

## RESEARCH ARTICLE

# Which Laboratory and Clinical Feature are different in Pregnant and Non-pregnant Women with COVID-19? A Cross-sectional Study in the West of Iran

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**Abstract: Background:** This study aimed to determine the differences in laboratory and clinical characteristics of pregnant and non-pregnant women with COVID-19 in Hamadan, the west of Iran.

**Material & Methods:** This cross-sectional study compared 135 pregnant with 135 non-pregnant women without underlying diseases and matched by age with COVID-19 from March 2020 to June 2021 in Hamadan, a western city in Iran. Their demographic characteristics, clinical symptoms, vital signs, and laboratory findings were evaluated using a preset checklist and contrasted between the two groups. The adjusted odds ratios (ORs) for the outcomes of illness were presented. A considerable amount of analysis was performed on all data using the SPSS version 26 software.

**Results:** In general, there was a significant association between most clinical symptoms and status of pregnancy. Although the Peripheral oxygen saturation with a pulse oximeter (SPO2) mean was significantly lower among non-pregnant compared to the pregnant women ( $89.19 \pm 4.52$  versus  $94.91 \pm 3.12$ ;  $p < 0.001$ ), the mean of heart rate was significantly lower among pregnant women compared to non-pregnant women ( $90.59 \pm 11.80$  versus  $96.50 \pm 15.02$ ;  $p = 0.001$ ). The percentage of low hemoglobin (Hb), abnormal Blood Urea Nitrogen, high Creatinine (CR), high Erythrocyte Sedimentation Rate and high Lactate Dehydrogenase was significantly higher in non-pregnant women compared to the pregnant women. Women with pregnancy compared to non-pregnant women and women with low Hb compared to normal Hb had a considerably increased chance of intensive care unit /death. Each unit increase in SPO2 and pulse rate resulted in a considerable reduction in this risk. In addition, women with high CR, shortness of breath and per unit rise in temperature had a considerably higher chance of staying in the hospital for a longer period of time.

**Conclusion:** The clinical and para-clinical manifestations of pregnant women with COVID-19 are different from non-pregnant women. Although there was a significant difference between the two groups due to mortality, the percentage of admission to the intensive care unit in pregnant women with COVID-19 is higher than in non-pregnant women. To avoid these adverse outcomes, pregnant women should take precautions to avoid COVID-19 infection.

**Keywords:** COVID-19, pregnant women, pregnancy outcome, neonatal, maternal-child health centers.

## 1. INTRODUCTION

Pregnancy is one of the most important period in a woman's life, during this period women undergo physical and

mental changes [1, 2]. These normal physiological changes in pregnant women, such as changes in the functioning of the immune system and lung efficiency, increase their sensitivity and vulnerability [3].

Viral pneumonia is one of the important factors that has many complications and may cause mortality in pregnant women [4]. Pneumonia is considered the third indirect cause of mortality in pregnant mothers [3]. Approximately 75% of

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pregnant women with pneumonia are hospitalized in special care units [3]. In epidemics related to viral infections such as influenza, SARS, and MERS, consequences like maternal morbidity and mortality, transmission of the virus from mother to fetus, and perinatal infections have been observed [5]. Viral pneumonia in pregnant mothers can have several adverse gynecological and obstetric side effects such as premature rupture of membranes (PROM), pre-term labor (PTL), intrauterine fetal death (IUFD), intrauterine growth restriction (IUGR) and even death of the mother [6]. Recently, COVID-19 was reported as the third outbreak of coronaviruses in the world and an acute respiratory syndrome. The most important and common clinical symptoms of COVID-19 include fever, headache, cough, fatigue or myalgia, muscle pain, sputum, and gastrointestinal symptoms [7]. This disease is considered one of the most important risks to public health, especially in vulnerable groups such as pregnant women and their infants [8].

Currently, there are many available studies about the effect of COVID-19 on pregnant women and their infants, and according to these studies, it has been shown that pregnant women and their infants are probably at greater risk compared to other people [4, 9]. Although some studies have not reported that pregnant women are at higher risk than other people [10]. In the studies about the clinical symptoms of COVID-19 during pregnancy, similar clinical symptoms were observed in pregnant and non-pregnant women [11, 12]. Also, there was no evidence that pregnant women are at higher risk of infection than other people [10]. Moreover, in the meta-analysis studies (2020) that were conducted in Iran to investigate pregnancy and newborn complications in pregnant women with COVID-19, cesarean delivery, pre-term birth, low birth weight, and premature infants were the most important outcomes of pregnancy results as well as, hospitalization of newborns in the NICU (neonatal intensive care unit), and fetal distress were the most likely neonatal outcomes [11].

