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Research article

The Influence of Climate on Critically Ill Pregnant COVID-19 Patients, as Revealed by the Inflammation Indexes, in Spring versus Autumn 2021 Infection

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Abstract: (1) Background: Seasonality is an important environmental factor that influences immune responses (2) Methods: In a retrospective study, we included all pregnant patients admitted to the Elena Doamna Obstetrics and Gynecology Hospital with a critical form of COVID-19 infection between 1 January and 1 December 2021. The blood counts collected on the specific A, H and E Brixia score- collection days, or the ones collected closest to those days, were considered in our study. We also studied the differences between the two groups regarding the inflammation indexes exhibited on those specific days: A (admittance), H (highest Brixia score), and E (end of hospitalization). (3) Results: The values of NLR, dNLR, SII, and AISI are significantly higher and IIC is significantly lower for the spring group versus the autumn group, especially on the H and E Brixia score-collection days. (4) Conclusions: These results suggest that severe-COVID-19 inflammation was significantly higher in the spring of 2021 in Romania than in autumn 2021, in regard to pregnant patients.

Keywords: severe COVID-19; pregnancy; spring; autumn; NLR; MLR; PLR; SII; SIRI; AISI.

1. Introduction

There was an amplification effect of the heat wave events on the magnitude of the severe COVID-19 outbreak, showing that climate change is leaving to more frequent extreme climate events and an increasing number of infectious diseases [1]. Meteorologal variables are the second most important determinants for COVID-19 transmission, especially ultraviolet radiation and temperature, but the associations with daily cases varied across different climate zones [2]. The increase in maximal temperature from winter to summer had strong correlation with the number of newly infected cases.[3]. COVID-19 transmission rate was lower in warm and wet seasons than in dry and cold ones. [4].

Seasonality is an important environmental factor that influences immune responses [5]. Seasonal variation in concentrations of fibrinogen and thrombin generation could explain approximately 11% of their total variations.[6]. Markers of systemic inflammation decreased significantly in summer compared to winter [7]. Even the risk of chronic inflammatory lesion of the placenta was 16% higher in the autumn and winter as compared to the summer [8].

COVID-19 can result in prolonged systemic inflammation in patients with the disease [9]. We observed increased inflammation rates, and increased complement and antibody activities, in severe versus non-severe forms of COVID-19 in pregnant patients [10]. Pregnancy alone was a risk factor for severe-COVID-19 disease, since more pregnant COVID-19 patients were admitted to the intensive care unit (ICU) and required invasive ventilation, in comparison to non-pregnant COVID-19 patients of a reproductive age [11]. On the other hand, according to Santa [12], the physiological conditions of pregnancy appear to favor COVID-19 infection and, at the same time, seem to protect pregnant patients from contracting severe forms of infection.

Compared to the pre-Delta variant period, the risk of ICU admissions during the Delta variant period was 41% higher for women of a reproductive age, and the risk of death was 3.33 times greater than the risk during the pre-Delta-variant period among women of a reproductive age [13]. However, few studies have examined the difference between severe cases of pregnant COVID-19 patients in spring versus autumn 2021 (when the Alpha, instead of the Delta, variant dominated in Romania).

The systemic inflammation indices NLR (neutrophil to lymphocyte ratio), SII (systemic inflammatory index), and SIRI (systemic inflammatory response index) presented a strong predictive power for severe-COVID-19 cases, invasive mechanical ventilation support, and low survival probability during hospitalization in Mexican patients [14], without specifying exactly when the indices were collected. On the other hand, according to Carranza Lira [15], there was no difference in the NLR (neutrophil to lymphocyte ratio) between groups and only the PLR (platelet to lymphocyte ratio) was significantly higher in the severe-disease group compared to the non-severe-disease group of pregnant COVID-19 patients. In the present study, we intend to study these indexes for pregnant Romanian, severe-COVID-19 patients.

The admission and day 7 NLR, dNLR (derived neutrophil to lymphocyte ratio), and PLR values had no prognostic relevance for the events occurring late during hospitalization; however, day 14 NLR, dNLR, and PLR values were independent predictors for progression to septic shock and mortality in intensive care unit patients [16]. According to other studies [17], severe cases of pregnant COVID-19 patients had higher NLR values, only upon admission, than non-severe-disease patients.

