

# COVID-19 and Perinatal Stress Experience – a Study Conducted as Part of the COVGEN Initiative

## COVID-19 und perinatales Stresserleben – eine Studie im Rahmen der COVGEN-Initiative



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### ABSTRACT

**Introduction** During the COVID-19 pandemic, stress and anxiety in the population increased due to concerns about people's own health and that of their relatives, as well as changes in everyday life due to measures taken to reduce the infection rate. Pregnant women are particularly stressed. The present study examines how the COVID-19 pandemic affects the stress experience and mental health of pregnant women and mothers of newborns and how care could be optimized.

**Methods** As part of the international COVGEN initiative (<https://www.covgen.org>) to investigate the effects of the COVID-19 pandemic on the peripartum period, pregnant and postpartum women were asked about their experience with stress using the COPE-IS (Coronavirus Perinatal Experiences – Impact Survey) questionnaire developed for this purpose and translated from the English. In addition, demographic data, pre-existing diseases, pregnancy complications and the care situation were recorded. The questionnaire was either administered as hardcopy to inpatients at the Department of Women's Health, University Hospital Tübingen, Germany, or online. All pregnant women and mothers who were pregnant or had given birth after the official start of the COVID-19 pandemic (11 March 2020) were eligible to participate.

**Results** Complete data sets of  $n = 156$  pregnant women and  $n = 221$  postpartum women were available for evaluation. The general stress level assessed with the COPE-IS was significantly increased by the COVID-19 pandemic in both, pregnant and postpartum women, with pre-existing conditions such as respiratory diseases and pregnancy-related diseases like gestational diabetes adding to the stress. The subjectively perceived quality of care/support during pregnancy also influenced the stress level.

**Conclusions** Fears of a COVID-19 infection and changes in preventive and aftercare services were a burden for the women surveyed. Intensified care during pregnancy and puerperium could help to stabilize the mental situation and reduce stress.

## ZUSAMMENFASSUNG

**Einleitung** Während der COVID-19-Pandemie haben Stress und Angst in der Bevölkerung zugenommen, bedingt durch Sorgen um die eigene Gesundheit und die der Angehörigen sowie Veränderungen des Alltags durch Maßnahmen zur Eindämmung der Infektionsrate. Schwangere Frauen sind besonders belastet. Die vorliegende Studie untersucht, wie sich die COVID-19-Pandemie auf das Stresserleben und die mentale Gesundheit schwangerer Frauen und Mütter von Neugeborenen auswirkt und wie die Versorgung optimiert werden könnte.

**Methoden** Im Rahmen der internationalen COVGEN Initiative (<https://www.covgen.org>) zur Erforschung der Auswirkungen der COVID-19-Pandemie auf die Peripartalzeit wurden

schwängere und postpartale Frauen mit einem zu diesem Zweck entwickelten und aus dem englischen übersetzten Fragebogen COPE-IS (Coronavirus Perinatal Experiences – Impact Survey) zu ihrem Stresserleben befragt. Zusätzlich wurden unter anderem demografische Daten, Vorerkrankungen, Schwangerschaftskomplikationen und die Versorgungssituation erfasst. Der Fragebogen wurde papierbasiert (stationäre Patientinnen am Department für Frauengesundheit des Universitätsklinikums Tübingen) und online angeboten. Es konnten alle schwangeren Frauen und Mütter teilnehmen, die nach offiziellem Beginn der COVID-19-Pandemie (11.03.2020) schwanger waren oder entbunden hatten.

**Ergebnisse** Es konnten vollständige Datensätze von  $n = 156$  schwangeren und  $n = 221$  postpartalen Frauen ausgewertet werden. Das mit dem COPE-IS erhobene allgemeine Stresslevel war sowohl bei schwangeren als auch bei postpartalen Frauen aufgrund der COVID-19-Pandemie signifikant erhöht, wobei Vorerkrankungen wie Atemwegserkrankungen und schwangerschaftsbedingte Erkrankungen wie Gestationsdiabetes den Stress zusätzlich verstärkten. Die subjektiv empfundene Qualität der Betreuung während der Schwangerschaft beeinflusste das Stressempfinden ebenfalls.