Some of the researchers investigated the laboratory symptoms of pregnant and non-pregnant women with COVID-19, and the results indicated that despite the normal level of white blood cells, hemoglobin, platelets and liver enzymes in both groups, there was a significant reduction of related lymphocytes in white blood cells and increase in cardiopulmonary resuscitation and transferees in the blood of pregnant women compared to the control group [13]. However, there was no report available about the death or severity of the disease in affected pregnant women compared to non-pregnant ones [14]. Recently, a study was performed in Iran to compare the clinical characteristics of pregnant mothers with COVID-19 and healthy pregnant mothers, and the results showed that the probability of pregnancy problems, newborn problems, pre-eclampsia and premature birth were higher in pregnant women with COVID-19 [15]. There have been few studies comparing symptoms as well as clinical and paraclinical characteristics, in two groups of pregnant and non-pregnant women with COVID-19 in Iran [16-18]. Hence, more studies are warranted in this field in order to make a better conclusion. For this purpose, in the present study, we investigated and compared the clinical, demographic, and laboratory factors of pregnant and non-pregnant women with COVID-19 hospitalized in Hamadan province

in order to identify more clinical features of this epidemic in pregnant and non-pregnant women and make an informed decision for treating the patients according to their pregnancy conditions.

## 2. MATERIAL AND METHODS

A total of 270 married women with COVID-19 participated in this cross-sectional study, which included 135 non-pregnant and 135 pregnant, with an age range of 18–45 years and without underlying diseases, between March 2020 to June 2021 in Hamadan, a city west of Iran.

Their disease was confirmed based on the positive real-time reverse transcriptase polymerase chain reaction (RT-PCR) test of upper respiratory nasopharyngeal swab samples.

The non-pregnant women were selected from hospitalized patients in Sina (Farshchiyan) hospital, which is a main center for COVID-19, and pregnant women were selected from COVID-19-positive pregnant women with gestational age of 37 to 40 weeks referred to Fatemeh hospital (a main Centre for obstetrics and gynecology) for delivery. The sample size was calculated using the formula and prevalence of abnormal WBC in pregnant and non-pregnant women with COVID-19 which was reported 0.13 vs. 0.27, respectively [19]. With a significant level of  $\alpha = 0.05$  and power of  $1 - \beta = 0.80$ , the number of 135 women was calculated per group. In this study, the inclusion criteria were married women patients in reproductive age (18–45 years), without underlying diseases and with positive SARS-CoV-2 infection confirmed by real-time polymerase chain reaction tests of nasopharyngeal swab samples.

Pregnant patients with pregnancy outcomes such as premature rupture of membranes (PROM), preeclampsia, eclampsia, decreased fetal movements, bleeding, abnormal amniotic fluid, and abnormal placenta were excluded.

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A trained nurse gathered the data from patients' medical records, which were recorded at the beginning of hospitalization and recorded in a predetermined checklist. This checklist consisted of pregnancy status, age (year), clinical features, vital signs, and laboratory findings as follows:

Clinical features: Clinical symptoms (exist or non-exist of fever, cough, shortness of breath, diarrhea, nausea, vomit, anorexia, odor disorder, taste disorder, muscular pain, fatigue, digestive problems, headache, sore throat); Vital signs: Temperature, systolic and diastolic blood pressure (mm Hg), heart rate (per minute), respiratory rate (per minute), Peripheral oxygen saturation with pulse oximeter (SPO<sub>2</sub>; percent); Laboratory findings: Blood Urea Nitrogen (BUN; mg/dL), White Blood Cells count (WBC;  $\times 1000\mu\text{L}$ ), hemoglobin (Hb; g/dL), Creatinine (Cr; mg/dL), Alkaline Phosphatase (ALP; U/L), platelet count ( $\times 1000\mu\text{L}$ ), Erythrocyte Sedimentation Rate (ESR; mm/h), Lactate Dehydrogenase (LDH; U/L), Serum Glutamic-Pyruvic Transaminase (SGPT; U/L), Serum Glutamic-Oxaloacetic Transaminase (SGOT; U/L),

C-reactive protein (CRP: negative, positive). The length of Hospitalization and survival status (alive or dead) were considered as outcome variables.

Descriptive statistics such as number (Percent), mean $\pm$  standard deviation (SD), median and Interquartile Range (IQR) were carried out for all covariates. Continuous characteristics between the two groups were compared using an independent t-test or Mann-Whitney. The chi-square or exact Fisher test were utilized to compare the qualitative characteristics of two groups. To explore the association between pregnancy status and laboratory factors, first, these factors were categorized into low, normal and high ranges according to pregnancy or non-pregnancy status and then a chi-square or exact Fisher test was performed. Moreover, the effect of potential risk factors on the aggravation of the disease (ICU experience or death) and the hospitalization length of COVID-19 ( $< 1$  week,  $\geq 1$  week) was assessed by an adjusted multiple logistic model and the odds ratio was reported. All analysis was conducted in SPSS (Version 26 software). A  $p$ -value less than 0.05 was considered significant.