The Brixia score, which evaluates the extent of changes in the lungs, was used as a time marker. The aim of this study is to assess the seasonal variation of the inflammation indexes in three specific periods during patients' hospitalization in an intensive care unit: upon admission (Brixia A day), the greatest lung involvement (Brixia H day), and at the end of hospitalization (Brixia E day), in the spring versus autumn group of pregnant, severe-COVID-19 patients. The inflammation indexes studied were the NLR, dNLR, MLR (monocyte to lymphocyte ratio), PLR, SII, SIRI, AISI (aggregate index of systemic inflammation), MCVL (mean corpuscular volume to lymphocyte ratio), and IIC (cumulative inflammatory index).

2. Materials and Methods

All pregnant patients admitted to the Elena Doamna Obstetrics and Gynecology Hospital with a critical form of COVID-19 infection between 1 January and 1 December 2021 were included the retrospective study. Patients who received conventional chest X-rays in another healthcare unit before/during admission to our hospital, where only the results were available and not the X-ray images, were excluded from the study. Patients were considered present a critical form of COVID-19 when they required admission to the ICU

due to having at least one of the following symptoms: severe dyspnea, oxygen saturation below 95%, extreme fatigue, and loss of state of consciousness. All pregnant patients admitted to the hospital were tested by RT-PCR upon admittance, and the positive-test patients were considered for the present study according to the severity of the disease. However, most severe cases of pregnant COVID-19 patients were directed to us from all over the county, because we are a hospital dedicated to obstetrics and gynecology patients with COVID-19; these patients already had a RT-PCR-positive test and arrived by ambulance with respiratory support [10].

Patients underwent conventional chest X-rays with abdomen shielding for fetal protection. A Siemens Polymobil 10 mobile X-ray installation was used. The Brixia scores were calculated for every chest image, and the following scores were considered: A score (upon admittance); H and L scores (the highest and lowest scores throughout the hospitalization period); and E score (the score at the end of hospitalization). For patients who received only one chest examination, the H score was considered. Since we had very few patients for which the L score was not the E or A score, we eliminated the L Brixia score from this study. The Brixia score was calculated by dividing the image of each lung into three zones, from the top of the lung to its base, and each zone was designated a number from 0 to 3 as follows: 0—normal image; 1—interstitial opacities; 2—interstitial and alveolar opacities, predominantly interstitial; and 3—interstitial and alveolar opacities, predominantly alveolar. The numbers collected from all quadrants were added, and a final Brixia score ranging from 0 to 18 was obtained [18].

The blood values for the specific A, H, and E Brixia score-collection days, or the closest ones to those days, were considered. We studied the differences between the two groups regarding the inflammation indexes on those specific days: A, H, and E [18].

The inflammation indexes studied were: NLR, dNLR, MLR, PLR, SII, SIRI, AISI, MCVL, and IIC.

We calculated the NLR as the absolute count of neutrophils divided by the absolute count of lymphocytes. We calculated the MLR as the absolute count of monocytes divided by the absolute count of lymphocytes. We calculated the PLR as the absolute count of platelets divided by the absolute count of lymphocytes. We calculated the dNLR as the absolute count of neutrophils divided by the difference between the absolute count of white blood cells and the absolute count of neutrophils. We calculated the SII as the absolute count of neutrophils multiplied by the absolute count of platelets divided by the absolute count of lymphocytes. We calculated the SIRI as the absolute count of neutrophils multiplied by the absolute count of monocytes divided by the absolute count of lymphocytes. We calculated the AISI as the absolute count of neutrophils multiplied by the absolute count of monocytes multiplied by the absolute count of platelets divided by the absolute count of lymphocytes. We calculated the MCVL as the mean corpuscular volume divided by the absolute count of lymphocytes. We calculated the IIC as the mean corpuscular volume multiplied by width of erythrocyte distribution multiplied by the absolute count of neutrophils divided by one thousand times the absolute count of lymphocytes.