**Schlussfolgerungen** Ängste vor einer COVID-19-Infektion und veränderte Vor- bzw. Nachsorgeangebote belasteten die befragten Frauen. Ein engmaschiges Betreuungsangebot während Schwangerschaft und Wochenbett könnte dazu beitragen, die mentale Situation zu stabilisieren und Stress zu verringern.

## Introduction

The global COVID-19 pandemic, which began in the winter of 2019/2020, represents a long-lasting exceptional situation that affects the people involved on different levels. In addition to worrying about being infected with COVID-19 themselves and becoming seriously ill, or having those close to them become ill, the measures ordered by the government also changed the lives to which people had become accustomed. Contact restrictions, in particular, led to serious changes in many areas of life. These, for example, included restrictions in the professional world, in the education sector, religious practice, leisure activities, but also in the health system [1, 2]. Such changes can have long-term effects on people's mental health [3]. Although some positive effects such as a "deceleration of everyday life" have been reported [4], various studies have meanwhile shown that a large part of the population reacts with increased stress and increased symptoms of depression and anxiety to the circumstances of the COVID-19 pandemic [5, 6, 7].

Stress during pregnancy can have negative effects on the mother and thus also on the mental and psychomotor development of the growing child [8, 9]. Risk factors for increased stress during pregnancy include stressful negative life events, lack of social and/or financial support, depression, anxiety or worry and complications during pregnancy [10, 11, 12]. If symptoms of

depression and/or anxiety occur during the pre- and postnatal period, these may not only affect the mother but also the child in the long term. Furthermore, symptom-related changes in maternal lifestyle and metabolism during and after pregnancy can have a negative influence on the fetal development and later on the postnatal development of the child [13, 14, 15, 16, 17]. Postnatal maternal anxiety and depression can also influence the mother's behavior towards the child or the mother-child interaction [18, 19, 20, 21, 22]. Therefore, the period of pregnancy as well as the postpartum period is a sensitive time for the mother and the long-term development of the child.

Especially in the vulnerable period of pregnancy, birth and puerperium, changes that occur due to the COVID-19 pandemic and the associated measures can trigger or even intensify worries and fears and thus increase the risk of developing prenatal and postnatal depression [23, 24]. To date, studies published on pregnancy during the COVID-19 pandemic show that anxiety symptoms in pregnant women generally appear to increase [5]. Stress symptoms, which may increase the risk of depressive symptoms or anxiety symptoms, as well as pregnancy-specific anxiety occur more frequently [25]. The increase in anxiety and depressive symptoms in pregnant women during the COVID-19 pandemic is a multinational trend and is not limited to individual countries [24, 26, 27, 28].

A detailed analysis of the experience and behavior of pregnant women and mothers in the postpartum period during the COVID-19 pandemic is warranted. Differentiated recording of worries and limitations, but also of possible coping strategies and helpful support, offers the opportunity to develop and implement interventions in time in order to reduce or avoid negative consequences for mothers and children. The COPE-IS (Coronavirus Peripartal – Impact Survey) questionnaire was developed as part of the international COVGEN initiative (<https://www.covgen.org>) to investigate the effects of the COVID-19 pandemic on the peripartum period and has been translated into various languages [29].

In the present study, pregnant women and mothers in the postpartum period were interviewed using the COPE-IS questionnaire. The evaluation focused on the subjective sense of stress caused by the COVID-19 pandemic. General level of stress, stress with regard to an own potential disease and stress with regard to a potential disease in the close family or circle of friends was compared to the care situation as well as to pre-existing diseases.

## Methods

### Subjects

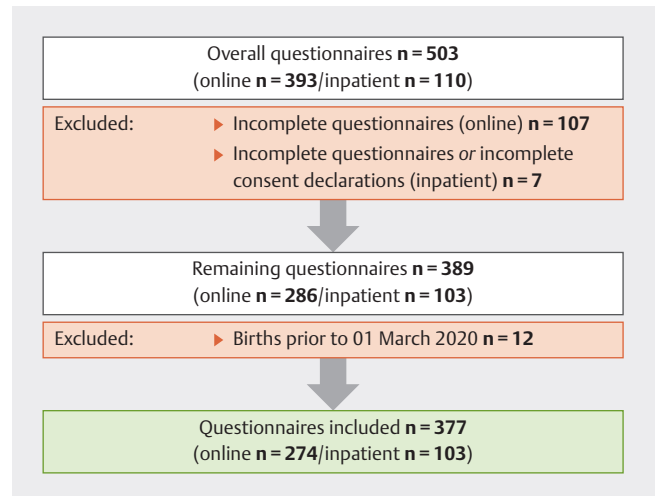
From the end of November 2020 to August 2021, a questionnaire-based cross-sectional study assessed the impact of the COVID-19 pandemic on the mental health of pre- and postpartum women. The criteria for inclusion were pregnancy or childbirth since the official start of the COVID-19 pandemic (11 March 2020), being of legal age and having German language skills.

