



## Systematic Review

## Covid-19 among 185 pregnant women across four countries: A systematic review

Donald S Christian<sup>1</sup>, Hardika J Khanpara<sup>1,\*</sup><sup>1</sup>Dept. of Community Medicine, GCS Medical College, Ahmedabad, Gujarat, India

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## ABSTRACT

**Background & Objective:** The aim of this systematic review was to report pregnancy and its outcomes of women who were affected by COVID-19 as pregnancy is known to be adversely affected by most of the viral outbreaks of recent times and it is too early to rule out COVID-19 from the list.

**Data Sources:** Electronic search was made across popular databases such as PubMed and Google Scholar with emphasize on keywords and their combinations keeping “COVID-19 and pregnancy” as a central theme.

**Study Eligibility Criteria:** The major inclusion criteria for articles was that they must have data on pregnant women who were tested positive for COVID-19 and they should have reasonable information on the outcomes of the current pregnancy.

**Study Appraisal and Synthesis Methods:** Median age of the women, gestational age at delivery, Co-morbidities, events during current pregnancy, maternal and fetal complications, mode of delivery, birth weight, APGAR scores of the neonate, neonatal outcome and COVID-19 test result of the neonate were the information which were tried to compare from the selected articles.

**Results:** Eight articles were screened and finalized for the systematic review which belonged to China, USA, UK and Singapore which in total had data for 185 pregnant women who were tested positive for COVID-19 and had undergone delivery. Similarly, the median age of the pregnant women was 30 years (29-33) and the median gestational of the women at the time of delivery was 36.75 (34-38) weeks. The caesarean rates was typically higher across the articles, with mean of 77.45%. Fever, cough and shortness of breath were the commonest presentations. The maternal and fetal complications were not significant. The most of the results of neonatal testing for COVID-19 turned out to be negative. The rate of premature births were highly variable.

**Conclusion:** The data thus far showed that the course of a COVID-19 pregnancy is much similar to a non-infected one. However, the rates of premature births were found higher at several occasions and need to be explored further. The possibilities of vertical transmission were almost nil. The outcomes of the pregnancies were also comparable to uninfected ones.

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## 1. Introduction

The current pandemic of COVID-19 has affected most of the parts of the world counting for more than 28 lac confirmed cases and more than 1.93 lac deaths globally.<sup>1</sup> The vulnerable groups include persons with extreme ages and comorbid conditions like Coronary Heart Disease, Hypertension or Diabetes.<sup>2</sup> The current knowledge suggest

that pregnancy is not a risk group as far as COVID-19 is concerned. But it should be remembered the lower immune status during pregnancy as well as the fact that Corona virus families have proven to be responsible for severe illnesses among pregnant women across the globe.<sup>3</sup> Physiological adjustments of pregnancy are likely to pose significant maternal and foetal morbidity and mortality.<sup>4</sup>

Although the data till date suggest that there is no increased risk to the pregnant women as compared to the non-pregnant women;<sup>5-7</sup> the rapidly spreading disease

\* Corresponding author.

E-mail address: [drhardika.kamani@gmail.com](mailto:drhardika.kamani@gmail.com) (H. J. Khanpara).

could have different implications in different settings as the time passes. Nevertheless, every emerging infections tended to affect pregnancy and foetal outcomes throughout the globe, most recent examples being H1N1 Swine flu and Zika virus.<sup>8</sup> Moreover, there is a need to consider pregnant women and their care separately in the health action plans against COVID-19 as there are reports of denials of care of pregnancy either in treatment or in vaccination, due to concerns of foetal safety in previous outbreaks of some of the recent emerging infections.<sup>9</sup> Even with the recent research and data on Corona virus and pregnancy, experts opine that there is need of large samples with epidemiological correlations to draw valid conclusions across the globe.<sup>10,11</sup> The objective of this systematic review was to report pregnancy and its outcomes of women who were affected by COVID-19 across the countries. Further, it might help the stakeholders to identify potential areas of research for COVID-19 with pregnancy, till the pandemic continuous in general public.

## 2. Methodology

### 2.1. Identification of studies

A computerized literature search using the Pubmed and Google Scholar database was conducted. The key words used were as following: "Corona virus and/or pregnancy", "Covid-19 and/or pregnancy", "Corona virus pregnancy outcomes", "2019-nCoV and/or pregnancy", "Corona virus and maternal infection" and "Corona virus and neonatal outcomes". Snowballing technique was used to search further articles. Only studies that showed outcomes of COVID-19 pregnancies were explored further. The types of study looked for were cross-sectional studies, case reports, case series, randomised trials, clinical trials as well as systematic reviews and meta-analysis. The consort guidelines were to be followed if randomised trials were to be included in the analysis.<sup>12</sup> The keywords were also adjusted to find out articles belonging to different countries as far as possible. In case of several consecutive reports of the same study, the latest one was used. Two investigators independently conducted the primary literature research using the key terms of searching. Then the data were independently reviewed and the studies not conforming to the eligibility and inclusion criteria were excluded. The remaining articles were further analysed for variations of time and place. In case of any conflicts between the investigators after independent search, consensus was reached by discussion and then the articles were finalised accordingly.