We divided the patients into two groups: the spring group (group 1, n = 11) hospitalized from January to May 2021, separated by a two-month period absent of severe cases from the autumn group (group 2, n = 7) hospitalized from August to the end of November 2021. This corresponded to the dominance of the Alpha variant of SARS-CoV-2 in spring and the Delta variant in autumn 2021 [19] in Romania. The median age was 32 (27, 37) years old in group 1 and 34 (30,37) years old in group 2 ($p = 0.55$) [18].

Statistical analysis was performed using SPSS version 18 software (SPSS Inc., Chicago, IL, USA). For descriptive measures, we computed the mean, standard deviation, and median and quartiles 1 and 3 (because the variables followed a non-normal distribution). To compare the data, the nonparametric Mann–Whitney U test was performed. The standard significance cut-off at $p = 0.05$ was used to determine our hypothesis [18].

3. Results

3.1. Brixia A Day

On the Brixia A day, upon admission, we obtained a significantly higher dNLR value for the spring group; however, all the inflammation indexes were elevated, except for MCVL and IIC, which *decrease* during the inflammation period (Table A1) and remained considerably low (Table 1).

Table 1. Inflammation indexes on the Brixia A day (day of the first chest X-ray upon admission) for the two groups: median (Quartile1 = Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 11	Autumn Group n = 7	*p*
NLR	3.64 (2.94; 4.85)	3.34 (1.81; 3.94)	0.23
dNLR	1.89 (1.21; 2.32)	1.24 (0.51; 1.52)	0.04
MLR	1.19 (0.76; 1.91)	2.17 (1.50; 3.37)	0.07
PLR	165.16 (87.27; 250.53)	156.25 (118.75; 198.14)	0.81
SII	764.29 (454.48; 1087.26)	534.37 (409.37; 802.50)	0.36
SIRI	3.81 (3.00; 18.33)	6.50 (6.07; 7.89)	0.47
AISI	879.74 (454.48; 5414.56)	1367.31 (1072.50; 1688.73)	0.74
MCVL	76.40 (46.24; 88.18)	79.65 (50.02; 90.34)	0.88
IIC	4.17 (3.49; 5.85)	3.90 (2.16; 4.67)	0.36

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

3.2. Brixia H Day

On the Brixia H day, the day that presented the highest Brixia score, which represents the greatest lung involvement, although most inflammation indexes were very elevated, and the MCVL and IIC scores were very low, there was a significantly higher elevation apparent for the spring group, regarding the dNLR, SII, and AISI values (Table 2)

Table 2. Inflammation indexes on the Brixia H day (day of the highest Brixia score on chest X-ray) for the two groups: median (Quartile1= Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 11	Autumn Group n = 7	*p*
NLR	4.28 (3.72; 6.54)	2.12 (0.61; 4.06)	0.08
dNLR	1.80 (1.38; 2.49)	0.72 (0.15; 1.52)	0.01
MLR	1.47 (1.19; 1.91)	2.22 (1.66; 2.96)	0.13
PLR	200.75 (105.96; 216.66)	143.91 (111.53; 171.87)	0.53
SII	1118.66 (1006.65; 1573.96)	477.95 (203.00; 670.31)	0.01
SIRI	10.93 (7.68; 15,.68)	5.51 (4.05; 6.50)	0.08
AISI	2782.21 (2061.88; 3711.55)	1331.48 (1072.50; 1699.79)	0.04
MCVL	49.79 (34.69; 70.95)	58.15 (32.53; 90.34)	0.81
IIC	4.97 (4.31; 7.36)	2.52 (0.71; 4.80)	0.08

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

3.3. Brixia E Day

On the Brixia E day, at the end of hospitalization, even though the inflammation indexes remained elevated, and the MCVL and IIC scores were very low, there was significantly higher elevation activity in the spring compared to the autumn group, regarding the NLR, dNLR, SII, and IIC values (Table 3).