### Questionnaire

The German version of the COPE-IS (<https://www.covgen.org>) was used. The online version of the questionnaire was promoted via posters and flyers, as well as via social media. For inpatients of the Department of Women's Health at the University Hospital of Tübingen a hardcopy version was used, as online access was not available for all patients during the inpatient stay.

For pregnant women (Item #P1–Item #P14 and Item #20–Item #80) and postpartum women (Item #1–Item #80), the questionnaire consists of a separate part and a common part (see additional materials S1). The items relate to the stress experience in connection with the COVID-19 pandemic and to altered experiences during pregnancy and after birth. Demographic data, the presence of other diseases and the availability of social support were also queried. The study was approved by the Ethics Committee of the Faculty of Medicine of the University of Tübingen (586/2020BO1), and all study participants gave their written consent to the participation and processing of their data.

The items “Overall level of stress related to the COVID-19 outbreak” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26) were each measured on a seven-step scale from 1 (“No distress”) to 7 (“Highly distressed”) and described by the median (Mdn) and the interquartile range (IQR). Also on a seven-step scale from 1 (“not supported”) to 7 (“very supported”), the extent of support from the



► **Fig. 1** Fig. Flow chart of the evaluated questionnaires. A total of 503 subjects participated in the study (393 outpatients used the online version and 110 inpatients the paper-and-pencil version of the questionnaire). One hundred and fourteen questionnaires were either incomplete or contained an incomplete declaration of consent and 12 participants had already given birth before the official start of the corona pandemic (01 March 2020). This meant that 377 women (274 outpatients and 103 inpatients) were included in the evaluation.

social network (Item #41, #42) before as well as during the COVID-19 pandemic was queried (i.e. at the time of the survey).

### Statistics

The data were not normally distributed (Kolmogorov-Smirnov test) and were analyzed by non-parametric tests (Kruskal-Wallis test, Mann-Whitney U test, Wilcoxon test). SPSS Statistics (version 27) was used for the statistical evaluation of the data. Results with a p-value from 0 to < 0.05 were considered significant.

## Results

### Study subjects

A total of 503 subjects participated in the study. One hundred and seven women from the online cohort and 7 women from the inpatient cohort were excluded because of incomplete questionnaires. Since a total of 12 women reported the last delivery date before 01 March 2020, they were also excluded from the study (► **Fig. 1**).

We were therefore able to evaluate questionnaires from 377 women. The online cohort consisted of 156 pregnant and 118 postpartum women. The inpatient cohort consisted of 103 postpartum women at the Department of Women's Health, University Hospital Tübingen (► **Table 1**).

► **Table 1** Description of the study population.

Subjects	
Included subjects; n (%)	377 (100.0)
▪ Pregnant outpatient	156 (41.4)
▪ Postpartum outpatient	118 (31.3)
▪ Postpartum inpatient*	103 (27.3)
Age; M (SD)	32.09 (3.8)
Pregnancy; n (%)	
▪ First pregnancy	211 (56.0)
▪ Previous pregnancy	166 (44.0)
Week of pregnancy; M (SD)	27.1 (9.7)
Week postpartum; M (SD)	10.4 (12.7)
Positive COVID-19 test**; n (%)	12 (3.2)
Annual household income; n (%)	
▪ over € 200 000	8 (2.1)
▪ € 160 000–199 999	10 (2.7)
▪ € 120 000–159 999	37 (9.8)
▪ € 100 000–119 999	37 (9.8)
▪ € 80 000–99 999	51 (13.5)
▪ € 60 000–79 999	70 (18.6)
▪ € 40 000–59 999	68 (18.0)
▪ € 20 000–39 999	47 (12.5)
▪ less than € 20 000	12 (3.2)
▪ unknown	37 (9.8)
Highest degree; n (%)	
▪ Doctorate	30 (8.0)
▪ Master's/State Examination	128 (34.0)
▪ Bachelor's degree	64 (17.0)
▪ Education	54 (14.3)
▪ Abitur/Fachabitur (German secondary school leaving exam/specialized secondary school leaving exam)	45 (11.9)
▪ Fachhochschulreife (German university entrance qualification)	27 (7.2)
▪ Intermediate school-leaving certificate	27 (7.2)
▪ Secondary school leaving certificate	2 (0.4)

