
Ht	40.8±3.75	41.5±4.22	0.11
PLT	260432± 117617.7	237772.3± 73424.69	0.6
WBC	7085±3524.17	6383.16±2685.26	0.07
Neutrophils	4861±3335.04	4497.22±2466.49	0.16
Lymphocytes	1592±773.98	1549.79±1075.08	0.35
ESR	39±25.46	40.57±25.01	0.37
Fibrinogen	469±175.93	479.12±154.04	0.43
LDH	476±277.4	496.41±228.23	0.28
CRP	133±259.3	62.92±91.63	0.09
GOT	39±25.81	43.39±30.59	0.19
GPT	41±31.97	45.19±30.42	0.19
D-dimer	1±3.39	0.54±0.68	0.09
Urea	37±18.88	37.48±15.01	0.47
Creatinine	1±0.25	1.03±0.21	0.43
Glycemia	119±60.8	138.59±97.31	0.1

Similar to a study by Kumar and colleagues (12), the serum hemoglobin concentration decreases during the disease due to its affinity for oxygen. In this sense, we found significant links between the two groups (P=0.04).

Table V: Characterization of groups according to antibiotic treatment administered during hospitalization

Treatment	COVID-19	COVID-19&OBESITY	P value
Cefort	34 (45%)	55 (53%)	0.029
Augmentin & Zinnat	14 (19%)	11 (11%)	0.05
Doxycycline	13 (17%)	19 (18%)	0.01
Azithromycin	13 (17%)	15 (15%)	0.05
Meropenem	3 (4%)	7 (7%)	0.44
Others	14 (19%)	17 (17%)	0.13

Similar to an article in Africa (13), our study noted the use of broad-spectrum antibiotic treatment with the highest share being third-generation cephalosporins (Cefoperzone, 53%), followed by a representative of the tetracycline class (Doxycycline, 18%), where we also found significant differences.

Regarding antiviral treatment: 24 patients received Remdesivir, of which 13 were obese, 78 patients received Favipiravir, of which 50 were obese; immunosuppressive therapy: 6 patients received Tocilizumab, of which only one case was obese; a combination of antiretroviral and hydroxychloroquine received 74 patients, of whom 43 were obese.

Table VI: Characterization of groups according to the form of the disease

Severity	COVID-19	COVID-19&OBESITY	P VALUE
Asymptomatic	4 (4%)	2 (2%)	0.1
Mild	20 (22%)	22 (21%)	0.06
Moderate	27 (36%)	50 (49%)	0.07
Moderately-severe	6 (8%)	6 (6%)	0.16
Severe	17 (19%)	23 (22%)	0.17

There were 128 patients under the age of 65 and 49 patients aged 65 years or older. Among those under 65, 83 patients (64.84%) had a moderate/severe form of SARS-COV2 infection, while 45 (35.16%) had mild forms. Of those over the age of 65, 87.76% had moderate/severe illness. In the general group, we did not find significant differences regardless of the form of infection.

Table VII: Characterization of groups according to LDH value at admission and form of disease

Severity	COVID-19	COVID-19&OBESITY	P VALUE
	477±275.8819	133±221.5095	
Asymptomatic/ Mild	320	104	0.0001
Moderate/ Moderately-severe	454	111	0.0002
Severe	612	224	0.09

Table VIII: Characterization of groups according to LDH value in dynamics and form of disease

Severity	COVID-19	COVID-19&OBESITY	P VALUE
Asymptomatic/ Mild	308	106	0.006
Moderate/ Moderately-severe	521	119	0.07
Severe	789	238	0.51

Regarding the degree of development of hemolysis, we followed the LDH value at admission and in dynamics. Contrary to an article in China that LDH values were severely associated (14), the results of our study showed an insignificant increase compared to the control group.

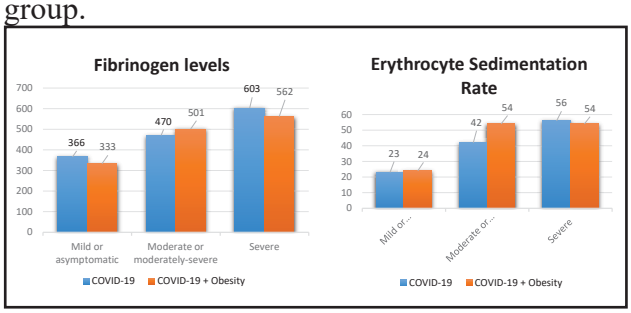


Figure 1: Characterization of groups according to the level of inflammatory markers- Fibrinogen (left), ESR (right)

Unlike McNeill`s article, according to which obese patients showed significantly higher values of inflammatory markers (15), the results of our study did not show significant differences.