Table 3. Inflammation indexes on the Brixia E day (day of the final chest X-ray prior to the end of hospitalization) in the two groups: median (Quartile1= Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 11	Autumn Group n = 7	*p*
NLR	3.28 (2.03; 5.64)	0.93 (0.33; 2.16)	0.02
dNLR	1.06 (0.91; 2.06)	0.28 (0.13; 0.78)	0.003
MLR	1.46 (1.00; 2.29)	1.95 (1.52; 2.60)	0.22
PLR	176.25 (114.84; 229.44)	132.63 (125.78; 158.16)	0.57
SII	1168.35 (692.44; 1674.15)	353.96 (179.35; 518.25)	0.008
SIRI	11.02 (5.90; 17.82)	4.89 (2.01; 7.18)	0.10
AISI	3488.63 (1853.87; 5947.37)	1495.20 (1076.15; 2578.24)	0.14
MCVL	39.16 (31.30; 44.71)	35.74 (28.94; 45.20)	0.85
IIC	3.92 (2.29; 6.36)	1.09 (0.39; 2.58)	0.02

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

3.4. Patients Released for Homecare

Some patients from the spring group were released for homecare; others were transferred to other hospitals, such as the intensive care unit in the Respiratory Disease Hospital, Infectious Disease Hospital, or Nephrology Hospital; while all the patients in the autumn group were released for homecare [11].

When comparing the inflammation indexes for the homecare-release patients in the spring (n = 4) [11] versus autumn (n = 7) group [11], there was no significant difference present on the Brixia A (Table 4), H (Table 5), and E (Table 6) days, except for the SII on the Brixia H day ($p = 0.038$).

Table 4. Inflammation indexes on the Brixia A day (day of the first chest X-ray upon admission) in the two groups of released-for-homecare patients: median (Quartile1= Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 4	Autumn Group n = 7	*p*
NLR	3.00 (2.48; 3.77)	3.34 (1.81; 3.94)	0.909
dNLR	1.51 (0.65; 2.32)	1.24 (0.51; 1.52)	0.305
MLR	0.98 (0.62; 2.33)	2.17 (1.50; 3.37)	0.210
PLR	148.03 (127.02; 182.28)	156.25 (118.75; 198.14)	0.909
SII	532.24 (454.48; 792.94)	534.37 (409.37; 802.50)	0.909
SIRI	3.00 (2.60; 12.08)	6.50 (6.07; 7.89)	0.304
AISI	454.48 (367.24; 3853.70)	1367.31 (1072.50; 1688.73)	0.425
MCVL	72.73 (46.24; 80.50)	79.65 (50.02; 90.34)	0.569
IIC	3.49 (2.91; 4.43)	3.90 (2.16; 4.67)	0.909

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

Table 5. Inflammation indexes on the Brixia H day (day of the highest Brixia score on chest X-ray) in the two groups: median (Quartile1= Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 4	Autumn Group n = 7	*p*
NLR	4.04 (3.07; 5.92)	2.12 (0.61; 4.06)	0.186
dNLR	2.03 (1.05; 2.84)	0.72 (0.15; 1.52)	0.058
MLR	1.37 (0.91; 2.80)	2.22 (1.66; 2.96)	0.257
PLR	174.00 (130.19; 200.75)	143.91 (111.53; 171.87)	0.450
SII	1052.15 (891.67; 1335.81)	477.95 (203.00; 670.31)	0.038
SIRI	12.75 (6.22; 19.64)	5.51 (4.05; 6.50)	0.450
AISI	2842.91 (1306.67; 7157.54)	1331.48 (1072.50; 1699.79)	0.345
MCVL	48.68 (36.00; 71.00)	58.15 (32.53; 90.34)	0.850
IIC	4.70 (3.57; 6.88)	2.52 (0.71; 4.80)	0.186

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

Table 6. Inflammation indexes on the Brixia E day (day of the final chest X-ray prior to the end of hospitalization) in the two groups: median (Quartile1= Percentile 25; Quartile3 = Percentile 75).