M = mean; n = number of subjects; SD = standard deviation.

\* Inpatients were administered the paper-and-pencil version of the questionnaire.

\*\* A positive COVID-19 test result or whether the patient was ill at the time of filling in the questionnaire was not recorded.

## Subjective stress level due to the COVID-19 pandemic

Study participants reported an increased overall level of stress (Item #58; Mdn = 4; IQR = 3) due to the COVID-19 pandemic

(► **Table 2**). In the overall cohort, this value differed significantly from the “1” stress scale (1 = “no stress”;  $p < 0.001$ ; Wilcoxon test). Similarly, study participants reported both an increased level of stress with regard to their own COVID-19-related symptoms or a potential illness (Item #25; Mdn = 3; IQR = 2), as well as an increased level of stress with regard to COVID-19-related symptoms or a potential illness in friends and family (Item #26; Mdn = 4; IQR = 3) (► **Fig. 2**). There was no significant difference between the online and inpatient cohort for any of these three items.

## Pre-existing diseases

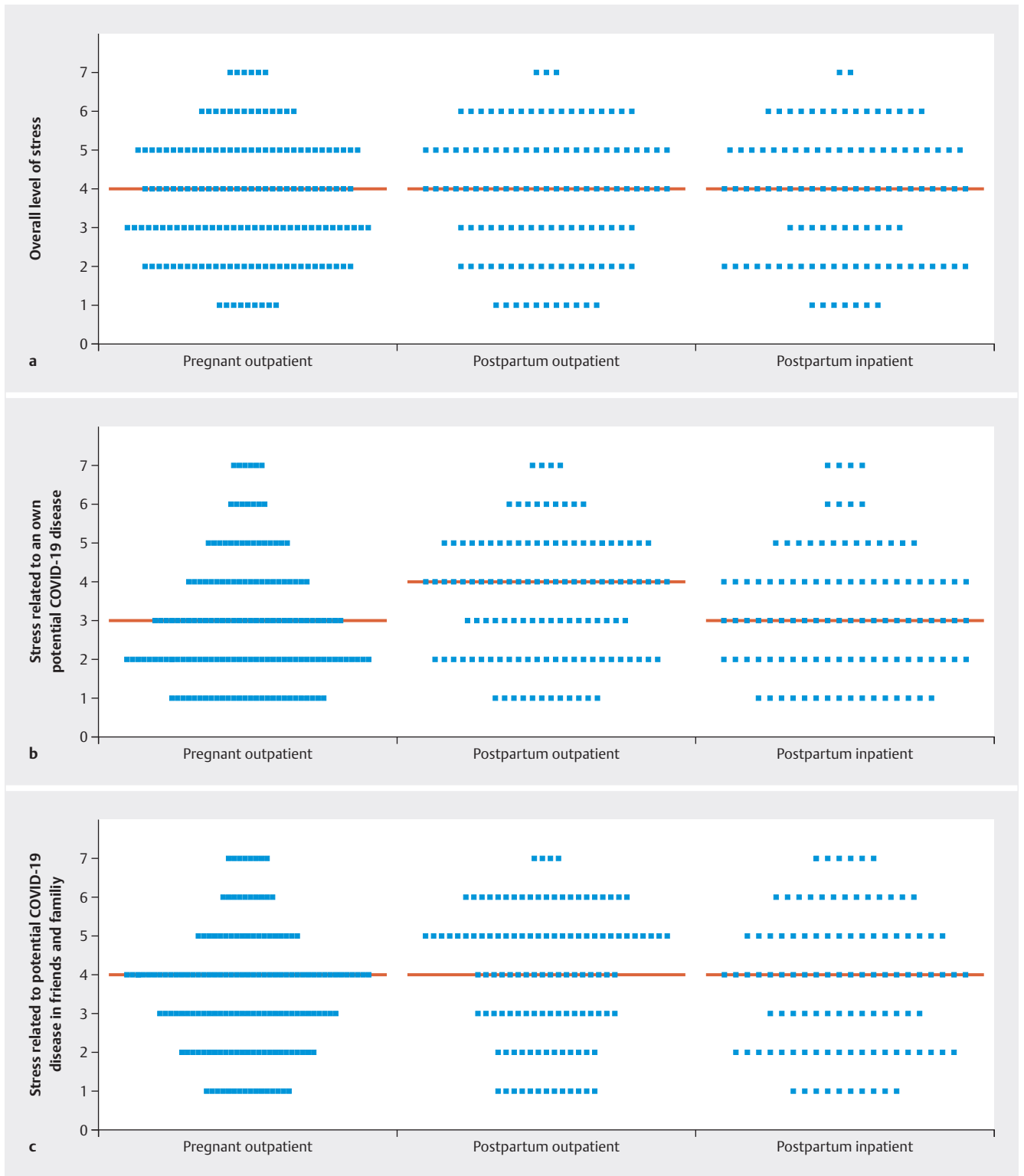
A total of 233 women (61.8%) reported the presence of pre-existing diseases in the household. Of these, 93 women (24.7%) had a pre-existing disease of their own; for 140 women (37.1%) diseases were present only in other members of the household. Options for pre-existing diseases were respiratory problems, diabetes, lung disease, heart disease, liver disease, cancer, disease-related immunodeficiency and affective disorder (Item #62, Item #63). For the qualities “How distressed are you about your own COVID-19-related symptoms or potential illness”, (Item #25;  $p = 0.003$ ; Kruskal-Wallis H test) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26;  $p = 0.022$ ; Kruskal-Wallis H test), the stress level was significantly different in the groups “no pre-existing disease”, “own pre-existing disease”, and “member of household with pre-existing