The Clinical Characteristics of Pregnant Women with Novel Coronavirus

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Abstract: Introduction: In December 2019, unexplained pneumonia occurred in Wuhan, China. This sudden public health event gradually attracted international attention. As of September this year, the clinical characteristics, laboratory characteristics, and CT findings of pregnant women with COVID-19 are mainly based on case reports, and there is no comprehensive systematic review. Methods: We conducted literature searches on multiple databases such as the Cochrane library, the researches that searched include retrospective studies, case-control studies and cohort studies. After screening the literature and reading carefully, the clinical characteristics, laboratory characteristics, and CT findings of pregnant women with COVID-19 have been extracted separately. Due to the limitations of the data, we have further qualitatively combined and described the data contained in the literature. Results: We retrieved 3337 articles. 51 articles were included for evaluation, including 43 case reports and 8 case controls. Among 51 articles, 36 studies were from China (70.58%), and 43 case reports included 1094 patients, with fever (N=360 32.91%), cough (N=307 28.06%) and dyspnea (N=76 6.95%) are the main clinical manifestations. The most common laboratory examination is Lymphopenia (N=181 6.54%), and the most common CT finding is Ground glass opacity (N=271 24.77%). The most frequent complication was ARDS (N=21 1.92%). Conclusion: Pregnant patients with COVID-19 are similar to non-pregnant patients in typical clinical features, laboratory features and CT findings. However, compared with non-pregnant patients, the prognosis and severity of comorbidities and complications appear to be more dangerous in pregnant patients.


1. Introduction

In December 2019, a series of pneumonia cases with unknown causes appeared in Wuhan (Hubei, China), with clinical manifestations similar to viral pneumonia[1]. Currently, COVID-19 is in a global pandemic trend. COVID-19, severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV) are all β-coronaviruses. Although the similarity to the SARS-CoV genome is 82%, COVID-19 is more infectious [2]. The virus is mainly transmitted through air, droplets, aerosols and contact, and it is speculated that bats are the intermediate host of SARS-CoV-2[3]. At present, the main clinical manifestations of patients with COVID-19 are fever, dry cough, fatigue, etc. Some patients are abdominal pain, diarrhea, pharyngeal pain, etc[4]. In the past SARS, about one-third of pregnant women died of this disease[5]. In light of historical lessons, we should pay attention to the pregnant groups infected during the COVID-19, pregnant women should be assessed as potential risk groups for the current COVID-19 pandemic[6]. Pregnant women, a kind of special susceptible population, are in an immunosuppressed state and are more likely to be infected by various pathogens, their clinical characteristics are different from those of other populations. Therefore, it is necessary to review and sort out the clinical characteristics of the reported pregnant women infected with COVID-19. At present, there is a lack of systematic analysis and evaluation of the clinical data of pregnant women. Aiming to make a systematic review and provide ideas for clinical strategies for obstetricians we have collected and sorted out the clinical characteristics of pregnant women, laboratory tests, CT results and other data.

2. Methods

This paper is a systematic evaluation and summary, and will make a meta-analysis when necessary. The original literature we used came from searching multiple databases.

2.1 Data Source

The search will be conducted in 6 databases including MEDLINE, Embase, Cochrane Library, Web of Science, CNKI and Wanfang. And the reference lists of relevant literatures were also searched. We will include studies published after December 2019, and only in English and Chinese. The searched studies include: Case reports, Case Series, Retrospective study, Case-control studies and cohort studies, Clinical research on which clinical data can be extracted.

We will use these search terms and relative variants: pregnancy, gravidity, pregnant women, gestation, novel coronavirus, novel coronavirus pneumonia, new coronavirus, COVID-19, 2019-nCoV, SARS-CoV-2.