Index	Spring Group n = 4	Autumn Group n = 7	*p*
NLR	1.96 (1.51; 2.41)	0.93 (0.33; 2.16)	0.317
dNLR	0.91 (0.88; 0.94)	0.28 (0.13; 0.78)	0.096
MLR	1.16 (0.60; 1.72)	1.95 (1.52; 2.60)	0.182
PLR	136.25 (111.42; 161.08)	132.63 (125.78; 158.16)	0.739
SII	692.44 (538.02; 846.85)	353.96 (179.35; 518.25)	0.182
SIRI	7.56 (2.01; 13.10)	4.89 (2.01; 7.18)	0.867
AISI	2657.00 (715.57; 4598.43)	1495.20 (1076.15; 2578.24)	1.000
MCVL	31.30 (25.87; 36.73)	35.74 (28.94; 45.20)	0.505
IIC	2.29 (1.77; 2.81)	1.09 (0.39; 2.58)	0.314

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

4. Discussion

Environmental factors were found to influence COVID-19 through four major interlinking mechanisms: increased risk of preexisting conditions associated with disease severity; immune system impairment; viral survival and transport; and behaviors that increase viral exposure. [20]. There was lower mobility rate in response to hot summer temperature [21]. Podavalenko [22] reported most cases of COVID-19 registered in the cold season, the least in June-August, with the maximum rate of hospitalization and mortality in September-December 2021. Wind speed, air temperature and solar radiation have positive and strong correlations with the confirmed cases and deaths in the cold season (autumn and winter) [23].

Transmission of SARS-CoV-2 may increase independently of temperature and specific humidity in periods with low levels of population immunity [24]. Seasonal variations in peripheral inflammatory markers were observed during pregnancy, when they peaked in the spring and had a trough in the autumn[25], which was confirmed by us.

In a previous study conducted on severe-case, pregnant COVID-19 patients, we observed no differences between the spring and autumn months, including maternal and fetal outcomes, except for the number of patients released for homecare and the number of days following admission when delivery occurred [18]. Furthermore, we showed that

there was a dramatic decrease in neutrophils, from the spring to autumn group at the end of the hospitalization period, suggesting that the infection in autumn determined a depletion of neutrophils; on the contrary, the spring variant determined a physiologic increase in the white blood cell count and neutrophils present during infection. In the present work, we studied the underlying inflammation indexes, in order to explain the differences between the maternal outcomes.

COVID-19 patients had higher levels of NLR, MLR, PLR, and dNLR than healthy subjects [26]. The neutrophil to lymphocyte ratio (NLR) significantly increased in pregnant patients with COVID-19 [27]. In the severe-COVID-19, pregnant patients, the neutrophil count (and IL-6) was significantly higher than in the non-severe-disease group [28]. A normal white cell count for COVID-19 patients in the intensive care unit may be misleading, while the neutrophil count, NLR, and dNLR are good prognosticators of the clinical outcome [29].

Dynamic changes in the NLR and dNLR independently predict the necessity of invasive mechanical ventilation and death rates for critically ill COVID-19 patients [16]. We agreed that the NLR and dNLR values increased during all the ICU hospitalizations for both groups of severe-COVID-19, pregnant patients, which was also in accordance with the results obtained by other authors [20-22,31-41].

Although all the NLR values increased for all three Brixia score-collection days, there was a significant difference in the increase at the end of hospitalization (Brixia E day) in the spring group compared to the autumn group. This suggested that inflammation was greater in the spring group, which was confirmed by the fact that many of the patients were transferred to other specialized intensive care units (respiratory/infectious/nephrology), and few were released into homecare in the spring group, while all patients in the autumn group were released into homecare.

The dNLR value was significantly higher in the spring group for all the three days, Brixia A, H, and E days, showing that inflammation was much greater in the spring group, and this evolution was even more obvious than that of the NLR.

Corroborating these values with the demonstration of Ardestani [26] that showed that the NLR and dNLR are reliable markers used to evaluate the severity of COVID-19, this means that the spring group had a more severe form of COVID-19, which was confirmed by the additional number of hospitalization days[19]

We agreed that the monocyte to lymphocyte ratio (MLR) significantly increased in pregnant patients with COVID-19 [26,29], and had a powerful predictive value for COVID-19 severity [32]. We also obtained increased MLR values for both groups, without any significant differences between the groups.

We agreed that the platelet to lymphocyte ratio (PLR) significantly increased in patients with COVID-19 [29,38]. We also obtained increased PLR values for all severe cases of pregnant COVID-19 patients; therefore, we did not agree with the authors who stated that the PLR could not predict poor clinical outcomes [37] and that the PLR was not an independent risk factor for disease severity and death for COVID-19 patients [40].