disease”. In the context of post-hoc analyses, women who themselves had a pre-existing disease reported a significantly increased stress level (► **Table 3**) (Item #25:  $p = 0.001$ ; Item #26:  $p = 0.021$ ). Particularly respondents with respiratory diseases experienced significantly increased stress levels with regard to own COVID-19-related symptoms or potential illness (Item #25;  $p = 0.002$ ; Mann-Whitney U test).

## Pregnancy-associated diseases

A total of 177 (46.9%) women reported the presence of pregnancy-associated diseases (Item #63, ► **Table 4**). Here, women with gestational diabetes (11.9%) had a significantly higher overall level of stress caused by the COVID-19 pandemic than unaffected women (Item #58;  $p = 0.006$ ; Mann-Whitney U test).

## Care/support and stress

The question regarding the professional care situation during pregnancy by a gynecologist or midwife (Item #P5 or Item #8) could be answered with “very well supported” ( $n = 293$ ), “somewhat well supported” ( $n = 78$ ) and “not very well supported” ( $n = 6$ ). For the evaluation, the response options were summarized as “somewhat well supported” and “not very well supported” (“less well supported”,  $n = 84$ ). Regarding the perceived stress levels for the qualities “overall level of stress” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26), significantly more stress was perceived when the care/support provided was less good (► **Table 5**).



► **Fig. 2** Fig. Subjective stress level due to the COVID-19 pandemic. For outpatients before or after childbirth and for inpatients, the distribution of answers 1 (“no distress”) to 7 (“highly distress”) is shown for items a “Overall level of stress related to the COVID-19 outbreak” (Item #58), b “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and c “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26). The red line corresponds to the respective median.

► **Table 2** Stress level due to the COVID-19 pandemic.

