

A systematic review and meta-analysis of the reported symptoms of Covid 19 in pregnancy

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Summary

Introduction: The percentage of Symptomatic pregnant and non-pregnant women infected with Covid 19 is the same. The common symptoms in pregnant women are cough, fever, sore throat and myalgia. The objective of this is systematic review and meta-analysis of the commonly reported symptoms of COVID 19 in pregnancy and to compare it to non-pregnant. **Methods:** Study Design; Systematic review and meta-analysis of published retrospective studies. Searches conducted from December 2019 - April 2020 on PubMed, Medline, EMBASE, ISI Web of Science Electronic database used to collect data, corresponding to the (PRISMA) Preferred Reporting Items for Systematic Meta-Analysis, using the following search terms: keywords "coronavirus, COVID-19, pregnancy". **Results:** Figure 1 presents the study flow diagram. We identify 114 records through database searching, sixteen further studies recognized through other sources, and 98 papers isolated after duplicates, leaving 32 reports. After screening for titles and abstracts, we found only 27 reports to be potentially suitable and rescued these reports in full text. We excluded seven studies; 20 did not report symptoms of groups of interest. In the process of Screening, 16 were screened. Ten of full-text articles assessed for appropriateness, six full-text articles omitted with reasons, and only Four studies [12-15] were included in the review. **Conclusion:** The only symptoms that are more common in pregnant than non-pregnant are the sore throat. That concluded that when pregnant women start to have sore throat care should be taken to exclude COVID-19 infection.

Key words: Coronavirus; COVID-19; Pregnancy.

Introduction

COVID-19, infection during pregnancy is very uncommon [1]. Earliest cases, reported were in Wuhan, China, December 2019 (The Virus SARS-CoV-2) [2]. It is Beta-coronavirus. The Host cell receptor is a structural analysis that suggests angiotensin-converting enzyme, receptor. The animal hosts are bats; animals might represent an intermediate host. The incubation period, the Mean 5.2 days (95% confidence interval [CI], 4.1-7.0); and the 95 % of the distribution was 12.5 days. It ranges, from 2-14 days. Time from illness onset until hospitalization with a mean of 12.5 days. (95% CI, 10.3-14.8), onset before Jan. 1 with a mean 9.1 days (95% CI, 8.6 9.7). Basic reproduction number OR 2.2 (95% CI, 1.4-3.9) [2]. Patient characteristics; nearly all reported patients are adults. Children have been infrequently reported (< 1% of cases). Age range; (10-89 years) the average age in years was 59 years. Male to female ration 56% - 44%. The mortality as a Case fatality rate overall Initial estimate is about 1%. Clinical manifestations were described from hospitalized patients, and the most common symptoms were Fever (83-100%) then Cough (59-82%), Myalgia (11-35%), Headache and Sore throat (7-8%) and finally Diarrhea (2-10%). Laboratory findings were Leukopenia (9-25%), Lymphopenia (35-70%) and Thrombocytopenia (5-12%). Radiographic abnormalities on chest

imaging were (100%) [3].

In general, pregnant women have many anatomical and physiological variations of pregnancy that affect the respiratory system and that increase liability to infections COVID-19, and the clinical progression of the disease in infected pregnant women delayed diagnosis of COVID-19, this is in due to pregnancy-associated rhinitis and physiologic dyspnea, which is common in pregnancy [4]. The immunosuppression of pregnant women impacts the severity of symptoms, particularly towards the end of pregnancy, pregnant women cannot clear respiratory secretion and decreased lung functional residual capacity [4]. During normal pregnancy, hormone such as estrogen and progesterone increase levels of angiotensinogen and renin, leading to an increase in ACE-2 levels [5] and increased expression of ACE2 may facilitate infection with COVID-19 [6]. What is the effect of coronavirus (COVID-19) infection on pregnancy, and what are the common symptoms [7]? Very minimal knowledge is known until today; this lack of reliable data makes the answer to many questions very difficult [8]. Early few studies showed that clinical features of pneumonia-related COVID-19 in pregnancy were similar to those in non-pregnant [9]. Little evidence exists to permit any reliable conclusions about the nature of COVID-19 infection in pregnancy [10, 11].