The study protocol was approved by the Research Council of Hamadan University of Medical Sciences with research ID 14000124451, and ethics code IR.UMSHA.REC.1400.007. All the participants provided their consent to participate in this study by signing the consent form.

### 3. RESULTS

The mean $\pm$  SD age of pregnant women was as similar as the non-pregnant group (31.31 $\pm$ 5.62 years vs. 31.72  $\pm$  6.21 years, respectively). In general, among all clinical symptoms, fever and cough had the highest prevalence (57.8%

and 56.3%, respectively), and fatigue and diarrhea had the lowest prevalence (3% and 4.9%, respectively). Based on Fig. (1), the prevalence of shortness of breath, diarrhea, nausea, vomiting, anorexia, odor and taste disorders, muscular pain and headache in pregnant women were significantly lower than in non-pregnant women. Despite the fact that more than 50% of patients in both groups had fever, pregnant women had a substantially greater prevalence of fever than non-pregnant women (64.9% vs 50.7%;  $p = 0.019$ ). Moreover, the results in Table 1 show that the temperature of pregnant women was significantly higher in comparison to the non-pregnant women (37.73 $\pm$ 0.76 versus 37.31 $\pm$ 0.76, respectively;  $p < 0.001$ ). SPO2 mean was significantly higher among pregnant compared to non-pregnant women (94.91 $\pm$ 3.12 versus 89.19 $\pm$ 4.52, respectively;  $p < 0.001$ ). The heart rate mean among pregnant women was significantly lower than non-pregnant women (90.59 $\pm$ 11.80 versus 96.50 $\pm$ 15.02, respectively;  $p = 0.001$ ). Based on our findings, the median (IQR) of hospitalization length in pregnant women was significantly lower than in non-pregnant women 4 (3-6) versus 5 (4-8), respectively;  $p < 0.001$ ). There was no significant difference in the prevalence of other clinical symptoms, vital signs, ICU admission, and the deaths of COVID-19 between the two groups.

The normal range and Mean $\pm$  SD of laboratory factors of the pregnant and non-pregnant women are reported in Table 2. According to the pregnant or non-pregnancy state, the laboratory variables in this table were divided into low, normal, and high ranges based on their normal range. Following that, using the chi-square or Fisher exact test, the associations between pregnancy status and laboratory variables were evaluated and presented in Table 3. Based on our findings, the prevalence of low Monocytes, low Platelet, and negative