	Overall level of stress Mdn (IQR)	Stress related to an own potential COVID-19 disease Mdn (IQR)	Stress related to potential COVID-19 disease in friends and family Mdn (IQR)
total; (n = 377)	4 (3)	3 (2)	4 (3)
Outpatient pregnant; (n = 156)	4 (2.75)	3 (2)	4 (2)
Outpatient postpartum; (n = 118)	4 (2.25)	4 (3)	4 (2)
Inpatient postpartum; (n = 103)	4 (3)	3 (2)	4 (3)

For outpatients before or after childbirth and for inpatients, the median of answers 1 (“no stress”) to 7 (“extremely high stress”) is shown for items “Overall level of stress related to the COVID-19 outbreak” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26). IQR = interquartile range; MDN = median; n = number of study participants

► **Table 3** Stress level in relation to pre-existing disease in the household.

	Overall level of stress Mdn (IQR)	Stress related to an own potential COVID-19 disease Mdn (IQR)	Stress related to potential COVID-19 disease in family and friends Mdn (IQR)
no pre-existing disease; (n = 144)	4 (3)	3 (2)	3 (3)
own pre-existing disease; (n = 93)	4 (2)	4 (3)*	4 (2)**
pre-existing disease in home environment (n = 140)	4 (2)	3 (2)	4 (3)
p-value***	0.157	0.003	0.022

The median of responses 1 (“no distress”) to 7 (“highly distressed”) for items “Overall level of stress related to the COVID-19 outbreak” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item # 25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26) is shown for subjects without own pre-existing diseases or diseases in the home environment, for women who themselves had a pre-existing disease and for subjects with pre-existing diseases in the home environment. In the context of post-hoc analyses (Dunn-Bonferroni), there was a significant difference compared to women who did not themselves have previous disease or diseases in the home environment: \*  $p = 0.001$ ; \*\*  $p = 0.021$ ; \*\*\* Kruskal-Wallis H test; IQR = interquartile range; Mdn = median; n = number of study participants

In addition, the respondents stated that the COVID-19 pandemic had weakened support from their social network (item #42; significant difference to 1 = “not supported”;  $p = 0.003$ ; Wilcoxon test). There was a discrepancy between the demand and supply of digital support services: 60.3% of pregnant women and 44.3% of postpartum women wished to learn more about virtual mother-child groups (Item #P14 or Item #19), but only 16.1% of postpartum women used virtual support services (Item #18).

## Discussion

The results of this questionnaire-based cross-sectional study show that women found their general stress levels to be significantly increased during and after pregnancy due to the COVID-19 pandemic. Pregnant women with pre-existing diseases (e.g., gestational diabetes or respiratory diseases) reported significantly higher stress levels than women without relevant pre-existing diseases. Women who felt less well cared for also reported a significantly higher level of stress compared to women who felt very well cared for.

► **Table 4** Pregnancy-associated diseases.

	Overall level of stress Mdn (IQR)	p*	Stress related to an own potential COVID-19 disease Mdn (IQR)	p*	Stress related to potential COVID-19 disease in family and friends Mdn (IQR)	p*
Gestational diabetes		0.006		0.394		0.510
▪ yes (n = 45)	5 (3)		3 (3)		4 (2)	
▪ no (n = 332)	4 (3)		3 (2)		4 (3)	
High blood pressure		0.182		0.186		0.800
▪ yes (n = 29)	4 (2)		3 (2)		4 (2)	
▪ no (n = 348)	4 (2.5)		3 (2)		4 (3)	
Cervical shortening		0.110		0.994		0.686
▪ yes (n = 24)	4.5 (3)		3 (3)		4 (3)	
▪ no (n = 353)	4 (3)		3 (2)		4 (3)	
Fetal growth retardation		0.600		0.878		0.447
▪ yes (n = 11)	4 (3)		3 (3)		3 (2.5)	
▪ no (n = 366)	4 (3)		3 (2)		4 (3)	

For subjects with or without pregnancy-associated disease, the median of responses 1 (“no distress”) to 7 (“highly distressed”) for items “Overall level of stress related to the COVID-19 outbreak” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26) is shown. IQR = interquartile range; Mdn = median; n = number of study participants; \* Mann-Whitney U test (presence of pregnancy-associated disease: yes versus no)

► **Table 5** Stress level in relation to the care situation.