Table 1. — Characteristics of involved studies (PICO).

Author	Journal	Year	Design	Population/Wt
Yan J	Am J Obs Gyne	23/4/2020	A retrospective review	116/63.4
Breslin N	Am J Obs Gyne MFM.	19/4/2020	A retrospective review	43/23.5
Liu D	Am J Roentgenol.	18/3/2020	A retrospective review	15/8.2
Huijun Chen	The Lancet	12/2/2020	A retrospective review	9/4.9
Total				183/100
(Control) Tian S	J Infect.	27/2/2020	A retrospective review	262

Table 2. — Common Symptoms Included Studies (PICO).

	Four Common	Reported	Symptoms	
Author	Fever	Cough	Myalgia	Sore throat
Yan J	59/116	33/116	15/116	10/116
Breslin N	37/43	14/43	5/43	4/43
Liu D	13/15.	9/15	3/15	2/15
Huijun Chen	7/9	4/9	2/9	1/9
Control				
Tian S	215/262	120/262	68/282	18/262

The objective of this study is systematic review and meta-analysis of the commonly reported symptoms of COVID-19 in pregnancy and to compare it to symptoms of non-pregnant.

Materials and Methods

(Systematic review and meta-analysis) of published retrospective studies.

Searches

Performed from December 2019 - April 2020 on PubMed. Medline, EMBASE, ISI Web of Science Electronic database used to collect data. Using the following search terms: keywords “coronavirus, COVID-19, pregnancy”.

Literature search strategy and eligibility criteria

The search approach, range criteria, data abstraction, study quality evaluation and statistical analyses illustrated below by the reporting of this review was guided by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines The PRISMA checklist was used while writing this analysis. Only full-text published retrospective studies that illustrate the common symptoms of Covid 19 during pregnancy

The study’s analysis primary outcome of interest was to compare the common symptoms in pregnant and non-pregnant. The search approach was limited to articles published in English December 2019 - April 2020 for PubMed. Medline, EMBASE, ISI Web of Science Electronic database further efforts were made to recognize all available studies, A total of four full-text retrospective articles preselected from 114 references, based on title and

abstract [12-15]. Two independent reviewers (A.J, H.H.) performed data selection and extraction according to the (PRISMA) Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement [17]. This systematic review was conducted according to (PICO) standard. Random-effect meta-analysis performed on symptoms all data. We performed data analyses using EXCEL and SPSS. We were used to calculating pooled estimated prevalence with odd ratio and 95% confidence intervals of clinical symptoms only.

Two authors independently completed an initial screening of the title and abstract of all articles and clinical studies to exclude documents considered irrelevant by both observers. Based on the pre-established inclusion criteria, the full texts of theoretically relevant articles were retrieved and assessed for inclusion by two review authors. The method of quality of the selected studies was estimated. Data were included in the meta-analysis. The following study details were collected to characterize the included studies, study authors, publication year, study design, and population. We used the symptom of control from a study which has a total of 262 non-pregnant [16] (Tables 1 and 2).

Results

Data analysis

Figure 1 presents the study flow diagram; we identify 114 records through database exploring, sixteen added studies Identified through other sources, and 98 papers removed after duplicates, leaving 32 reports. After screening for titles and abstracts, we found only 27 reports to be theoretically eligible and rescued these reports in full text. We eliminated seven studies; 20 did not report symptoms of groups

