Impact of the COVID-19 Pandemic on Maternal Well-Being during Pregnancy

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Abstract: The outbreak of a pandemic has negative psychological effects. We aimed to determine the impact of the SARS-CoV-2 pandemic during pregnancy and identify the risk factors for maternal well-being. A multicenter, prospective, population-based study was carried out that included women (n = 1320) who were pregnant during the SARS-CoV-2 pandemic in Barcelona (Spain) compared against a pre-pandemic cohort (n = 345). Maternal well-being was assessed using the validated World Health Organization Well-Being Index Questionnaire (WHO-5 Index). Pregnant women attended during the COVID-19 pandemic showed worst WHO-5 well-being scores (median (IQR) of 56 (36–72) for the pandemic cohort vs. 64 (52–76) for the pre-pandemic cohort p < 0.001), with 42.8% of women presenting a poor well-being score vs. 28% for the pre-pandemic cohort (p < 0.001). Presence of a previous psychiatric disorder (OR 7.1; 95% CI 2.6–19, p < 0.001), being in the third trimester of pregnancy (OR 1.7; 95% CI 1.5–2, p = 0.001), or requiring hospital admission for COVID-19 (OR 4.7; 95% CI 1.4–16.7, p = 0.014), significantly contributed to low maternal well-being during the COVID-19 pandemic (multivariate analysis). Being infected by SARS-CoV-2 was not associated with a lower well-being score. We conclude that, during the COVID-19 pandemic, there were higher rates of poor maternal well-being; the infection of SARS-CoV-2 itself did not worsen maternal well-being, but other factors as psychiatric disorders, being in the third trimester of pregnancy or hospital admission for COVID-19 disease did.

Keywords: COVID-19; SARS-CoV-2; pandemic; well-being; pregnancy; psychiatric disorders; anxiety; depression

1. Introduction

Severe acute respiratory coronavirus 2 (SARS-CoV-2) is a global challenge for healthcare sectors and individuals. Since the outbreak, many countries have adopted strict measures, such as lockdowns, aimed at mitigating the spread of the disease [1]. Previous evidence has revealed the negative psychological impact, in terms of anxiety, depression,
and post-traumatic stress symptoms [2,3] associated to the outbreak of a pandemic and its consequences on the general population, particularly on people who have quarantined [3,4].

The coronavirus 19 disease (COVID-19) has been widely studied in pregnant women. Mostly, pregnant women with SARS-CoV-2 infection remain asymptomatic and the overall rate of complications has been found to be similar to that of non-infected women [5], except close to delivery in the third trimester, where the rate of complications increases [5–7]. However, this population might still be vulnerable to medical and social risks [8]. Changes in preventive health-care seeking behavior due to lockdown and healthcare policies (prenatal care and pregnancy follow-up) may increase pregnancy-related stress disorders, have a negative effect on well-being, increase the risk of post-partum depression, and exacerbate other mental health problems [4]. During the initial spread of COVID-19 in 2020, pregnant women had less prenatal visits, relatives were not allowed to attend prenatal and postnatal visits, there was uncertainty regarding fetal transmission, and strict health measures led to social isolation [9].

Many studies have assessed the negative impact of the pandemic on maternal psychological status during pregnancy [10–12], but few studies have compared this impact to a previous pre-pandemic cohort [13] based on laboratory confirmation of SARS-CoV-2 infection [14–17]. Most current published studies on maternal psychological impact of the COVID-19 pandemic focus on depressive disorders, mental stress, or anxiety, leaving maternal well-being aside. Assessing well-being may provide a better and more general picture of the impact the pandemic has on the physical and psychological status during pregnancy.

It remains unclear whether the impact on maternal well-being is related to the COVID-19 infection itself, its severity, symptomatology, or if it is secondary to pandemic lockdown and social restrictions. The aim of this study was to examine the impact of the COVID-19 pandemic and lockdown on maternal well-being during pregnancy and identify its risk factors.

2. Materials and Methods

2.1. Study Design and Participants

A multicenter, prospective, population-based study was carried out between March 2020 and May 2020 in Barcelona, Spain [5,18]. SARS-CoV-2 infection was confirmed in all participants by the presence of antibodies and/or real-time polymerase chain reaction (RT-PCR), as described elsewhere [5]. Inclusion criteria: pregnant women who attended the participating university hospitals (Hospital Clinic, Hospital Sant Joan de Déu, and Hospital de Sant Pau) for first/second trimester screening for Down’s syndrome (10–16 weeks of gestation) or admitted to the hospital for obstetric causes or delivery and were able to undergo a well-being assessment. Pregnant women referred for a SARS-CoV-2 diagnosis outside the catchment area of the participating centers were excluded from the study. The study was approved by the Ethics Committee of each of the participating hospitals (HCB: HCB-2020-0434, HSJD: PIC-56-20, HSP: IIBSP-COV-2020-38). All participants signed their informed consent before being included in the study.

The pandemic cohort was compared to a previous cohort of pregnant women recruited between February 2017 and October 2019 before the COVID-19 pandemic [19] (Table A1).

2.2. Aims of the Study

The primary purpose of the study was to evaluate maternal well-being, assessed with the World Health Organization’s Well-Being Index (WHO-5) [20]. The WHO-5 consists of a five-item scale that measures quality of life and psychological well-being based on patients’ feelings within the last 15 days. The raw score ranges from 0 to 25, 0 representing the worst possible and 25 the best possible quality of life. Women were classified according to their well-being status as having a poor (≤52) or a favorable (>52) WHO-5 score [21]. The questionnaire was self-administered at recruitment. Comparisons of well-being scores between pandemic and pre-pandemic cohorts were carried out.
The second aim of this study was to assess maternal and pregnancy variables that may act as potential risk factors for a poorer well-being status, as well as data related to SARS-CoV-2 infection, quarantine, and lockdown.