2.2 Selection of Studies and Data Extraction

Document management will be conducted by Endnote X9 software. The software will be used to filter duplicate studies first, and then delete duplicate researches by reading titles, abstracts and other relevant information. The PRISMA literature screening flow chart is shown in Figure 1.
According to the inclusion criteria and exclusion criteria, the literature will be further screened. In this process, the controversial literature will be screened after obtaining the full text. Further detailed screening and data extraction of the researches will be carried out simultaneously by two professionally trained reviewers. After discussion by the review team, a unified data extraction table (Excel spreadsheet) will be made. The extracted information will include: the characteristics and methods of the study: the publication time of the study type literature, the source of the case and the name of the author, etc. Demographic characteristics of the subjects: mean age-based diseases and pregnancy complications. The clinical characteristics, diarrhea and shortness of breath of the subjects. Results the data included in the index included: such as the laboratory white blood cell count and the number of cases with increased ast. Bias risk assessment and other information. If there are any questions or puzzles about the original research in the process of data extraction, we will contact the author through email to get specific answers.

2.3 Risk of Bias Assessment

Two reviewers will independently evaluate and cross check the risk of bias. Discrepancies on the risk of bias will be resolved through discussion with a third review author. The risk of bias assessment chart of inclusion studies will be produced by using Review Manager 5.3 software.

2.4 Data Analysis and Synthesis

Through literature search and report analysis, there may be less cohort studies or RCTs for pregnant women with covid-19 during the epidemic period, so the types and amount of data included in the literature have certain limitations. We will make further qualitative combination and description of the data included in the literature.

3. Results

3.1 Case report

Among the 44 case reports included, 11 reports mentioned ICU, a total of 91 cases, accounting for 8.32% of the total cases (1094 cases). 10 reports mentioned 32 cases (2.93%) of diabetic complications. 8 reports mentioned complications of hypertension. 1 report mentioned cardiovascular disease. The most common clinical symptoms were fever and cough, followed by myalgia or fatigue, and dyspnea. A total of 360 cases of fever (32.91%) were mentioned in 31 reports. 33 reports mentioned cough, a total of 307 cases (28.06%). 13 reports mentioned myalgia or fatigue, a total of 59 cases (5.39%). 14 reports mentioned dyspnea, 76 cases (6.95%). Some articles mentioned diarrhea, sore throat, headache, sputum production and other symptoms. Lymphopenia, high C-reactive protein and leucocytosis were the most significant laboratory characteristics. Lymphopenia was mentioned in 21 reports, with a total of 181 cases (16.54%). 16 reports mentioned high C-reactive protein, 79 cases (7.22%). Fourteen articles mentioned 63 cases of leucocytosis (5.76%). Among the imaging findings, ground glass opacity, chest ray bilateral pneumonia and chest X-ray unilateral pneumonia were the main CT features. There are 21 articles mentioned ground glass opacity, 271 cases (24.77%), 20 articles mentioned chest X-ray bilateral pneumonia, 142 cases (12.98%), 13 articles mentioned chest X-ray unilateral pneumonia Pneumonia, a total of 52 cases (4.75%). In the included studies, only a few reports mentioned complications such as shock and acute kidney injury. Some results are shown in Table 1.
### 3.2 Case-control