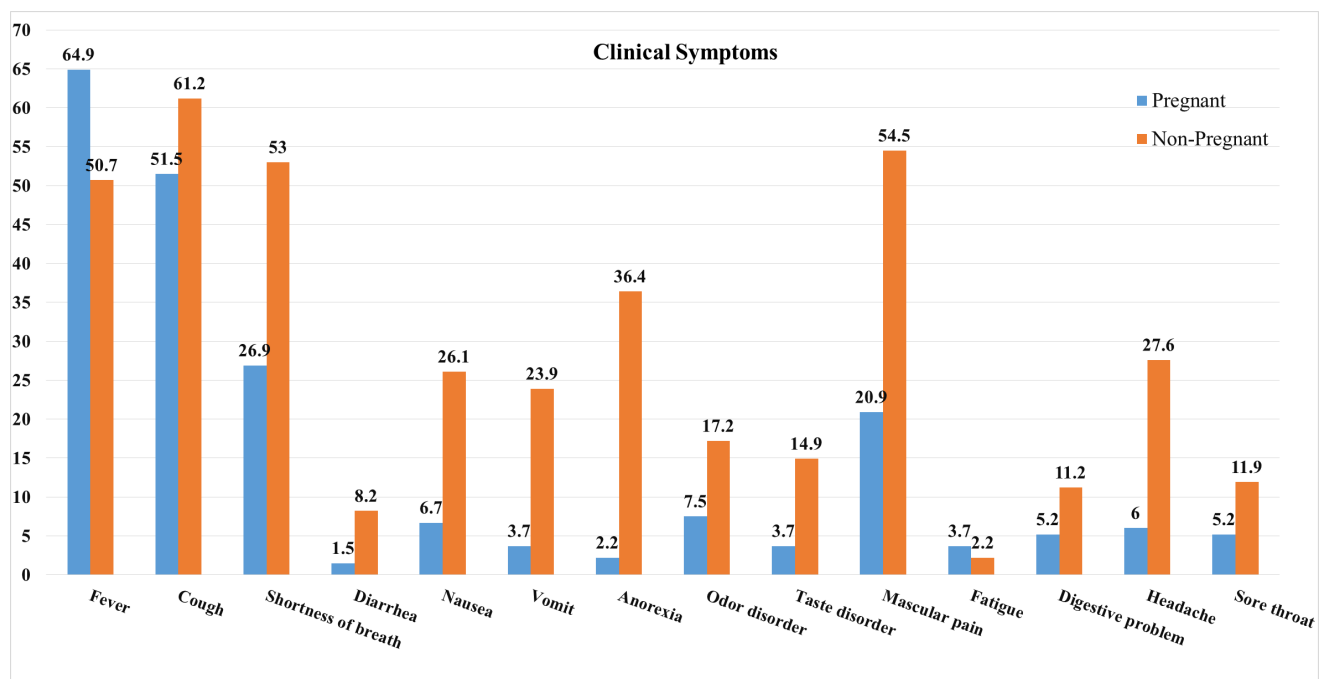


Fig. (1). The percentage of clinical symptom according to pregnancy status. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

Table 1. Comparison of characteristics of pregnant and non-pregnant women with COVID-19.

| -                                     | Pregnant (n=135) N (%) | Non-pregnant (n=135) N (%) | p-value <sup>a</sup> |
|---------------------------------------|------------------------|----------------------------|----------------------|
| Age (years)(Mean± SD)                 | 31.31±5.62             | 31.72 ± 6.21               | 0.572 <sup>b</sup>   |
| <b>Vital sign</b>                     |                        |                            |                      |
| Systolic (mm Hg)                      | 117.07±9.29            | 115.39±11.90               | 0.151                |
| Diastolic (mm Hg)                     | 72.70±8.12             | 74.35±9.35                 | 0.111                |
| Heart Rate (per minute)               | 90.59±11.80            | 96.50±15.02                | 0.001                |
| Respiratory rate (per minute)         | 20.10±1.74             | 20.02±3.60                 | 0.201                |
| Temperature                           | 37.73±0.76             | 37.31±0.76                 | <0.001               |
| SPO2 (percent)                        | 94.91±3.12             | 89.19±4.52                 | <0.001               |
| <b>Outcome</b>                        |                        |                            |                      |
| Hospitalization length (median (IQR)) | 4 (3-6)                | 5 (4-8)                    | <0.001               |
| ICU admin                             | 9 (6.7%)               | 3 (2.2%)                   | 0.076 <sup>c</sup>   |
| Death (N (%))                         | 7 (5.2%)               | 2 (1.5%)                   | 0.172 <sup>d</sup>   |

ICU: Intensive Care Unit; IQR: Interquartile range; SD: Standard Deviation SPO2: The Peripheral oxygen saturation with pulse oximeter. a. Mann-Whitney. b. Independent t-test. c. Chi-square. d. Exact fisher test.

Table 2. Characteristics of Para-clinical features of pregnant and non-pregnant women with COVID-19.

| -                   | Pregnant Women (n=135) |               | Non-Pregnant Women (n=135) |               |
|---------------------|------------------------|---------------|----------------------------|---------------|
|                     | Normal Range           | Mean±SD       | Normal Range               | Mean±SD       |
| WBC (×1000μL)       | 5.6-16.9               | 8.09±3.44     | 4-10.8                     | 6.22±3.33     |
| Lymphocyte (%)      | 20-40                  | 25.36±13.60   | 20-40                      | 24.88±11.80   |
| Monocytes (%)       | 4.7-12.5               | 1.92± 0.97    | 4.7-12.5                   | 3.08± 1.45    |
| Neutrophile (%)     | 40-74                  | 72.10±13.71   | 40-74                      | 70.36±12.12   |
| Hb (g/dl),          | 9.5-15.0               | 12.31±1.33    | 11.7-15.7                  | 13.15±1.49    |
| BUN (mg/dL)         | 3-13                   | 7.54±2.66     | 7-20                       | 12.11±11.19   |
| Cr (mg/dL)          | 0.4-0.9                | 0.86±1.04     | 0.5-0.9                    | 0.93±0.78     |
| Platelets (×1000μL) | 146-429                | 184.88±60.09  | 130-400                    | 198.25±73.69  |
| ESR (mm/h)          | 4-70                   | 44.13±19.07   | 0-20                       | 37.79±23.11   |
| LDH (U/L)           | 82-524                 | 468.67±183.52 | 100-260                    | 515.71±200.58 |
| Alp (U/L)           | 17-229                 | 215.19±125.90 | 33-96                      | 147.36±125.57 |
| SGOT (U/L)          | 4-32                   | 42.95±73.02   | 7-40                       | 39.97±36.20   |
| SGPT (U/L)          | 2-25                   | 32.59±52.46   | 7-45                       | 39.47±38.63   |
| CRP (+)             | ---                    | 68 (57.1%)    | ---                        | 67 (72.0%)    |