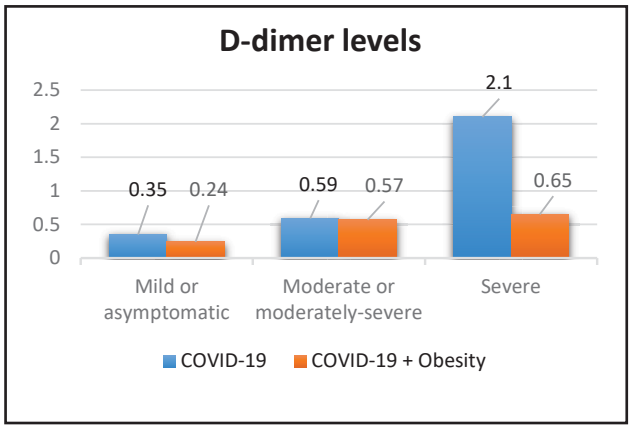


Figure 2: Characterization of groups according to the level of D-dimers

In contrast to Mehanna`s article that high levels of D-dimers have been shown in patients with COVID-19 and obesity (16), the results of our study did not show significant differences.

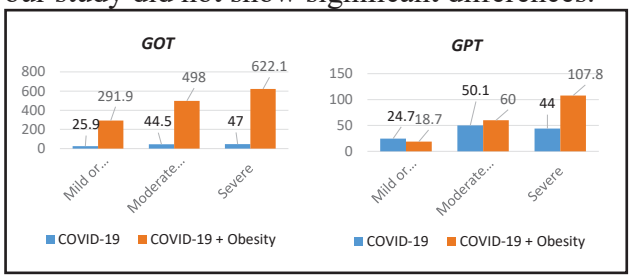


Figure 3: Characterization of groups by transaminase level: GOT (left) and GPT (right)

In our study we observed significant increases in serum transaminases, similar to other articles, including Wu (17).

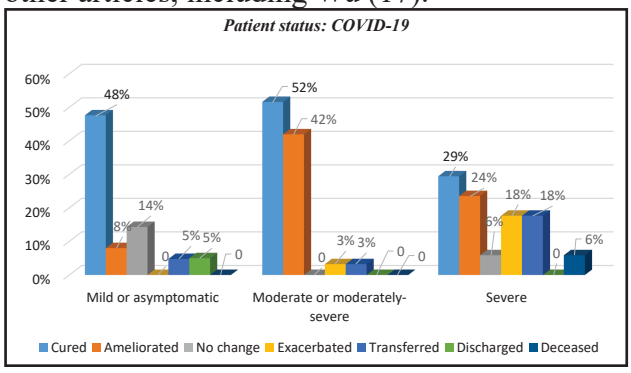


Figure 4: Evolution of patients in the control group

In our study, we observed an improvement in most cases, mainly in the moderate and moderate-severe form (46%), followed by the severe forms with 43%. In addition, 17 patients were transferred to other hospital units for additional care, 9 of them with aggravated clinical status, the others remaining hospitalized. Only one death was reported, unlike other articles that demonstrated increased morbidity and mortality in patients with obesity and SARS-COV2 infection.

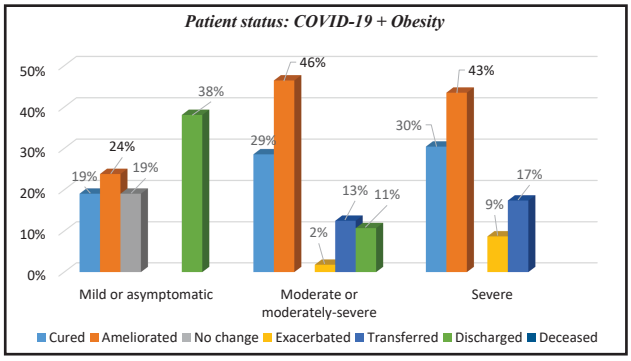


Figure 5: Evolution of patients in the study group

Discussions

Parameters assessment is important in stratifying the risk of patients with SARS-COV2 infection, so unlike a study conducted in Denmark, we found the following: male sex, age up to 65 years, comorbidities such as essential hypertension, diabetes, cardiovascular and thyroid disorders have been associated with an increased risk of adverse outcomes of severe SARS-COV2 infection; there were no significant differences in lymphocyte value; inflammation blood markers: although all patient had the inflammatory syndrome, the value of leukocytes, fibrinogen, and C-reactive protein was higher in patients with a BMI between 30 and 34.99 kg/m2 (grade I obesity). Regardless of the type and severity of the symptoms of infection, in dynamics, patients with obesity have prothrombotic status due to chronic inflammation and impaired fibrinolysis. Thus, we consider accurate markers to predict the risk of a negative prognosis as D-dimers, and in our study, we did not find significantly higher values. On the other hand, the data support a higher prevalence of elevated levels of marker of liver damage, both at admission and in evolution, and our study also demonstrated this fact. Also, another factor that defines a negative prognosis is obstructive sleep apnea syndrome, caused by acute respiratory distress and obesity-hypoventilation syndrome, and in this regard, our study showed that patients needed long-term

oxygen therapy at home, dyspnea resting and persisting at discharge. Medical imaging plays a decisive role in the management of the disease based on which it is possible to intervene early for diagnosis and treatment, so our study showed a high risk of moderate/severe forms compared to the control group. Regarding the treatment administered, according to the guidelines, broad-spectrum antibiotics were mainly used, the evolution of the disease in most cases being for improvement, and only one death was reported. Although the vaccination rate was relatively low, the vaccine proved to some extent effective in the study group.