2.3. Data Collection

Baseline and socioeconomic characteristics (working status, housing characteristics, and availability of green areas during lockdown) were obtained from a structured questionnaire, and medical and obstetric histories from the medical records at recruitment.

COVID-19 symptoms were recorded at hospital admission using a structured questionnaire that included questions on risk factors and COVID-19 suggestive symptoms noticed between mid-February 2020 and the time of SARS-CoV-2 testing. Women who tested positive, completed the same questionnaire again 4–5 weeks later. Symptomatic SARS-CoV-2 infected women were defined as having at least one of the following symptoms: fever, dry cough, anosmia or ageusia, dyspnea, myalgia, diarrhea, sore throat, skin rash, or discoloration of fingers and/or toes. More details can be found in Appendices A and B.

Pregnancy, delivery, and neonatal data were obtained from electronic medical files at delivery and during the postpartum period.

2.4. Statistical Analysis

For the primary outcome, the analyses were based on WHO-5 scorings. Secondary analyses were assessed by comparing the cohort of women who were pregnant during the SARS-CoV-2 pandemic against the pre-pandemic group. Quantitative variables were assessed for normality using Shapiro–Wilk’s test: normally distributed variables were compared using the t-test and expressed as mean and standard deviation (SD). Non-normally distributed variables were compared using the U-Mann–Whitney test and expressed as median and interquartile range (IQR). Qualitative variables were compared using χ² or Fisher’s exact tests. Logistic regression analyses were performed to assess the association between maternal well-being and potential risk factors adjusted by gestational age at recruitment. A p-value < 0.05 was considered as statistically significant. The analyses were performed on SPSS v26 (New York, NY, USA).

3. Results

3.1. Characteristics of the Study Population

During the pandemic, 1320 women were recruited; 444 (33.6%) were in the first trimester (median (IQR) gestational age 10.7 weeks (9.9–12.1)) and 876 (66.4%) in the third trimester (median (IQR) gestational age 39.7 weeks (38.6–40.6)) of pregnancy. Table 1 summarizes the baseline characteristics of the population and Table 2 shows pregnancy and neonatal outcomes. Most women (n = 851, 64.5%) had a vaginal delivery; 202 (15.3%) were positive for SARS-CoV-2 at recruitment, determined by either presence of antibodies (n = 200) and/or positive RT-PCR (n = 26) (Table A3). Table A1 summarizes the characteristics of the pre-pandemic cohort.

| Characteristics | Total Cohort (n = 1320) |
|-----------------|-------------------------|
| Age (years)     | 33.3 (29.1–37)          |
| Ethnicity       |                         |
| White           | 858 (65%)               |
| Latin American  | 297 (22.5%)             |
| Black           | 23 (1.7%)               |
| Asian           | 81 (6.1%)               |
| Others          | 61 (4.6%)               |
Table 1. Cont.

| Characteristics                        | Total Cohort (n = 1320) |
|----------------------------------------|-------------------------|
| **Education level**                    |                         |
| Not educated                           | 31 (2.3%)               |
| Primary                                | 86 (6.5%)               |
| Secondary                              | 361 (27.3%)             |
| Vocational                             | 191 (14.5%)             |
| University                             | 651 (49.3%)             |
| **Working status**                     |                         |
| Employed                               | 930 (70.5%)             |
| Unemployed                             | 262 (19.8)              |
| Housewife                              | 113 (8.6%)              |
| Student                                | 15 (1.1%)               |
| **Low socio-economic status**          |                         |
| Low socio-economic status              | 417 (31.6%)             |
| **Tobacco use during pregnancy**       |                         |
| Tobacco use during pregnancy           | 127 (9.6%)              |
| **Pre-pregnancy BMI (kg/h^2)**         | 24.1 (4.7)              |
| **Medical history**                    |                         |
| Obesity (BMI > 30)                     | 157 (11.9%)             |
| Psychiatric disorders *                | 28 (2.1%)               |
| Cardiac diseases                       | 45 (3.4%)               |
| Respiratory disorders                  | 65 (4.9%)               |
| Diabetes Mellitus                      | 18 (1.4%)               |
| Thyroid diseases                       | 91 (6.9%)               |
| **Obstetric history**                  |                         |
| Nulliparous                            | 724 (54.9%)             |
| Assisted reproductive technologies     | 98 (7.4%)               |

Data expressed as n (%), median (IQR), or mean (SD). BMI: Body Mass Index. * Psychiatric disorders requiring therapy during pregnancy.

Table 2. Pandemic cohort pregnancy and neonatal outcomes.

| Characteristics                                          | Total Cohort (n = 1320) |
|----------------------------------------------------------|-------------------------|
| **Preeclampsia**                                         | 57 (4.3%)               |
| Threatened/spontaneous preterm delivery                  | 55 (4.2%)               |
| Preterm premature rupture of the membranes               | 40 (3%)                 |
| Stillbirth                                               | 7 (0.5%)                |
| Induction of labor                                       | 509 (38.6%)             |
| **Gestational age at recruitment**                       |                         |
| In first trimester                                       | 10.7 (9.9–12.1)         |
| In third trimester                                       | 39.7 (38.6–40.6)        |
| **Gestational age at delivery**                          | 39.2 (2.2)              |
| Prematurity (<37 weeks)                                 | 84 (6.4%)               |
| **Mode of delivery**                                    |                         |
| Vaginal delivery                                         | 851 (64.5%)             |
| Operative vaginal delivery                               | 123 (9.3%)              |
| Cesarean section                                         | 346 (26.2%)             |
| Fetal distress                                           | 123 (9.3%)              |
| Female gender                                            | 616 (46.7%)             |
| **Birth weight (grams)**                                | 3280 (2985–3580)        |
| Birth weight percentile                                 | 48 (24–74)              |
Table 2. Cont.

| Characteristics                              | Total Cohort (n = 1320) |
|----------------------------------------------|-------------------------|
| Small for gestational age (<10th centile)    | 154 (11.7%)             |
| Severe small for gestational age (<3rd centile) | 52 (3.9%)            |
| Large for gestational age (>90th centile)    | 157 (11.9%)             |
| 5-min Apgar 5 score                          | 9.9 (0.7)               |
| Neonatal complications                       | 52 (3.9%)               |

Data expressed as n (%), median (IQR), or mean (SD).