Table 3. Distributional of Para-clinical features in pregnant and non-pregnant women with COVID-19.

| -           | Non-Pregnant Women (n=135) | Pregnant Women (n=135) | p-value <sup>a</sup> |
|-------------|----------------------------|------------------------|----------------------|
| WBC         |                            |                        |                      |
| Normal      | 85 (69.1)                  | 99 (73.3)              | 0.275                |
| Low         | 29 (23.6)                  | 32 (23.7)              |                      |
| High        | 9 (7.3)                    | 4 (3.0)                |                      |
| Lymphocyte  |                            |                        |                      |
| Normal      | 57 (50.0)                  | 66 (53.2)              | 0.322                |
| Low         | 47 (41.2)                  | 53 (42.7)              |                      |
| High        | 10 (8.8)                   | 5 (4.0)                |                      |
| Monocytes   |                            |                        |                      |
| Normal      | 14 (13.2)                  | 2 (2.0)                | 0.002                |
| Low         | 92 (86.8)                  | 99 (98.0)              |                      |
| Neutrophile |                            |                        |                      |
| Normal      | 64 (56.1)                  | 58 (46.8)              | 0.190 <sup>b</sup>   |
| Low         | 1 (.9)                     | 4 (3.2)                |                      |
| High        | 49 (43.0)                  | 62 (50.0)              |                      |
| Hb          |                            |                        |                      |
| Normal      | 119 (90.2)                 | 133 (98.5)             | 0.003                |
| Low         | 13 (9.8)                   | 2 (1.5)                |                      |
| BUN         |                            |                        |                      |
| Normal      | 105 (81.4)                 | 117 (94.4)             | <0.001               |
| Low         | 19 (14.7)                  | 1 (.8)                 |                      |
| High        | 5 (3.9)                    | 6 (4.8)                |                      |
| Cr          |                            |                        |                      |
| Normal      | 98 (74.2)                  | 107 (86.3)             | 0.016                |
| High        | 34 (25.8)                  | 17 (13.7)              |                      |
| Platelet    |                            |                        |                      |
| Normal      | 118 (90.8)                 | 97 (71.9)              | <0.001               |
| Low         | 12 (9.2)                   | 38 (28.1)              |                      |
| ESR         |                            |                        |                      |
| Normal      | 28 (23.1)                  | 83 (92.2)              | <0.001               |
| High        | 93 (76.9)                  | 7 (7.8)                |                      |
| LDH         |                            |                        |                      |
| Normal      | 4 (5.1)                    | 87 (77.0)              | <0.001               |
| High        | 74 (94.9)                  | 26 (23.0)              |                      |

(Table 3) Contd....

| -        | Non-Pregnant Women (n=135) | Pregnant Women (n=135) | p-value <sup>a</sup> |
|----------|----------------------------|------------------------|----------------------|
| Alp      |                            |                        |                      |
| Normal   | 27 (30.7)                  | 18 (50.0)              | 0.120                |
| Low      | 5 (5.7)                    | 1 (2.8)                |                      |
| High     | 56 (63.6)                  | 17 (47.2)              |                      |
| SGOT     |                            |                        |                      |
| Normal   | 85 (69.7)                  | 81 (69.2)              | 0.941                |
| High     | 37 (30.3)                  | 36 (30.8)              |                      |
| SGPT     |                            |                        |                      |
| Normal   | 91 (75.2)                  | 66 (71.0)              | 0.487                |
| High     | 30 (24.8)                  | 27 (29.0)              |                      |
| CRP      |                            |                        |                      |
| Positive | 67 (72.0)                  | 68 (57.1)              | 0.025                |
| Negative | 26 (28.0)                  | 51 (42.9)              |                      |

a. Chi-square. b. Exact fisher test.

CRP in pregnant women was significantly higher than in non-pregnant women, with percentages of 98.0% versus 86.8%,  $p = 0.002$  for Monocytes, 28.1% versus 9.2%,  $p < 0.001$  for Platelet, and 42.9% versus 28%,  $p = 0.025$  for CRP. In comparison to pregnant women, non-pregnant women had a considerably greater proportion of low Hb, aberrant BUN, high Cr, high ESR, and high LDH. Their percentages of these laboratory factors were respectively 9.8% versus 1.5%,  $p = 0.003$  for Hb, 18.6% versus 5.6%,  $p < 0.001$  for BUN, 25.8% versus 13.7%,  $p = 0.016$  for Cr, 76.9% versus 7.8%,  $p < 0.001$  for ESR, 94.9% versus 23%,  $p < 0.001$  for LDH. No significant association was reported between pregnancy in the women with COVID-19 and WBC, Lymphocyte, Neutrophile, Alp, SGOT, and SGPT.