Conclusions

Obesity and its associated comorbidities remain a significant determinant in the results of SARS-COV2 infection, and data may vary from study to study, depending on the epidemic impact of the disease. As the pandemic progressed, the medical units also improved their level of care. The doctors developed their knowledge and experience in clinical management and increased awareness among patients. Our research has highlighted the need for interdisciplinary collaboration to improve the care of patients with this comorbidity, implement weight loss strategies, follow more closely, and treat other comorbidities.

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References.

1. Townsend N, Vogel C, Allender S, Halloran A, Sorensen K, Wilding J, et all. World Health Organization European Regional Obesity Report. Copenhaga (Danemarca), 2022. p. 1-2.
2. Bolsoni-Lopez A, Furieri Barros L, Cardoso Alonso Vale MI. Obesity and Covid-19: a reflection on the relationship between pandemics. Rev Gaucha Enferm. 2021; 42(spe):e20200216. doi:https://doi.org/10.1590/1983-1447.2021.20200216
3. Ritter A, Kreis NN, Louwen, Yuan J. Obesity and COVID-19: Molecular mechanisms linking both pandemics. PubMed Central. 2020;21(16): 5793. doi: 10.3390/ijms21165793
4. Sudhakar M, Winfred SB, Meiyazhagan G, Venkatachalam DP. Mechanisms contributing to adverse outcomes of COVID-19 in obesity. Mol Cell Biochem. 2022;477, p.1155-1193. Doi: https://doi.org/10.1007/s11010-022-04356-w
5. Farzi R, Aghbash PS, Eslami N, Azadi A, Shamekh A, Hemmat N, et all. The role of antigen-presenting cells in the pathogenesis of COVID-19. PubMed Central. 2022;233:153848. doi: 10.1016/j.prp.2022.153848
6. Dicker D, Golan R, Baker JL, Busetto L, Fruhbeck G, Goossens GH, et all. Vaccinating people with obesity for COVID-19: EASO call for action. PubMed Central. 2021;14(3): 334-335. doi: 10.1159/000516524
7. Chirila S, Hangan T, Gurgas L. BMI Calculator in Microsoft Excel. ARS Medica Tomitana. 2011;17(4):70-7.
8. Liu W, Tao ZW, Wang L, Yuan ML, Liu K, Zhou L, et all. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. PubMed Central. 2020;133(9), p.1032-1038. Doi: 10.1097/CM9.0000000000000775
9. Anderson M, Geleris J, Anderson D, Zucker J, Nobel YR, Freedberg D et all, Body Mass Index and risk for intubation or death in SARS-COV2 Infection. American College of Physicians Journals. 2020;173(10), p.782-790. Doi: https://doi.org/10.7326/M20-3214
10. Garg S, Kim L, Whitaker M, Cummings C, Holstein R, Prill M et all. Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 – COVID-NET, 14 states, March 1-30. MMWR Morb. Mortal. Wkly Rep. 2020;69(15):458–464. DOI: 10.15585/mmwr.mm6915e3
11. Utku AC, Budak G, Karabay O, Guclu E, Okan HD, Vatan Asli. Main symptoms in patients presenting in the COVID-19 period.

Scott Med J, 2020:0036933020949253. doi: 10.1177/0036933020949253
12. Kumar A, Arora A, Sharma P, Anikhindi SA, Bansal N, Singla V, et all. Clinical features of COVID-19 and factors associated with severe clinical course: A systematic review and meta-analysis. SSRN. 2020. doi: 10.2139/ssrn.3566166
13. Adebisi YA, Jimoh ND, Ogunkola IO, Uwizeyimana T, Olayemi AH, Ukor NA, et all. The use of antibiotics in COVID-19 management: a rapid review of national treatment guidelines in 10 African countries. Trop Med Health. 2021;49:51. Doi: https://doi.org/10.1186/s41182-021-00344-w
14. Yan H, Vijay A, Jiang F, Zheng N, Hu Y, Ye H, et all. Serum glucose, lactate dehydrogenase and hypertension are mediators of the effect of body mass index on severity of COVI-19. Endocrinol Diabetes Metab. 2021;4(2): e00215. Doi: 10.1002/edm2.215
15. McNeill JN, Lau ES, Paniagua SM, Liu EE, Wang JK, Bassett IV, et all. The role of obesity in inflammatory markers in COVID-19 patients. Obes Res Clin Pract. 2021;15(1): 96-99. doi: 10.1016/j.orcp.2020.12.004
16. Mehanna O, Askary AE, Ali E, Esawy BE, FathAlla T, Gharib AF. Impact of obesity and its associated comorbid conditions on COVID-19 presentation. Diabetes Metab Syndr Obes. 2021;14: 409-415. doi: 10.2147/DMSO.S287779
17. Wu S, Zhou K, Hebert AM, Bena J, Kashyap S. Impact of metabolic Syndrome on severity of COVID-19 illness. Met Syndr and Related Disorders. 2022; 20(4): 191-198. Doi: https://doi.org/10.1089/met.2021.0102