3.2. Maternal Well-Being

The median (IQR) WHO-5 score in the overall pandemic cohort was 56 (36–72); the score in 565 women (42.8%) was ≤52, suggestive of poor well-being, whereas in 755 participants (57.2%) it was >52, indicating favorable well-being (Figure 1).

![Figure 1. Maternal WHO-5 well-being outcomes for the pandemic cohort.](image)

WHO-5 results for pregnant women during the COVID-19 pandemic (median (IQR) 56 (36–72)) were worse than for the pre-pandemic cohort (n = 345), (median (IQR) 64 (52–76)) (p < 0.001). In the pandemic cohort, 42.8% of women had a poor well-being score vs. 28% for the pre-pandemic cohort (p < 0.001) (Figure A1). Results were adjusted by ethnicity and psychiatric disorders (Table A1).

Table 3 shows the characteristics of the COVID-19 cohort, classified according to maternal WHO-5 well-being. No significant statistical differences were found for maternal age, ethnicity, socioeconomic status, BMI, parity, or assisted reproductive technologies. However, the existence of previous maternal psychiatric disorders was a significant contributor to low maternal well-being (4.1% vs. 0.6% in case of a favorable well-being, p < 0.001) (Figure 2a).

Table 3. Pandemic cohort baseline characteristics based on maternal well-being (WHO-5).

| Characteristics | WHO-5 ≤ 52 (n = 565) | WHO-5 > 52 (n = 755) | p-Value |
|-----------------|-----------------------|----------------------|---------|
| Age (years)     | 32.8 (28.8–37)        | 33.6 (29.6–37.2)     | 0.050   |
| Ethnicity       |                       |                      |         |
| White           | 367 (65%)             | 491 (65%)            | 0.977   |
| Latin American  | 135 (23.9%)           | 162 (21.5%)          | 0.294   |
| Black           | 6 (1.1%)              | 17 (2.3%)            | 0.102   |
| Asian           | 37 (6.5%)             | 44 (5.8%)            | 0.589   |
| Others          | 20 (3.5%)             | 41 (5.4%)            | 0.105   |
Table 3. Cont.

| Characteristics                  | WHO-5 ≤ 52 (n = 565) | WHO-5 > 52 (n = 755) | p-Value |
|----------------------------------|-----------------------|----------------------|---------|
| Education level                  |                       |                      |         |
| Not educated                     | 13 (2.3%)             | 18 (2.4%)            | 0.921   |
| Primary                          | 35 (6.2%)             | 51 (6.8%)            | 0.683   |
| Secondary                        | 168 (29.7%)           | 192 (25.6%)          | 0.092   |
| Vocational                       | 76 (13.5%)            | 115 (15.2%)          | 0.363   |
| University                       | 273 (48.3%)           | 378 (50.1%)          | 0.530   |
| Working status                   |                       |                      |         |
| Employed                         | 396 (70.1%)           | 534 (70.7%)          | 0.801   |
| Unemployed                       | 107 (19%)             | 154 (20.4%)          | 0.520   |
| Housewife                        | 54 (9.6%)             | 59 (7.8%)            | 0.259   |
| Student                          | 7 (1.2%)              | 8 (1.1%)             | 0.761   |
| Low socio-economic status        | 182 (32.2%)           | 235 (31.1%)          | 0.674   |
| Tobacco use during pregnancy     | 53 (9.4%)             | 74 (9.8%)            | 0.798   |
| BMI (kg/m²)                      | 24 (4.6)              | 24.2 (4.8)           | 0.340   |
| Medical history                  |                       |                      |         |
| Obesity (BMI > 30)               | 67 (11.9%)            | 90 (11.9%)           | 0.972   |
| Psychiatric disorders *          | 23 (4.1%)             | 5 (0.7%)             | <0.001  |
| Cardiac diseases                 | 13 (2.3%)             | 32 (4.2%)            | 0.085   |
| Respiratory disorders            | 29 (5.1%)             | 36 (4.8%)            | 0.762   |
| Diabetes Mellitus                | 6 (1.1%)              | 12 (1.6%)            | 0.414   |
| Thyroid diseases                 | 30 (5.3%)             | 61 (8.1%)            | 0.049   |
| Obstetric history                |                       |                      |         |
| Nulliparous                      | 314 (55.6%)           | 411 (54.4%)          | 0.681   |
| Assisted reproductive technologies| 36 (6.4%)             | 62 (8.2%)            | 0.207   |

Data expressed as n (%), median (IQR), or mean (SD). BMI: Body Mass Index. * Psychiatric disorders requiring therapy during pregnancy.

Figure 2. Maternal WHO-5 well-being outcomes for the pandemic cohort based on the presence of psychiatric disorders (a) and trimester of pregnancy (b).