	Overall level of stress Mdn (IQR)	Stress related to an own potential COVID-19 disease Mdn (IQR)	Stress related to potential COVID-19 disease among family and friends Mdn (IQR)
Very well supported; (n = 292)	4 (3)	3(2)	4 (3)
Less well supported; (n = 84)	4.5 (3)	4 (3)	4 (2)
P value*	<0.001	0.016	0.044

For subjects with very or less well support, the median of answers 1 (“no distress”) to 7 (“highly distressed”) is shown for items “Overall level of stress related to the COVID-19 outbreak” (Item #58), “How distressed are you about your own COVID-19-related symptoms or potential illness” (Item #25) and “How distressed are you about COVID-19-related symptoms or potential illness in friends and family” (Item #26). IQR = interquartile range; Mdn = median; n = number of subjects; \* Mann-Whitney U test

These findings largely coincide with results reported in the currently available literature. For example, Moyer and colleagues (2020) [20] also report that women in pregnancy had an increased stress level and increased pregnancy-associated fears due to the COVID-19 pandemic. The study participants were predominantly worried about household conflicts, losing their jobs or becoming infected with COVID-19. Stepowicz and colleagues [30] also found that pregnant and postpartum women showed increased anxiety symptoms during the COVID-19 pandemic. The stress and anxiety levels were also significantly increased in women with pre-existing diseases compared to women without pre-existing diseases. Simi-

lar results were shown by Mappa et al. [26], who also investigated anxiety during pregnancy. It should be emphasized that these two previous studies were published at the beginning of 2020, at a time when less was known about COVID-19, the disease characteristics, the course of disease and the approval of vaccines could not yet be estimated. We now know that the transplacental infection of the fetus is rather a rare event and that the vaccination of pregnant women is classified as safe [31, 32, 33]. In addition, the prevalence of a SARS-CoV-2 infection in the context of a pregnancy was low during the study period [34].

Women with pregnancy-related diseases or at-risk pregnancies are a particularly vulnerable group [35, 36]. In the present study, women with gestational diabetes had a significantly increased perception of stress. There was however no significant association between the stress experience and gestational hypertension, cervical insufficiency or fetal growth retardation, although there was only a small number of cases in each group. A larger sample size would be required to investigate associations of at-risk pregnancies and stress during the COVID-19 pandemic in more detail and in particular to evaluate any specific correlations with the week of pregnancy at the time of the survey.

Women who found the care situation by a gynecologist or midwife to be less adequate also described an increased stress level. Considering the influence of support during pregnancy and after birth as well as the general social support, a study by Lebel and colleagues in particular confirms an association with depression and anxiety disorders [24]. Among other things, the authors described social support and taking part in sports as protective factors. Nearly two thirds of respondents wanted more virtual-based support, although only a small proportion of participants actually used such support when it was available.

A limiting factor of the present study is that perceived stress was measured at only one time point during the pandemic period, which proceeded in three waves up till the time of the evaluation. This means that the extent that lockdown measures and restrictions influenced the feeling of stress, for instance, cannot be determined. Given the international differences between health care systems and country-specific political decisions on pandemic containment, cross-national interpretation of the results is limited. In addition, the questionnaire was only developed with the emergence of the COVID-19 pandemic and can therefore not be compared to a control group (consisting of women whose pregnancies and postpartum periods were not affected by the COVID-19 pandemic). Accordingly, we asked to what extent stress levels were increased by the COVID-19 pandemic, although it cannot be ruled out that other factors contributed to a subjectively increased sense of stress during that period of time. We used a questionnaire from the international COVGEN initiative that remains to be validated [29, 37]. A reference value for the perception of stress is therefore not available. Similarly, the comparison with a control group is not possible at the present time, as the effects of the COVID-19 pandemic affect the entire population. Accordingly, we examined the extent to which the general feeling of stress significantly differed from the stress scale of “1” (1 = “no stress”). The drop-out rate due to incomplete questionnaires was particularly high among the online cohort. A potential rationale may be that less time was available in the home environment for the online cohort to complete the questionnaire than in the inpatient context. This can lead to a distortion of the results and a corresponding overestimation of the influence of COVID-19 on the stress experience.

## Conclusions

Women during and after pregnancy are particularly affected by COVID-19. The presence of pregnancy-associated diseases contributes to an increased stress experience due to COVID-19. In particular, women with less social support or with pre-existing diseases should be identified at an early stage in order to provide targeted further support that is available independently of lockdown measures.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

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