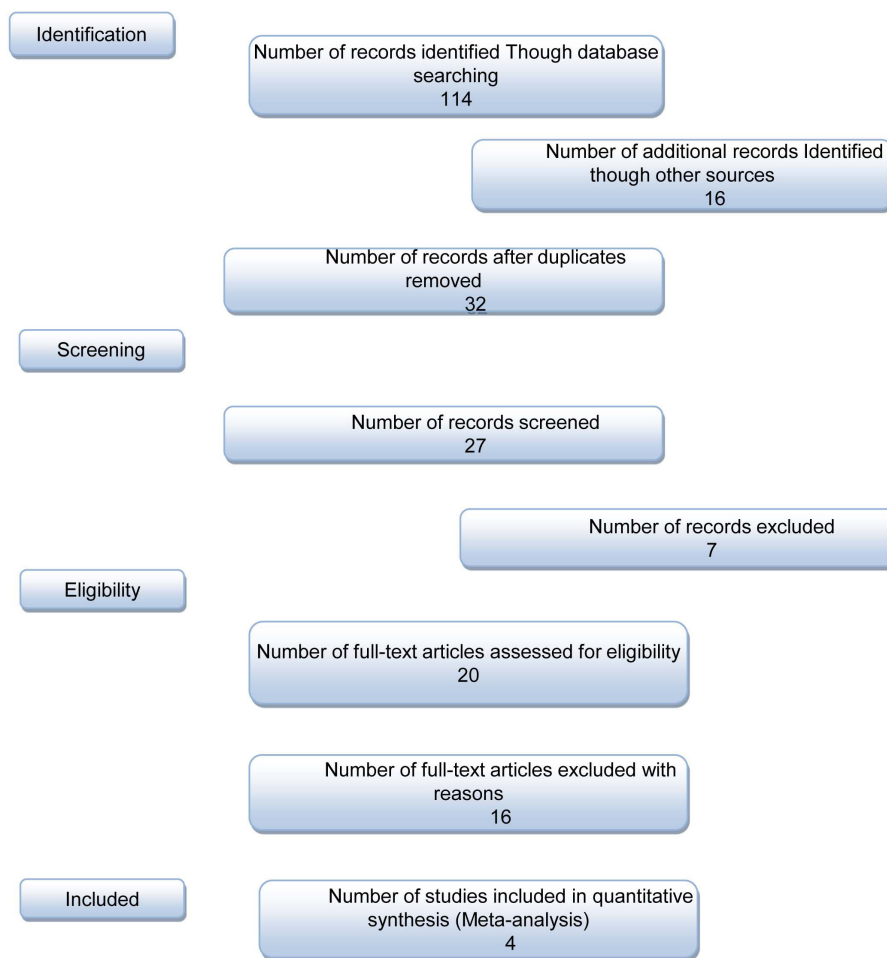


Figure 1. — Presents the literature search. (Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement) (PRISMA).

of interest. In the process of Screening, 16 were screened. Ten of full-text articles assessed for eligibility, six full-text articles excluded with reasons only Four studies [12-15], included in the review.

Sensitivity analysis

To weigh the impact of the study, sensitivity analyses of symptoms were accomplished by inspection of the forest plot. Therefore, the meta-analysis was repeated in the first step by step guide Pooled effect sizes were considered statistically significant at $P < 0.05$. In addition to computed estimations of between-study variance, the statistical heterogeneity crosswise the studies were calculated by chi-square statistic, and the value of I2 statistic judged inconsistency. An I2 value of over 50% indicated substantial heterogeneity. Each outcome was analyzed independently [18].

Risk ratios (R.R.s) with two-sided 95% CI were assessed for dichotomous outcomes using a random-effect model. Although we explored the data using both the static effect models and random-effect models, results in the text are only described from random-effect models due to underlying heterogeneity in the studies.

To assess the impact of the weight of the study, sensitivity analyses were performed by visual inspection of the forest plot exposed in ascending order of study weight in another hand.

Data from four appropriate articles were isolated and united into the meta-analysis. The meta-analysis of four studies reported symptoms of COVID 19 in pregnancy. Only English language and time restrictions 2019 and 2020. Relevant literature was also scanned through cross-references of identification in the reference lists within retrospective studies in participants that fulfilled the following criteria COVID 19 during pregnancy. We also added one retrospective study of symptoms of Covid 19 in non-pregnant to compare the symptoms with those in pregnancy [16].

Table 1 illustrate the characteristic of the patients in the four studies and the number of cases, which included in the review of Covid 19 in pregnancy total of 183 cases, and (Wt. 63.4, 23.5, 8.2, 4.9) and 1 study of non-pregnant 262 cases (Control). Table 2 shows the number of four common reported symptoms, fever, cough, myalgia and sore throat in each study and the control.