Regarding pregnancy and neonatal outcomes, being in the third trimester of pregnancy was significantly associated to worse maternal well-being (median (IQR) score 48 (I32–64) (p < 0.001) (Figure 2b). This association was not seen for preeclampsia, prematurity, cesarean section, or fetal distress among others (Table 4).
Table 4. Pregnancy and neonatal outcomes for the pandemic cohort based on WHO-5 well-being.

| Characteristics                          | WHO-5 ≤ 52 (n = 565) | WHO-5 > 52 (n = 755) | p-Value |
|-----------------------------------------|-----------------------|----------------------|---------|
| Trimester                               |                       |                      | <0.001  |
| First trimester                         | 117 (20.7%)           | 327 (43.3%)          |         |
| Third trimester                         | 448 (79.3%)           | 428 (56.7%)          |         |
| Preeclampsia                            | 28 (5%)               | 29 (3.8%)            | 0.324   |
| Threatened/spontaneous preterm labor    | 29 (5.2%)             | 25 (3.6%)            | 0.147   |
| Preterm premature rupture of the membranes | 15 (2.7%)           | 25 (3.3%)            | 0.491   |
| Stillbirth                              | 3 (0.5%)              | 4 (0.5%)             | 0.998   |
| Induction of labor                      | 226 (40%)             | 283 (37.5%)          | 0.353   |
| Gestational age at delivery             | 39.1 (2.3)            | 39.3 (2.1)           | 0.316   |
| Prematurity (<37 weeks)                 | 40 (7.1%)             | 44 (5.8%)            | 0.357   |
| Mode of delivery                        |                       |                      |         |
| Vaginal delivery                        | 361 (63.9%)           | 490 (64.9%)          | 0.705   |
| Operative vaginal delivery              | 56 (9.9%)             | 67 (8.9%)            | 0.551   |
| Cesarean section                        | 148 (26.2%)           | 198 (26.2%)          | 0.990   |
| Fetal distress                          | 61 (10.8%)            | 62 (8.2%)            | 0.110   |
| Female gender                           | 269 (47.6%)           | 347 (46%)            | 0.552   |
| Birth weight (grams)                    | 3260 (2940–3560)      | 3295 (3020–3595)     | 0.076   |
| Birth weight percentile                 | 45 (21–74)            | 50 (27–74)           | 0.47    |
| Small for gestational age (<10th centile)| 67 (11.9%)           | 87 (11.5%)           | 0.851   |
| Severe small for gestational age (<3rd centile)| 22 (3.9%)       | 30 (4%)              | 0.941   |
| Large for gestational age (>90th centile)| 68 (12%)            | 89 (11.8%)           | 0.891   |
| 5-min Apgar score                       | 9.8 (0.8)             | 9.9 (0.7)            | 0.268   |
| Neonatal complications                  | 29 (5.1%)             | 23 (3%)              | 0.054   |

Data expressed as n (%), median (IQR), or mean (SD).

Regarding SARS-CoV-2 infection, the infection itself did not have an effect on the level of maternal well-being (p = 0.812) (Figure 3a). However, presence of severe symptoms (fever, cough, or dyspnea) and hospital admission for COVID-19 were associated with a lower well-being score (Table 5 and Figure 3b). No SARS-CoV-2 infection cases were reported in newborns.
Table 5. Symptoms and diagnosis of SARS-CoV-2 infection and COVID-19 disease in the pandemic cohort based on the level of maternal WHO-5 well-being.

| Characteristics                                      | WHO-5 ≤ 52 (n = 565) | WHO-5 > 52 (n = 755) | p-Value |
|------------------------------------------------------|-----------------------|----------------------|---------|
| Positive SARS-CoV-2 testing                          | 88 (15.6%)            | 114 (15.1%)          | 0.812   |
| Symptoms of SARS-CoV-2 infection within the last 10 weeks | 95 (16.8%)            | 87 (11.5%)           | 0.006   |
| Fever                                                | 25 (4.4%)             | 19 (2.5%)            | 0.056   |
| Dry cough                                            | 44 (7.8%)             | 31 (4.1%)            | 0.004   |
| Difficulty breathing or shortness of breath          | 17 (3%)               | 12 (1.6%)            | 0.082   |
| Diarrhea                                             | 20 (3.5%)             | 16 (2.1%)            | 0.117   |
| Other respiratory symptoms                           | 9 (1.6%)              | 8 (1.2%)             | 0.534   |
| Myalgia                                              | 17 (3%)               | 17 (2.3%)            | 0.390   |
| Skin rash                                            | 5 (0.9%)              | 4 (0.5%)             | 0.438   |
| Loss of taste or smell                               | 15 (2.7%)             | 12 (1.6%)            | 0.176   |
| Other                                                 | 10 (1.8%)             | 16 (2.1%)            | 0.651   |
| **Combination of symptoms predictable for SARS-CoV-2 infection** |                       |                      |         |
| At least two symptoms or anosmia                     | 44 (7.8%)             | 39 (5.2%)            | 0.052   |
| At least three symptoms or anosmia                   | 22 (3.9%)             | 20 (2.6%)            | 0.202   |
| Fever, cough and dyspnea                             | 8 (1.4%)              | 1 (0.1%)             | 0.005   |
| **Symptom-related COVID-19 severity**                |                       |                      |         |
| Mild                                                 | 2 (14.5%)             | 79 (10.5%)           | 0.026   |
| Moderate                                             | 5 (0.9%)              | 7 (0.9%)             | 0.936   |
| Severe                                               | 8 (1.4%)              | 1 (0.1%)             | 0.005   |
| **COVID-19 disease**                                 |                       |                      |         |
| Admission for COVID-19 disease                       | 15 (2.7%)             | 3 (0.4%)             | <0.001  |
| Pneumonia                                            | 3 (0.5%)              | 1 (0.1%)             | 0.192   |
| Severe pneumonia                                     | 2 (0.4%)              | 1 (0.1%)             | 0.403   |
| Oxygen support                                       | 2 (0.4%)              | 1 (0.1%)             | 0.403   |
| Admission to intensive care unit                     | 1 (0.2%)              | 1 (0.1%)             | 0.837   |
| Invasive ventilatory support                         | 1 (0.2%)              | 0 (0%)               | 0.248   |

Data are expressed as n (%). RT-PCR: Real Time Polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Multivariate analyses revealed significant contribution to low maternal well-being with the presence of psychiatric disorders (OR 7.1; 95% CI 2.6–19, p < 0.001), being in the third trimester of pregnancy (OR 1.7; 95% CI 1.5–2, p < 0.001), or hospital admission for COVID-19 (OR 4.7; 95% CI 1.4–16.7, p = 0.014) (Table 6). No association was found between SARS-CoV-2 infection itself and a reduced well-being score.