Based on the results in Table 4, the risk of ICU/death was significantly decreased for one unit increase in SPO2 and pulse rate. Their estimated adjusted odds ratios (OR) were 0.78 (0.66, 0.93) and 0.89 (0.81, 0.96), respectively. Additionally, women who were pregnant compared to women who were not (OR: 19.15, 95% CI: 7.06, 77.74;  $p = 0.006$ ) and women who had low hemoglobin compared to those who did not (OR: 19.22, 95% CI: 1.46, 52.31;  $p = 0.024$ ) had considerably greater odds of being admitted to the hospital or dying. There was no significant association between the death/ICU of COVID-19 with age and CRP.

Our findings in Table 5 show that the risk of hospitalization length of more than one week was statistically decreased in the patients for a one-unit increase in SPO2 and increased in the patients for a one-unit increase in temperature. The adjusted ORs estimates for them were respectively 0.89 (0.83, 0.97) and 1.58 (1.06, 2.36). Additionally, the risk of hospitalization length of more than one week in women experiencing shortness of breath and women with high CR was respectively 1.99 (1.08, 3.67) times greater in women experiencing shortness of breath and 2.07 (1.04, 4.12) times greater in women with Normal CR. The duration of the

COVID-19 hospitalization was not significantly correlated with any other factors.

#### 4. DISCUSSION

The clinical and Para-clinical characteristics and the outcomes of pregnant and non-pregnant women of reproductive age with COVID-19 were studied. Most of the studies in this field compared the Para-clinical characteristics of pregnant and non-pregnant women without considering their pregnancy status [4, 7, 20], and this comparison without considering the individual's pregnancy status can lead to incorrect judgments. This research makes a substantial addition by classifying the clinical traits as normal or abnormal depending on whether they are pregnant or not before comparing them. With respect to the CDC report, the most common symptoms of COVID-19 are cough, fever, myalgia, fatigue, headache and shortness of breath, generally [21]. The present findings showed that the most common clinical symptoms in non-pregnant women are cough (61.2%), muscle pain (54.5%), shortness of breath (53.0%) and fever (50.7%), respectively, and in pregnant women, the symptoms include fever (64.9%), cough (51.5%), shortness of breath (26.9%) and muscle pains (20.9%). The initial symptoms in pregnant women are different compared to the non-pregnant women. However, contrary to the present results, Ellington *et al.* employed a large sample size, and reported fever as the most common symptom in both groups of pregnant and non-pregnant women [22]. In this research, compared to non-pregnant women's cough, pregnant women were more likely to have fever. Additionally, non-pregnant women had much greater rates of shortness of breath, diarrhea, nausea, vomiting, anorexia, smell and taste problems, muscular discomfort, and headaches than pregnant women. Consistent with the present study, Vizheh *et al.* showed that the most common symptom of the disease in pregnant mothers was fever and in non-pregnant mothers was a cough [23]. Similar to



**Table 4. Association between COVID-19 death and potential risk factors using adjusted odds ratio.**

| -            | Discharged<br>Mean (SD) | ICU/Death<br>Mean (SD) | OR (95% CI)         | p-value |
|--------------|-------------------------|------------------------|---------------------|---------|
| Age          | 31.46 (5.97)            | 32.31 (5.02)           | 0.92 (0.81, 1.05)   | 0.326   |
| SPO2         | 92.18 (4.67)            | 90.19 (6.68)           | 0.78 (0.66, 0.93)   | 0.006   |
| Pulse Rate   | 93.86 (13.95)           | 88.50 (10.17)          | 0.89 (0.81, 0.96)   | 0.005   |
| Status       | N (%)                   | N (%)                  | -                   | -       |
| Non-pregnant | 130 (51.2)              | 5 (31.3)               | ---                 | ---     |
| Pregnant     | 124 (48.8)              | 11 (68.8)              | 19.15 (7.06, 77.74) | 0.006   |
| <b>CRP</b>   |                         |                        |                     |         |
| Negative     | 74 (37.2)               | 3 (23.1)               | ---                 | ---     |
| Positive     | 125 (62.8)              | 10 (76.9)              | 2.9 (0.6, 13.95)    | 0.183   |
| <b>HB</b>    |                         |                        |                     |         |
| Normal       | 238 (94.8)              | 14 (87.5)              | ---                 | ---     |
| Low          | 13 (5.2)                | 2 (12.5)               | 19.22 (1.46, 52.31) | 0.024   |