In each study, we looked at the most common symptoms,

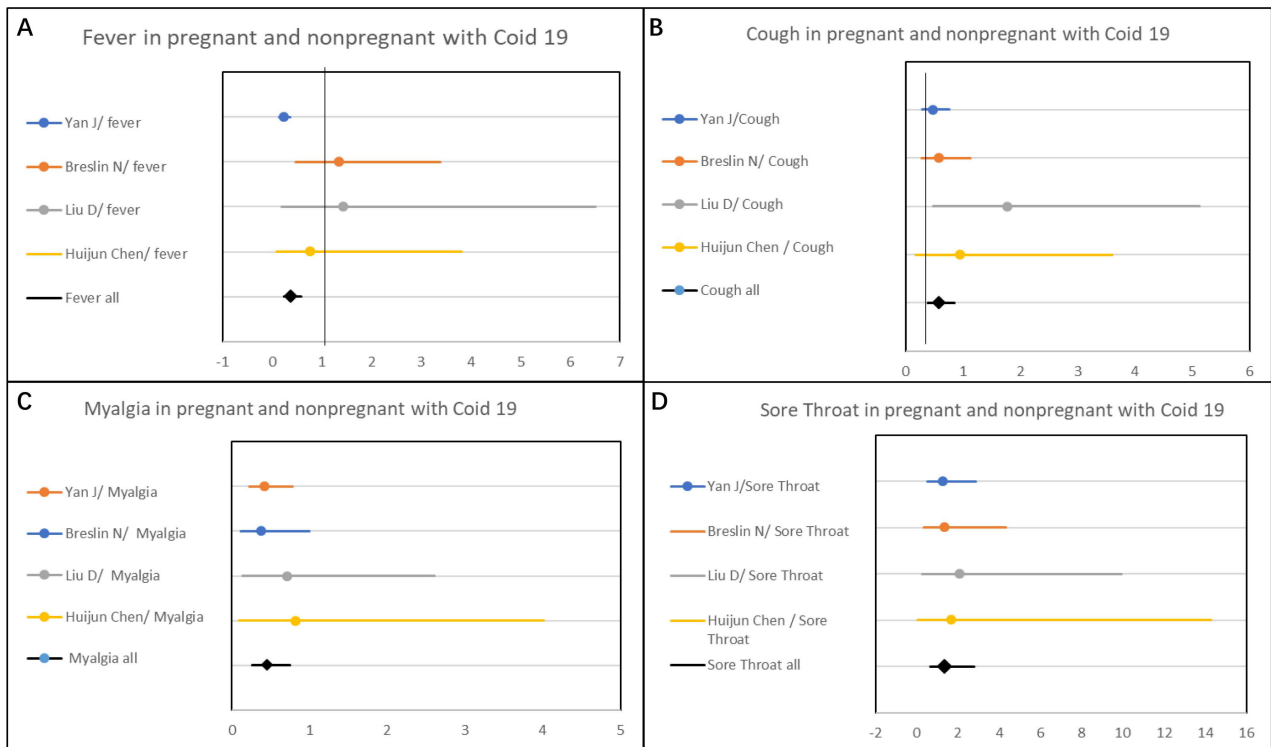


Figure 2. — Forest plot for the four studies.

mainly. Fever, cough, myalgia and sore throat and after calculating the percentage and odds ratio and 95% confidence limit and graphically presented each symptom as Forest plot for the four studies (Figure 2).

Forest plot A, B and C showing in total that symptom (fever), cough and myalgia is more common in non-pregnant with Covid 19 than pregnant women. Forest plot D showing in the total that Sore Throat is more common in pregnant with Covid 19 than non-pregnant (Figure 2).

Discussion

Pregnant women included in the list of people who are at moderate chance to get Covid 19 infection, and no evidence is more likely to get seriously ill from the infection. The main symptoms of coronavirus are fever, cough, myalgia and sore throat and a loss of smell or taste (anosmia) in non-pregnant. In pregnancy, a different study showed different symptoms compare to non-pregnant.

In our study, we analyze four retrospective case series, a number of pregnant women in each were (43, 15, 9 and 116 pregnant women) diagnosed as positive for COVID-19 clinically showed similar symptoms to non-pregnant more than 86% had mild illness, 9.3% were severely ill, and 4.7% were critically ill [12-16].

In pregnant women, the majority of patients were presented with fever and cough, myalgia and sore throat while laboratory tests yielded lymphocytopenia. C.T. findings of these patients were consistent with previous reports of non-pregnant patients, (Ground-glass opacities) at the early

stage. These patients need follow-up images after delivery.