Table 6. Multivariate analysis of factors associated to poor maternal WHO-5 well-being in the pandemic cohort.

| Univariate Analysis | Multivariate Analysis |
|---------------------|-----------------------|
|                     | OR (95% CI) | p-value | OR (95% CI) | p-value | Betta Coefficient |
| Baseline maternal characteristics |               |         |               |         |                  |
| Age (years)          | 0.98 (0.96–1) | 0.051   |               |         |                  |
| Gestational age at recruitment (weeks) | 1.04 (1.03–1.05) | <0.001 | 1.04 (1.03–1.05) | <0.001 |                  |
| Non-European ethnicity | 1 (0.8–1.3)  | 0.977   |               |         |                  |
| Low socio-economic status | 1 (0.8–1.3)  | 0.674   |               |         |                  |
| Tobacco use during pregnancy | 0.95 (0.7–1.4) | 0.789 | 0.95 (0.7–1.4) | 0.789 |                  |
| Psychiatric disorders | 6.4 (2.4–16.9) | <0.001 | 6.4 (2.4–16.9) | <0.001 | 1.947 |
| Thyroid diseases     | 0.6 (0.4–1)   | 0.051   |               |         | 0.83 |
| Nulliparity          | 1 (0.8–1.3)   | 0.661   |               |         |                  |
| Assisted reproductive techniques | 0.7 (0.5–1.2) | 0.208 | 0.7 (0.5–1.2) | 0.208 |                  |
| Pregnancy outcomes   |               |         |               |         |                  |
| Trimester (first vs. third) | 1.7 (1.5–1.9) | <0.001 | 1.7 (1.5–1.9) | <0.001 | 0.537 |
| Induction of labor   | 1.1 (0.9–1.4) | 0.353   |               |         |                  |
| Cesarean section     | 0.99 (0.8–1.3) | 0.99     |               |         |                  |
| SARS-CoV-2 status  |               |         |               |         |                  |
| Positive SARS-CoV-2 testing | 1 (0.8–1.4) | 0.812   |               |         |                  |
| Presence of at least one COVID-19 symptom | 1.5 (1.1–2.1) | 0.006 | 1.5 (1.1–2.1) | 0.006 |                  |
| Presence of fever, cough and dyspnea | 10.8 (1.3–86.8) | 0.025 | 10.8 (1.3–86.8) | 0.025 |                  |
| Presence of severe COVID-19 symptoms | 10.8 (1.3–86.8) | 0.025 | 10.8 (1.3–86.8) | 0.025 |                  |
| Hospital admission for COVID-19 | 6.8 (1.9–23.7) | 0.002 | 6.8 (1.9–23.7) | 0.002 | 1.565 |

Data are expressed as n (%). OR: Odds Ratio; CI: confidence interval; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19: Coronavirus 19 disease.
3.3. Lockdown Characteristics

Four hundred and eighty participants of the pandemic cohort answered a structured questionnaire on lockdown characteristics (Table A2). Most pregnant women remained isolated in their usual residence \((n = 448; 93.3\%)\) without older people at home \((n = 434; 90.4\%)\) and the majority \((n = 439; 91.5\%)\) were not concerned with the general impact of the pandemic, although 332 \((69.2\%)\) communicated they were worried about their pregnancy and their fetus. No significant contributors to maternal well-being status were identified (Table A2).

4. Discussion

4.1. Main Findings

The well-being score in almost half \((43\%)\) of our study population is low. This has been related to symptoms of depression \([21]\). Thus, maternal well-being status during the COVID-19 pandemic is affected. This is more evident when we compare pandemic versus pre-pandemic cohorts, where 28% of the latter cohort had poor well-being scores. Additionally, there are risk factors that contribute to a worse well-being during pregnancy, such as previous psychiatric disease, being in the third trimester of pregnancy, and hospital admission for COVID-19 disease. The infection of SARS-CoV-2 itself did not increase the risk of a lower well-being condition, but the severity of COVID-19 disease requiring hospitalization did.

Well-being is broadly defined as ‘the quality and state of a person’s life’ \([22]\) and consists of two components: feeling healthy and relatively robust and being able to carry out ones job and other tasks satisfactorily \([23]\). Fear related to childbirth is multidimensional and, under normal circumstances, only around 20% of pregnant women experience excessive concern regarding future events in pregnancy \([23]\). Feelings of well-being are key to the overall health of an individual but can be affected by physical and emotional trauma.

Several studies have reported a compromised maternal mental status during the COVID-19 pandemic \([3,12,16,24]\). Higher depressive rates in comparison to pre-pandemic subjects \([13]\) and prevalence of depressive and anxiety symptoms ranging around 15–19% and 11–31%, respectively, \([12,16]\) have been found. However, most of these works are based on maternal depression and anxiety scales and a limited number use maternal well-being as an assessment of maternal physical, mental, and social health \([23]\).

Few studies have compared pandemic cohort data to a previous pre-pandemic cohort, suggesting worse maternal anxiety and depression levels in patients assessed during the COVID-19 pandemic. Wu et al. reported higher depression symptoms in patients during the pandemic in comparison to a pre-pandemic cohort and found a positive association with the number of newly COVID-19 confirmed cases, suspected cases, and deaths \([13]\). Similarly, in a study by Berthelot et al., the authors found that COVID-19 pandemic-affected women were more likely to present depressive and anxiety symptoms, especially those with a previous psychiatric diagnosis or low income \([25]\). Zanardo et al. reported higher scores for anhedonia and depression in comparison to 100 previous patients \([26]\). Interestingly, Dong et al. found that anxiety levels of pregnant women were the same as before the pandemic, while the level of depression was significantly higher. The authors reported no differences in terms of gestational age or testing positive for SARS-CoV-2 infection \([17]\). Perzow et al. compared 135 patients pre- and post-pandemic and determined higher levels of anxiety and depression during the pandemic \([27]\). To the best of our knowledge, ours is the first study that assesses maternal well-being before and after the pandemic.