The SII is a newly diagnosed biomarker in patients with severe COVID-19 [43]. High SII values in early pregnancy could also be used as an additional marker for the prediction of miscarriage [44]. We confirmed that the SII values were significantly higher in complicated cases of pregnant COVID-19 patients [45]. We also obtained increased SII values for both groups of patients. Dynamic changes in SII values independently predict the necessity for invasive mechanical ventilation and death outcomes for critically ill COVID-19 patients [30]. We partly confirmed that, on the Brixia A day, patient numbers 6 and 11 in the spring group, who presented the highest SII values (3136.87 and 2452.06, respectively), did not require mechanical ventilation, while patients with half the SII values, which were still high, did require ventilation (patients 1, 3, and 6 in the spring group). The case was the same for patient 3 in the autumn group, who required ventilation. On the Brixia H day, we agreed with the results obtained by Moisa [30], which considered patients in the spring group, where mechanical ventilation was associated with very-high SII values. As

for the autumn group, the only patient who required mechanical ventilation had the lowest SII value (203). On the Brixia E day, the patient with the highest SII value (2040.11), the same patient (11) in the spring group, did not require mechanical ventilation. Moreover, the SII values were significantly higher in the spring compared to the autumn group, both on Brixia H and Brixia E days, suggesting that inflammation was greater on these days in the spring compared to the autumn group.

We agreed that the SIRI values were significantly higher for complicated cases of pregnant COVID-19 patients [45]. All severe-COVID-19, pregnant patients in both groups had elevated values of SIRI, without displaying any significant differences between them.

We agreed that the AISI was a predictor of severity and ICU admission for COVID-19 patients [46]. All severe-COVID-19, pregnant patients had elevated AISI levels. Moreover, AISI was significantly higher in the spring compared to the autumn group on Brixia H day, displaying the greatest lung involvement, showing that the spring group had a more severe form of severe COVID-19.

We agreed that the mean corpuscular volume to lymphocyte ratio (MCVL) and cumulative inflammatory index (IIC) decreased and predicted complications during the COVID-19 pandemic [47]. Our patients had decreased MCVL and IIC values, and presented a severe form of COVID-19. There was no significant difference in the MCVL values between the spring and autumn groups. The IIC values were oddly significantly higher in the spring than in the autumn group on Brixia E day, at the end of the hospitalization period—these results did not make sense. IIC did not correlate with the other inflammation indexes, which suggested higher inflammation rates in the spring group. The IIC did not explain the necessity for numerous patients from the spring group to be transferred to other ICUs, while all the patients in the autumn group were released into homecare.

This study presented several limitations. First, the number of severe-COVID-19, pregnant patients that we assessed was very small, and a larger study on an increased number of patients would be required to confirm these values. Second, other studies, conducted in other countries, would be required in order to determine whether other populations of pregnant patients with a severe form of COVID-19, presented the same variations.

5. Conclusions

There was seasonal variation in inflammatory indexes. The values of NLR, dNLR, SII, and AISI were significantly higher and of IIC were significantly lower in the spring versus the autumn group, suggesting that severe-COVID-19 inflammation cases were significantly higher in the spring of 2021 in Romania than in autumn 2021, regarding pregnant patients.

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Data Availability Statement: All the data are available from the corresponding author upon reasonable request.

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Appendix A

Table A1. The normal values of inflammation indexes.

Index	Normal Values	References
NLR	1.76 (0.83–3.92)	[48,49]
dNLR	2	[50]
MLR	0.12-0.47	[51]
PLR	120 (61–239)	[48]
SII	459 (189–1168)	[48]
SIRI	0.69	[52]
AISI	434	[53]
MCVL	<94.91	[47]
IIC	<13.36	[47]

NLR = neutrophil to lymphocyte ratio, dNLR = derived neutrophil to lymphocyte ratio, MLR = monocyte to lymphocyte ratio, PLR = platelet to lymphocyte ratio, SII = systemic inflammatory index, SIRI = systemic inflammatory response index, AISI = aggregate index of systemic inflammation, MCVL = mean corpuscular volume to lymphocyte ratio, IIC = cumulative inflammatory index.

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