In a case-control study of 17 patients, which grouped by anesthetic regimens, there were 5 cases of anemia, 1 case of pregnancy induced hypertension, 2 cases of gestational diabetes mellitus, 17 cases of cesarean section, 3 cases of general anesthesia (18%), 14 cases of continuous epidural anesthesia (82%), 4 cases of fever (29%), 4 cases of cough (29%), 1 case of diarrhea (7%), 1 case of fatigue (7%), 2 cases of chest tightness (14%). In a study on the clinical and CT features of the COVID-19, there were 41 patients with an average age of 30 (22-42 years), including 4 cases of gestational diabetes mellitus and 3 cases of gestational hypertension. There were 9 cases (56%) with normal body temperature in laboratory diagnosis group and 16 cases (64%) in clinical diagnosis group. All patients had cough symptoms. The number of leukocytes and neutrophils in pregnant group was higher than that in non-pregnancy group. In a case-control study of the outcomes of pregnant women with COVID-19, 11 of the 16 confirmed cases had pregnancy complications, including 3 cases of pregnancy induced hypertension and 2 cases of hypothyroidism. There were 4 cases (25%) of fever in the confirmed group and 1 case (5.6%) in the suspected group. In the suspicious group, cough, sore throat and dyspnea were found in 1 case (5.6%). In the confirmed group, 8 cases (50%) were unilateral pneumonia and 7 cases (43.8%) were bilateral pneumonia. In the suspected group, 10 cases (55.6%) had unilateral pneumonia and 7 cases (38.9%) had bilateral pneumonia. In a study of clinical outcomes of pregnancy, the mean age of the case group (36.46±6.89) was significantly lower than that of the control group (31.97±6.24). There was no significant difference in the incidence of cough and fever between the two groups. In addition to AST, SLT, CRP creatinine, hemoglobin level, D-dimer, other laboratory data were similar between the two groups. A study of the clinical characteristics and laboratory tests of COVID-19 in pregnant women showed that the median age of pregnant women was 29.9 years, while the median age of non-pregnant women was 30.0 years. In the pregnancy group, there were 2 cases of gestational diabetes mellitus (6.6%), 5 cases of pregnancy induced hypertension (16.7%), 1 case of intrahepatic cholestasis of pregnancy (3.3%), 1 case of twin pregnancy (3.3%). Fever, cough, asthma, anorexia and other symptoms were observed in both groups. There were 8 cases of asymptomatic pregnant women (26.7%). In a seropidemiological study on pregnant women with COVID-19, 125 (14.3%) of 874 pregnant women were positive for IgG, IgM or IgA COVID-19 antibody. 31 (24.8%) had at least three symptoms or loss of smell, and 8 (6.4%) had dyspnea. In a retrospective description of acute respiratory syndrome in pregnant women with COVID-19, the age range was 29 to 37.6 in the outpatient follow-up group and 29 to 35.5 in the inpatient group. Only 10 out of 52 inpatients showed positive results of PT-PCR. There were 2 (4%) cases of diabetes mellitus and 2 (4%) cases of pregnancy induced hypertension in the outpatient follow-up group, and 5 (10%) cases of gestational diabetes mellitus and pregnancy induced hypertension in the inpatient treatment group. In a study on vaginal delivery outcomes of pregnant women with COVID-19, a total of 55 patients were included. There was no significant difference in maternal age, body mass index and mode of delivery between the two groups. All the 55 patients received CT examination of lung at admission, 3 of them were normal and 52 had abnormal changes in different degrees.

### 4. Discussion

Beginning in late December 2019, the COVID-19 has gradually spread to all parts of the country and overseas. The COVID-19 epidemic has been declared as a public health emergency of international concern. So far, the epidemic is still developing, according to the case reports and case controls we included showed that 36 articles (70.58%) were from China and most were from hospitals in Wuhan, 5 articles (9.80%) were from the United States, 2 articles (3.92%) from...
Turkey and France, South Korea, Britain, Iran and other countries (1.86%).

The results of the case report study we included showed (N=1094) the clinical symptoms of the patients were mainly fever (N=560 32.91%) and cough (N=307 28.06%) but what cannot be missed is that a few patients still have muscles acid fatigue (N=59), headache (N=25), diarrhea (N=22) and anemia (N=76) and other clinical symptoms. In laboratory tests, lymphopenia (N=181 16.54%), C reaction Protein (N=79 7.22%) and leukocytosis (N=63 5.76%) are the main ones. In addition, the Blood sedimentation rate of some patients has increased. Creatine kinase, IL6, IL10, AST and ALT have also increased. In the CT report, most patients have bilateral lung infections (12.98%), and CT features mostly point to ground-glass changes (24.77%). In clinical symptoms and laboratory tests, COVID-19, SARS, and MERS all have similarities. It is worth mentioning that some special clinical symptoms have appeared in some studies, such as loss of smell[7]. The appearance of this sign suggests that patients with COVID-19 infection may have cranial nerves and ear, nose and throat damage. Laboratory tests are more special. According to our included case reports and case controls, the nucleic acid test (PT-PCR) of some patients at admission was negative while the clinical symptoms and laboratory tests do not rule out the possibility of illness. Therefore, we cannot completely rely on PT-PCR test results and ignore clinical symptoms and important data in laboratory tests.