Our results suggest that the existence of a previous psychiatric maternal condition is as a risk factor for worse maternal well-being. Similarly, some studies have reported that a previous psychiatric disorder diagnosed in pregnant women is as a risk factor for depression symptoms during the COVID-19 pandemic \([25,28,29]\). The stage of pregnancy had a unique association with anxiety and the level of well-being. Zeng et al. reported that the third trimester of pregnancy at the time of the COVID-19 pandemic seemed to be associated with a worse maternal well-being, with even worse results in comparison to the
post-partum period [12]. On the contrary, Saccone et al. found worse results in anxiety and psychological impact in pregnant women in the first trimester [24]. Other authors found no differences according to gestational age [11,17,30].

COVID-19 symptoms and infection have been described as anxiety factors [31] and predictors for post-traumatic stress disorder [32]. However, these studies did not consider the differences between confirmed SARS-CoV-2 infected and healthy patients. SARS-CoV-2 infection may increase the level of anxiety and worsen mental condition; our data do not confirm this hypothesis as found in other studies with smaller sample sizes [15,17]. We report worse maternal well-being in SARS-CoV-2 infected mothers with severe symptoms or requiring hospital admission due to COVID-19 disease for respiratory and or medical support according to our center protocols at the time of the study.

4.2. Clinical Relevance

Our results suggest the potential utility of maternal well-being screening during the COVID-19 pandemic, especially in patients with a previous diagnosis of mental illness and in their third trimester of pregnancy, close to delivery. There is no negative effect of SARS-CoV-2 maternal infection on their well-being. However, well-being is affected in pregnant women who require hospital admission for moderate to severe COVID-19 disease, who might benefit from a psychological support during their hospital stay.

4.3. Strengths and Limitations

Some of the strengths of this study include a very well characterized population of pregnant women, laboratory confirmation of SARS-CoV-2 infection in all women in different pregnancy stages and during the first wave of COVID-19 pandemic, where strict restriction measures were applied. The short and simple WHO-5 questionnaire can screen depressive symptoms and evaluate subjective well-being in pregnant populations, which can be helpful in daily clinical practice, especially when healthcare pressure is high. There are several limitations to this study. The WHO-5 questionnaire was self-administration with no psychiatric screening thereafter, there were no postpartum depression or anxiety symptoms follow-ups, and baseline characteristics of the pre-pandemic and pandemic cohorts were not identical. To overcome these limitations, we applied careful statistical adjustments. Moreover, our study did not include a follow-up of postpartum depression or anxiety symptoms that could be considered in future studies.

5. Conclusions

In conclusion, the COVID-19 pandemic is a challenge for pregnant women in terms of well-being, especially in their third trimester of pregnancy. Previous psychiatric disorders are associated to higher risk of poor well-being. The well-being of pregnant women testing positive for SARS-CoV-2 infection is not affected, except when presenting severe infection-related symptomatology or requiring hospitalization due to COVID-19 disease, in which cases poorer well-being was reported.

Author Contributions: F.C. (Francesca Crovetto), F.C. (Fátima Crispi) and E.G. conceived and designed the study. E.L., F.C. (Francesca Crovetto) and M.D.G.-R. were responsible of the study protocol at each hospital and ensured the correct execution of the study. F.C. (Francesca Crovetto), F.C. (Fátima Crispi) and E.L. were the supervisors at each of the three hospitals for day-to-day running of the study, including participant recruitment and data collection. R.P., M.L., C.T., A.C., D.B. and I.C. were responsible of medical file revision and data collection at the three participating hospitals. I.C., J.S., M.F. and L.Y. performed the data analyses. F.C. (Francesca Crovetto) supervised the data analysis. R.P. and F.C. (Francesca Crovetto) drafted the first version of manuscript. E.G. is the principal investigator of the project. None of the authors received any compensation for their contribution. All authors have read and agreed to the published version of the manuscript.
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Appendix A.

Appendix A.1. COVID-19 Evaluation

COVID-19 symptoms were recorded at hospital admission using a structured self-prepared questionnaire that included questions about risk factors and COVID-19 suggestive symptoms noticed between mid-February 2020 and the time of SARS-CoV-2 testing. All positive women completed the same questionnaire again 4–5 weeks later. Symptomatic SARS-CoV-2 infected women were defined as having at least one of the following symptoms: fever, dry cough, anosmia or ageusia, dyspnea, myalgia, diarrhea, sore throat, skin rash, or discoloration of fingers and/or toes.

Appendix A.2. Sample Collection

Maternal blood samples were drawn from peripheral veins in first and third trimester participants, at recruitment. Samples were centrifuged at 1500 × g for 10 min at 4 °C and sera immediately stored at −80 °C until further analysis. For SARS-CoV-2 IgG and IgM/IgA antibody determination, the COVID-19 VIRCLIA® Monotest (Vircell Microbiologist, Granada, Spain) was used. Indeterminate results were re-tested (VITROS® Immunodiagnostic Products Anti-SARS-CoV2 Total Tests, Ortho Clinical Diagnostics, Rochester, NY, USA) and classified as positive or negative. Likewise, results positive for IgM + IgA but negative for IgG in women reporting no symptoms suggestive of COVID-19 during the 10 weeks prior testing were re-tested with Luminex and classified as positive or negative [33]. A serological result was considered positive if any of the following were found: (a) IgG positive, (b) IgM + IgA positive in women with symptomatic COVID-19, (c) IgM + IgA positive confirmed by two tests (Vircell and Luminex).