**Table 5. Association between the hospitalization length of COVID-19 and potential risk factors using adjusted odds ratio.**

| -                          | < 1 week (N=193)<br>Mean (SD) | >= 1 week (N=77)<br>Mean (SD) | OR (95% CI)       | p-value |
|----------------------------|-------------------------------|-------------------------------|-------------------|---------|
| Age                        | 31.28 (5.83)                  | 32.10 (6.13)                  | 1.03 (0.98, 1.08) | 0.274   |
| SPO2                       | 92.80 (3.81)                  | 90.02 (6.40)                  | 0.89 (0.83, 0.97) | 0.006   |
| Respiratory rate           | 19.87 (2.8)                   | 20.55 (2.83)                  | 1.05 (0.95, 1.15) | 0.359   |
| Temperature                | 37.46 (0.76)                  | 37.66 (0.85)                  | 1.58 (1.06, 2.36) | 0.023   |
| -                          | N (%)                         | N (%)                         | -                 | -       |
| <b>Shortness of Breath</b> |                               |                               |                   |         |
| No                         | 125 (65.1)                    | 36 (47.4)                     | ---               | ---     |
| Yes                        | 67 (34.9)                     | 40 (52.6)                     | 1.99 (1.08, 3.67) | 0.027   |
| <b>Status</b>              |                               |                               |                   |         |
| Non-pregnant               | 89 (46.1)                     | 46 (59.7)                     | ---               | ---     |
| Pregnant                   | 104 (53.9)                    | 31 (40.3)                     | 0.79 (0.37, 1.67) | 0.531   |
| <b>CR</b>                  |                               |                               |                   |         |
| Normal                     | 151 (83.9)                    | 54 (71.1)                     | ---               | ---     |
| High                       | 29 (16.1)                     | 22 (28.9)                     | 2.07 (1.04, 4.12) | 0.039   |

these results, in another systematic study by Durray *et al.*, it was concluded that non-pregnant women were at a higher risk of experiencing symptoms, such as headache, myalgia, fever, phlegm, chest tightness, wheezing, and diarrhea [12]. However, many other studies and systematic reviews reported similar clinical characteristics among pregnant and non-pregnant women with COVID-19 [24-28].

The current study's findings on vital signs revealed that during hospitalization, pregnant women's percentage of peripheral oxygen saturation (SPO2) was much greater than that of non-pregnant women, and their heart rates were also lower. Vizheh *et al.* showed that the SPO2 of pregnant women was higher than that of non-pregnant women [23]. However, Kotosso *et al.* showed that the SPO2 of pregnant wom-

en was lower than that of the non-pregnant women, and the researchers concluded that in pregnant women, it does not necessarily mean severe lung damage; in fact, oxygen saturation during pregnancy can be affected by other physiological factors [29]. However, these physiological changes may cause the pregnant woman to be more susceptible to respiratory and thromboembolic complications [30].

With respect to the results, the hospitalization length of pregnant women was significantly shorter than that of the non-pregnant women. In this regard, Mohr-Sasson *et al.* indicated that the duration of hospitalization of the pregnant mothers was shorter than that of the non-pregnant women [13]. Given that pregnant women in this research had a much greater risk of ICU/death than non-pregnant women. The hospitalization of pregnant women seems to have been avoided, which is surprising given that pregnant women are more vulnerable to infectious diseases owing to the well-known blunting of immune responses during pregnancy. In another study on 409462 women of reproductive age, in which 23434 women were pregnant (9%), it was concluded that the probability of being admitted to the ICU and receiving mechanical ventilation was higher in pregnant women in comparison to non-pregnant women. However, the mortality risk in both groups was similar [22]. Although the hospitalization rate in ICU was higher in pregnant women than in non-pregnant women, a significant difference between the two groups was observed in this regard. In a research conducted in India, pregnant women with severe COVID-19 had a higher likelihood of requiring intubation, mechanical ventilation, and hospitalization to the ICU [31]. Another study in Sweden reported that in pregnant women, the risk of ICU admission was higher than in non-pregnant women. Pregnant women were more likely to be hospitalized in the ICU and receive mechanical ventilation, although no difference was observed in the severity of illness between the two groups [12]. Pregnancy is linked to increased risk of hospitalization in the ICU and ventilation, according to a meta-analysis conducted by Wang *et al.* (2022). These results imply that pregnancy itself may cause complications and morbidities in women with severe COVID-19 [32]. Physiological and immunological changes that occur during pregnancy can raise the risk or severity of certain infections [12, 33, 34]. Hence, pregnant women inhibit the activity of lymphocytes T during pregnancy, which leads them to maintain immunosuppression and be susceptible to viral infection [32, 35]. Moreover, due to the mother's body's high immunosuppressive level during pregnancy, various changes in architecture, physiology, and biochemistry will take place, including an increase in oxygen consumption, heart rate, and the upward protrusion of the diaphragm [33, 36]. The changes in the breathing system are significantly affected during pregnancy, under the effect of high levels of estrogen and progesterone, and the restriction of lung expansion that occurs during pregnancy can make women susceptible to respiratory pathogen infections. One of the prominent features of pregnancy is the pro-inflammatory state [36], which may have dangerous effects on the mother and the fetus. These events make pregnant women prone to more severe and longer periods of illness. The risk of unfavorable outcomes may be increased when pregnancy and COVID-19 coexist since pregnancy was a risk factor for ICU admission compared to non-pregnant