We compare a total of 183 pregnant women considering each symptom fever, cough, myalgia and sore throat separately in each study to the symptom of control from a study which has a total of 262 non-pregnant. It was found that the only symptoms that are more common in pregnant than non-pregnant are the sore throat. That concluded that when pregnant women start to have sore throat care should be taken to exclude COVID-19 infection.

When we analyze publication, that deals with COVID-19 in pregnancy. None of the findings indicates that COVID-19 infections induce labour to pregnant women. (18.2). Until now, there are no suggestive data that supports the serious threat of early pregnancy loss with COVID-19, or miscarriage [19, 20]. (Fetal compromise and preterm rupture of membranes were reported in few cases to cause preterm birth, but the exact relation between preterm birth and covid-19 is still unclear [21].

Transmission in Early studies, there was no reported evidence for vertical transmission of COVID-19 from mother to child in late pregnancy [22]. In few recent reports indicate that vertical transmission can occur. An early study reported two neonates to be infected with COVID 19 transmission likely to occur in the postnatal period [23].

It is unclear yet whether comorbidity arising during pregnancy, such as cardiac failure diabetes, hypertension, diabetes, and hypercoagulability might be additional risk factors for pregnant women as they do for non-pregnant people. Vertical transmission from mother to fetus does not

occur during the last trimester, and no data were collected in the first and second trimester.

Pregnant women should be admitted to the maternity suite once they are in spontaneous or induced labor, proper care has been given to them during the pandemic of covid-19 [24].

Every health care provider staff: the obstetric consultant, anaesthetists, the midwife-in-charge, the neonatologist consultant, the charge nurse, and the infection control team should be informed. As for emergency scenarios a local policy should state to reduce the number of staff members entering the room. The team should continue maternal observations and assessment as per standard practice, with oxygen saturations. If a woman develops a fever, which is one of the most typical symptoms, further investigation should be done. For all patients in labour, continuous electronic fetal monitoring is recommended [25].

In the Case of acute changes and worsening of the woman's symptoms, an assessment regarding the benefits and risks of continuing the labour versus proceeding to emergency caesarean birth. The neonatal team should be given enough time to allow them to attend entering the room/theatre. If there are no contraindications, then Cord clamping is advised after birth, until today there is currently no clear evidence to favour the delivery mode. It should be discussed with the woman, taking into consideration any obstetric indications and patients' preferences. The presence of COVID-19 should not influence the mode of birth unless the woman's respiratory condition urge an intervention for delivery if vaginal secretions are negative for COVID-19 [26].

The time of the second stage of labour shall be shortened with elective instrumental delivery.

An individualized informed discussion and decision should be made for an asymptomatic woman who is getting hypoxia or being exhausted.

Regarding analgesia: the presence of coronaviruses is not contraindicated to (epidural or spinal analgesia), and this is to minimize the use of general anaesthesia. As for patient with a single- microbiological filter, Entonox can be used [27].

Risk of venous thromboembolism should be assessed, and patients should have prophylactic LMWH and have a longer course of prophylactic LMWH [28].

A covid-19 suspected woman should have an individual assessment for an elective (planned) caesarean section. There should be an individualized evaluation with consideration of urgency of delivery, and risk of transmission. Obstetric management of elective caesarean delivery should be according to usual practice [28]

Planned induction of labours or elective caesarean section, an individual assessment should be made regarding the urgency of planned induction of labour for women currently in self-isolation because of suspected COVID-19 affecting either themselves or household contact. If delaying the induction of labour is not safe, the general advice for services

providing care to suspected/confirmed COVID-19 admitted women should be followed [28].

Conclusions

The only symptoms that are more common in pregnant than non-pregnant are the sore throat. That concluded that when pregnant women start to have sore throat care should be taken to exclude COVID-19 infection.

Author Contribution

A.J., H.H. designed the study protocol and search, data extraction. Aj and H.H. critical, independent review with contributed to statistical analysis and interpretation of data. A.J. drafted the manuscript with H.H. critically revising the manuscript.

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Conflict of Interest

The authors declare having no conflict of interest related to this work.

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