Nasopharyngeal swab samples for SARS-CoV-2 RNA RT-PCR were collected in all third trimester pregnancies recruited at hospital admittance. Samples were collected in Micronics tubes with Zymo DNA/RNA Shield Lysis buffer. RNA was extracted using the Quick-DNA/RNA Viral MagBead kit (Zymo) and the TECAN Dreamprepp robot. Five microliters of RNA solution were added to 15 µL of the rRT-PCR master mix (Luna Universal Probe One-Step RT-qPCR Kit; New England Biolabs) and used for amplification of the SARS-CoV-2 N1 and N2 regions, as well as the human RNase P gene as control, as described in the CDC-006-00019 CDC/DDID/NCIRD/Division of Viral Diseases protocol released 3/30/2020. A SARS-CoV-2 positive result was considered if Ct values for N1, N2, and RNase P were below 40. Samples discordant for N1 and N2 were repeated and samples with a Ct ≥ 40 for RNase P were considered as invalid.

SARS-CoV-2 infection was defined by either a positive serological result or RT-PCR in nasopharyngeal swabs.
Appendix B.

**Table A1.** Baseline characteristics of pre-pandemic and COVID-19 pandemic pregnant women cohorts.

| Characteristics                                      | Pre-Pandemic (n = 345) | Pandemic (n = 1320) | p-Value |
|------------------------------------------------------|------------------------|---------------------|---------|
| **Ethnicity**                                        |                        |                     |         |
| White                                                | 279 (80.9%)            | 858 (65%)           | <0.001  |
| Latin American                                       | 49 (14.2%)             | 297 (22.5%)         | 0.001   |
| Black                                                | 6 (1.7%)               | 23 (1.7%)           | 0.997   |
| Asian                                                | 6 (1.7%)               | 81 (6.1%)           | 0.001   |
| Others                                               | 5 (1.4%)               | 61 (4.6%)           | 0.007   |
| **Tobacco use during pregnancy**                     |                        |                     |         |
|                                                      | 27 (7.8%)              | 127 (9.6%)          | 0.305   |
| **Pre-pregnancy BMI (kg/m^2)**                       |                        |                     |         |
|                                                      | 23.8 (4.8)             | 24.1 (4.7)          | 0.29    |
| **Medical history**                                  |                        |                     |         |
| Obesity (BMI > 30)                                   | 39 (11.3%)             | 157 (11.9%)         | 0.762   |
| Psychiatric disorders *                              | 15 (4.3%)              | 28 (2.1%)           | 0.020   |
| Thyroid diseases                                     | 31 (9%)                | 91 (6.9%)           | 0.184   |
| **Obstetric history**                                |                        |                     |         |
| Nulliparous                                          | 203 (58.8%)            | 725 (54.9%)         | 0.192   |
| Data are expressed as n (%) or median (IQR) or mean (SD). BMI: Body mass index. * Psychiatric disorders requiring therapy during pregnancy.