women with COVID-19 [32]. Additionally, pregnant women often receive greater care for viral infections, which may help to mitigate the risk of serious negative effects including a higher mortality rate. In the examination of laboratory results, the prevalence of low monocyte, low platelet and negative CRP in pregnant women were significantly higher than non-pregnant women. Moreover, the prevalence of low Hb, abnormal BUN, high Cr, high ESR, and high LDH in non-pregnant women was reported to be significantly higher than the pregnant women. There was no significant relationship between pregnancy in women with COVID-19 and WBC, lymphocyte, neutrophil, Alp, SGOT and SGPT. These results may be explained by the relative immunological suppression that occurs during pregnancy as well as the immunodeficiency that occurs after COVID-19 infection. Studies on COVID-19 laboratory data in two groups of pregnant and non-pregnant women have produced varying conclusions. Contrary to our results, in the research of Vizheh *et al.*, in pregnant women, Cr levels were lower, ESR was lower, Hb was higher, and platelets were higher than in the non-pregnant women [12]. In Mohr-Sasson *et al.*'s research, no significant difference was reported among BUN, LDH, Cr, ESR, Hb and lymphocytes in two groups [13]. In general, in previous studies, in contrast to the non-pregnant group with COVID-19, pregnant mothers had similar values, such as changes in the number of leukocytes and platelets (increase or decrease), and increased CRP levels [23, 37, 38]. Leukopenia, lymphopenia, elevated LDH, and CRP have also typically been among the most prevalent laboratory signs in pregnant women compared to the non-pregnant group in most studies. Zha *et al.* reported mild differences in the laboratory characteristics of pregnant women compared to non-pregnant women, however, they suggested that these differences were in terms of the immunological and physiological changes during pregnancy rather than a disease [39]. The major difference between this study, and previous studies is that the laboratory features in this study were categorized to normal or abnormal based on status of pregnancy (normal range in pregnant or non-pregnant women) before comparison between two groups, while in previous studies, the numerical values of these features were compared in two groups without considering the pregnancy status of women. It seems that such a comparison leads to incorrect judgments in this regard.

The first benefit of this study is that pregnant women with COVID-19 were investigated during all three trimesters, as opposed to many other studies that only looked at pregnant women in the last months of pregnancy. Furthermore, in other studies, the comparison of laboratory findings in two pregnant and non-pregnant groups was only based on the findings, whereas in this study, these findings were converted into normal and abnormal based on the pregnancy status of the mothers, and then, the comparison was made. One of the limitations of the present study is that the patients who were not admitted to the hospital were not included in the study, which may cause bias in the generalization of findings. It is suggested that in the future, studies with a larger sample size and considering the severity of the disease should be conducted. Moreover, the risk of inherent bias exists as most of the data were collected retrospectively.



## CONCLUSION

It can be concluded that clinical and para-clinical manifestations of pregnant women are different from non-pregnant women. Although pregnant women spent less time in the hospital than non-pregnant women did, there was a significant difference in the two groups' risks of dying or being admitted to an intensive care unit. Considering the daily increase in the disease burden, **this** data will help healthcare workers to more easily identify patients who are susceptible to this disease and be able to make an informed decision when treating patients. In light of these findings, pregnant women should be thoroughly cared for as part of their pregnancy follow-up in a specialist gynecology and obstetrics department and should be examined for underlying diseases. Finally, prospective studies are better suited to evaluate the medium and long-term effects of COVID-19 on the mother-child pair.

## LIST OF ABBREVIATIONS

|        |   |   |
|--------|---|---|
| IQR    | = | Interquartile Range                             |
| IUFD   | = | Intrauterine Fetal Death                        |
| IUGR   | = | Intrauterine Growth Restriction                 |
| PROM   | = | Premature Rupture of Membranes                  |
| PTL    | = | Pre-term Labor                                  |
| RT-PCR | = | Reverse Transcriptase Polymerase Chain Reaction |
| SD     | = | Standard Deviation                              |

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the ethics committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1400.007).

## HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional and research committees and with the 1975 Declaration of Helsinki, as revised in 2013.

## CONSENT FOR PUBLICATION

All the participants informed their consent to participate in this study by signing the consent form.

## STANDARDS OF REPORTING

STROBE guidelines were followed.

## AVAILABILITY OF DATA AND MATERIALS

The data and supportive information **are** available within the article.

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None.

## CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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