In terms of comorbidities and complications, the case report studies we included showed that the incidence of acute respiratory distress syndrome in patients was much higher than that of acute myocardial injury and acute kidney injury. In a similar study, the results showed that in terms of complications and deaths, one-third of patients had ARDS[8]. Although the incidence of acute kidney injury and acute heart injury is low, the final result often leads to serious consequences of multiple organ failure. Therefore, medical personnel are fighting the epidemic. In the process, we should not only focus on the main comorbidities, but also pay attention to the special and serious complications, which brought by the COVID-19, in order to facilitate the prognosis. In the case report we included, there were 32 patients with diabetes (2.93%), there are 24 patients (2.19%) with hypertension, and relatively few people with cardiovascular disease, only 5 (0.46%). Complications, which be vigilant, are rare but often fatal factors.

We drew several meaningful conclusions from the included case reports. Firstly, due to the lack of strong evidence, it is not true that COVID-19 will cause severe complications in pregnant women who have vaginal delivery or cesarean section and their newborns[9]. Secondly, general anesthesia and epidural anesthesia are safe for pregnant women with COVID-19, but epidural anesthesia may have the risk of excessive blood pressure reduction[10]. Thirdly, under full evaluation of delivery conditions and strict protection measures, when ordinary COVID-19 pregnant patients deliver vaginally, they will not aggravate the symptoms of COVID-19 and will not increase the risk of COVID-19 infection in their newborns[11]. Fourthly, in some aspects, such as the appearance of bloody mucus in the vagina and the increase of D-dimer, it is more common in pregnant COVID-19 patients. Therefore, the clinical symptoms and experiments of pregnant COVID-19 patients and non-pregnant COVID-19 patients room characteristics seem to be different, and different treatment options should be actively adopted[12]. Fifthly, in the management of pregnant women with COVID-19, since the incidence of complications and decomposition rates in the late pregnancy may increase, the management of the late pregnancy should be focused[13]. Last but not least, in some pregnant patients with COVID-19 who have clinical features and no indications for laboratory examinations, the application of chest CT has the effect of early detection, evaluation of the severity of the disease and evaluation of treatment options[14].

We found 5 cohort studies on pregnant women infected with COVID-19 in the search results. From this, we have got some conclusions, a study conducted in an Italian Obstetrics and Gynecology Hospital showed an increase in BMI before pregnancy and the increase in breathing and heartbeat frequency during admission often lead to the occurrence of serious diseases[15]. At admission, clinicians should evaluate the patient’s vital signs changes and BMI before and after pregnancy, and pay attention to the risk of complications in high-risk pregnant women. A study from the United States on the study of pregnant women with critically severe COVID-19 mentioned that the incidence of critically severe ARDS is very high, and pregnant women who are critically severe in the third trimester often give birth due to infection[16]. The reason for mentioning these two cohort studies is that pregnant women infected with COVID-19 may be involved in serious diseases that are difficult to treat. Therefore, while clinicians pay attention to clinical symptoms in the clinical process, they should also pay attention to complications and demographic data to prevent adverse outcomes.

5. Clinical Significance

A study from the Ministry of Health Ankara City Hospital in Turkey attempts to study the clinical process and clinical efficacy of pregnant women with COVID-19 under the treatment of the hospital[17]. It is worth noting that the results of this study are similar to those of the studies we included. The clinical features of pregnant women with COVID-19 are mainly fever, cough, myalgia and dyspnea. In addition, the study shows that all pregnant women with COVID-19 in the study have a milder clinical course. We have concluded that, through personalized management and treatment of suspected and confirmed patients, and multi-faceted treatment of cases, better clinical outcomes can be obtained. The aim of the research is systematically summarizing the clinical and laboratory characteristics of pregnant women infected with COVID-19 by including a large amount of literature data. CT report characteristics and demographic data are convenient for clinicians to make individualized management and treatment, so as to obtain a relatively good prognosis.

6. Conclusion

Our research analysis shows that compared with non-pregnant adults, pregnant women infected with COVID-19 have great similarities in typical clinical features, laboratory tests, and CT features. What cannot be ignored is that some atypical
clinical features appeared in some of our included literature. It is worth pointing out that even though there is no current research showing that COVID-19 has the risk of vertical transmission in utero, the prognosis and severity of complications and complications in patients infected with COVID-19 during pregnancy seem to be more dangerous. Obviously, this conclusion still needs a lot of clinical trial data to prove. Therefore, the need for comprehensive evaluation and individualized management for pregnant patients to prevent adverse consequences deserves the attention of clinicians.

References