**Table A2.** Self-administered questionnaire on COVID-19 pandemic-related conditions.

| Characteristics                                      | Total Cohort (n = 480) | WHO-5 ≤ 52     | WHO-5 > 52 | p-Value |
|------------------------------------------------------|------------------------|----------------|-----------|---------|
| **SARS-CoV-2 diagnosis by laboratory test**           |                        |                |           | 0.079   |
| Yes                                                  | 7 (1.5%)               | 10 (3.4%)      | 2 (1%)    |         |
| No                                                   | 473 (98.5%)            | 267 (96.6%)    | 207 (99%) |         |
| **Contact with a symptomatic SARS-CoV-2 person**     |                        |                |           | 0.098   |
| Yes                                                  | 42 (8.8%)              | 21 (7%)        | 24 (11.2%)|         |
| No                                                   | 438 (91.3%)            | 278 (93%)      | 190 (88.8%)|         |
| **Know someone diagnosed by SARS-CoV-2**             |                        |                |           | 0.247   |
| Yes                                                  | 129 (26.9%)            | 74 (24.4%)     | 62 (29%)  |         |
| No                                                   | 351 (73.1%)            | 229 (75.6%)    | 152 (71%) |         |
| **Degree of concern about SARS-CoV-2 epidemic**      |                        |                |           | 0.888   |
| I'm very worried                                      | 192 (40%)              | 112 (37.2%)    | 94 (44.1%)|         |
| I'm quite worried                                     | 222 (46.3%)            | 141 (46.8%)    | 97 (45.5%)|         |
| I'm a little worried                                  | 59 (12.3%)             | 45 (15%)       | 18 (8.5%) |         |
| Don't care                                           | 7 (1.5%)               | 3 (1%)         | 4 (1.9%)  |         |
| **Worry of getting the disease yourself or a family member** |                  |                |           | 0.537   |
| I'm very worried                                      | 279 (58.1%)            | 170 (56.1%)    | 133 (62.1%)|         |
| I'm quite worried                                     | 159 (33.1%)            | 107 (35.3%)    | 63 (29.4%)|         |
| I'm a little worried                                  | 40 (8.3%)              | 25 (8.3%)      | 17 (7.9%) |         |
| Don't care                                           | 2 (0.4%)               | 1 (0.3%)       | 1 (0.5%)  |         |
| **Effect on the pregnancy and fetus concerns**       |                        |                |           | 0.220   |
| I'm very worried                                      | 332 (69.2%)            | 202 (66.9%)    | 156 (72.9%)|         |
| I'm quite worried                                     | 84 (17.5%)             | 58 (19.2%)     | 32 (15%)  |         |
| I'm a little worried                                  | 53 (11%)               | 33 (10.9%)     | 24 (11.2%)|         |
| Don't care                                           | 11 (2.3%)              | 9 (3%)         | 2 (0.9%)  |         |
| **Personal economic concern**                        |                        |                |           | 0.944   |
| I'm very worried                                      | 226 (47.1%)            | 146 (48.2%)    | 102 (47.7%)|         |
| I'm quite worried                                     | 148 (30.8%)            | 88 (29%)       | 66 (30.8%)|         |
| I'm a little worried                                  | 86 (17.9%)             | 55 (18.2%)     | 38 (17.8%)|         |
| Don't care                                           | 20 (4.2%)              | 14 (4.6%)      | 8 (3.7%)  |         |
| **Impact on global economy concerns**                |                        |                |           | 0.110   |
| I'm very worried                                      | 199 (41.5%)            | 124 (40.9%)    | 93 (43.5%)|         |
| I'm quite worried                                     | 198 (41.3%)            | 116 (38.3%)    | 94 (43.9%)|         |
| I'm a little worried                                  | 72 (15%)               | 55 (18.2%)     | 24 (11.2%)|         |
| Don't care                                           | 11 (2.3%)              | 8 (2.6%)       | 3 (1.4%)  |         |
| Characteristics                                      | Total Cohort (n = 480) | WHO-5 ≤ 52 | WHO-5 >52 | p-Value |
|------------------------------------------------------|------------------------|------------|-----------|---------|
| Excessive worrying                                   |                        |            |           |         |
| Yes                                                  | 41 (8.5%)              | 36 (11.9%) | 14 (6.5%) | 0.092   |
| No                                                   | 439 (91.5%)             | 267 (88.1%)| 200 (93.5%)|         |
| Does the pregnant woman have enough information      |                        |            |           |         |
| regarding the effects of the virus on pregnancy and  |                        |            |           |         |
| the fetus                                            |                        |            |           |         |
| Yes                                                  | 216 (45%)              | 141 (47.2%)| 89 (41.6%)| 0.332   |
| No                                                   | 264 (55%)              | 160 (52.8%)| 125 (58.4%)|         |
| Isolation in primary residence                       |                        |            |           |         |
| Yes                                                  | 448 (93.3%)             | 277 (91.4%)| 199 (93%) | 0.515   |
| No                                                   | 32 (6.7%)               | 26 (8.6%)  | 25 (7%)   |         |
| People at risk living at home                        |                        |            |           |         |
| Yes                                                  | 46 (9.6%)               | 27 (8.9%)  | 23 (10.8%)| 0.548   |
| No                                                   | 434 (90.4%)             | 275 (91%)  | 189 (89.2%)|         |
| Terrace or garden at home                            |                        |            |           |         |
| Yes                                                  | 251 (52.3%)             | 158 (53.2%)| 111 (52.1%)| 0.809   |
| No                                                   | 229 (47.7%)             | 139 (46.8%)| 102 (47.9%)|         |
| Work                                                 |                        |            |           |         |
| No                                                   | 419 (87.3%)             | 266 (88.1%)| 184 (86%) | 0.748   |
| Yes, from home                                       | 51 (10.6%)              | 29 (9.6%)  | 25 (11.7%)|         |
| Yes, at my usual place of work                       | 10 (2.1%)               | 7 (2.3%)   | 5 (2.3%)  |         |
| How many times a week does she go out                |                        |            |           |         |
| Never                                                | 162 (33.8%)             | 97 (32%)   | 78 (36.4%)| 0.352   |
| One or two times a week                              | 232 (48.3%)             | 146 (48.2%)| 106 (49.5%)|         |
| Between three and five times a week                  | 52 (10.8%)              | 36 (11.9%) | 19 (8.9%) |         |
| Six or more times a week                             | 34 (7.1%)               | 24 (7.9%)  | 11 (5.1%) |         |
| Coping with isolation                                |                        |            |           | <0.001  |
| Very well                                            | 94 (19.6%)              | 69 (23.1%) | 28 (13.1%)|         |
| Pretty well                                           | 309 (64.4%)             | 197 (65.9%)| 136 (63.8%)|         |
| Poorly                                               | 68 (14.2%)              | 29 (9.7%)  | 42 (19.7%)|         |
| Very poorly                                          | 9 (1.9%)                | 4 (1.3%)   | 7 (3.3%)  |         |
| Mental health before the pandemic                     |                        |            |           | 0.069   |
| Excellent                                            | 106 (26.6%)             | 75 (29.8%) | 38 (21.5%)|         |
| Very good                                            | 180 (45.2%)             | 115 (45.6%)| 65 (41.8%)|         |
| Good                                                 | 97 (24.4%)              | 56 (22.2%) | 41 (24.6%)|         |
| Regular                                              | 11 (2.8%)               | 4 (1.6%)   | 10 (5.6%) |         |
| Bad                                                  | 4 (1%)                  | 2 (0.8%)   | 2 (1.1%)  |         |

Data are expressed as n (%). SARS-CoV-2: severe acute respiratory syndrome coronavirus.

Table A3. Prevalence of SARS-CoV-2 infection during pregnancy.

| Characteristics                                      | Total Cohort (n = 1320) |
|------------------------------------------------------|-------------------------|
| SARS-CoV-2 positive (RT-PCR and/or Ab)                | 202 (15.3%)             |
| First trimester                                       | 82 (40.6%)              |
| Third trimester                                       | 120 (59.4%)             |
| RT-PCRa positive                                      | 26 (3%)                 |
| Ab for SARS-CoV-2 infection IgM/A/G                   |                          |
| Negative                                             | 1120 (84.8%)            |
| Positive                                             | 200 (15.2%)             |

Data are expressed as n (%) or median (IQR); SARS-CoV-2: severe acute respiratory syndrome coronavirus; RT-PCR: Real Time Polymerase chain reaction; Ab: Antibody. Data available only for 876 cases (Third trimester participants).


**Figure A1.** WHO-5 well-being level in pre-pandemic ($n = 345$) and pandemic ($n = 1320$) cohorts.

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