### 2.2. Data extraction

The following information was extracted from each study: Study design, authors, date of publication and study area. The date of publication/acceptance was given more

emphasiseas most of the literature would fall in 2020. For actual analysis, the information sought for were median age of the women, gestational age at delivery, Co-morbidities, events during current pregnancy, maternal and foetal complications, mode of delivery, birth weight, APGAR score, neonatal outcome and COVID-19 test result of the neonate. The variation, in the form of study area was given due emphasise, even if some of the information was lacking in some articles.

The articles suited most for the purpose were given priorities. Articles were further screened for relevance, complete information, the number of patients and heterogeneity of authors/study area. A comparison was made through a table regarding all the desired information. The median (with range) was preferred over the mean for numerical data, as it was a skewed distribution. Only symptoms of fever, cough and shortness of breath were considered for the analysis to simplify comparison and to avoid multiple symptoms. The corresponding authors were not contacted due to time constrain in ongoing pandemic. The quality of articles were assessed subjectively. Ethical approval was not required for this systematic review.

## 3. Results and Discussion

Considering the symptoms of the Covid-19 infection among the pregnant women, fever, cough and shortness of breath were the most common symptoms without any bias for countries. Especially, in Singapore article,<sup>17</sup> the proportions of females with fever (84%) were significantly high (Table 1). On the other hands, the proportions of cough was more than two third in article by Breslin N et al. for USA.<sup>14</sup> The mode of delivery was also ascertained from the articles. It was also observed that proportions premature births were significantly higher (78.18%) for the article by Dashraath P et al. at Singapore.<sup>17</sup> The proportion was also significant for the article by E. Mullins et al., which came out to be 46.87% among the 32 deliveries.<sup>13</sup> The incidences of maternal and foetal complications were also tried to found out. It can be seen that there were very few occasions of maternal complications from all these observations. The still birth rates were not significant and they were equally observed among China, Singapore and UK. However, in Singapore data the rates of IUGR (16.36%) were found to be significant.

The rates of Caesarean section was also found out from all the articles. The mean caesarean rate was found to be about 77.45% from the available data (Table 1). It is to be noted that in articles from Khan et al. and Liu et al., both from China, the caesarean rates were 100% and 90.9% respectively. These higher rates have implications of utmost care during the intervention.<sup>15,16</sup> The standard aseptic precautions in such pandemic are much warranted. The APGAR score at 1 min was found to 8.64 on an average from all the available data of the eight articles (Table 1).

**Table 1:** The analysis of eight article showing pregnancy outcomes of COVID-19 positive women (N=185)

Articles	Article 1 <sup>13</sup>	Article 2 <sup>14</sup>	Article 3 <sup>15</sup>	Article 4 <sup>16</sup>	Article 5 <sup>13</sup>	Article 6 <sup>14</sup>	Article 15	Article 8 <sup>16</sup>
<b>Number of women (N)</b>	7	13	7	55	32	43	17	11
<b>Median Maternal Age (range) in years</b>	30 (29-35)	30 (22-36)	33 (29-34)	31 (23-40)	30 (25-40)	29 (23-35)	29 (24-34)	32(27-37)
<b>Gestational age at delivery (weeks)</b>	34 (31-39)	35 (25-38)	38 (37-41)	34 (29-40)	36.5 (31-39)	37.0 (32.6-38.9)	37.82 (35-41)	37(36-38)
<b>Comorbid conditions</b>	None	None	Hypothyroidism:1, Poly Cystic Ovaries: 1	NA	12.5 %	Obesity:60.5% Asthma: 18% Diabetes: 7 %	None	Gestational Diabetes:1, Placenta Previa:1
<b>Events during pregnancy</b>	Fetal distress, Vaginal bleeding	Fever, Dyspnoea	Fever: 6 Abdominal Pain: 4 Fetal movements:1	Fever :84% Cough:28% Dyspnoea:18%	Fever: Sore throat	Fever: 48.3% Cough:65.5% Dyspnoea: 24.1%	Fever: 18% Cough:35% Dyspnoea:12%	Fever: 9 Cough:6 Dyspnoea: 0
<b>C-section proportions</b>	71.42 %	76.92 %	100%	NA	84.37 %	18.6 %	100%	90.9 %
<b>Birth weight (grams)</b>	2325 (1520-3800)	NA	3250 (3000-3500)	NA	NA	NA	3104 (2300-3750)	NA
<b>Maternal Complications</b>	NA	Premature rupture of membrane: 1 Multi Organ Dysfunction: 1	Uterine scarring :3	Mechanical ventilation: 2	Mechanical ventilation: 2 Multi organ dysfunction :1	Respiratory failure: 1, Septic shock: 2	Preterm delivery: 5	None
<b>Foetal Complications</b>	NA	Foetal distress:3 Still birth: 1	None	IUGR: 9 Still birth: 2	Still birth: 1	None	NA	None
<b>Premature delivery</b>	NA	Yes : 6 No: 4	NA	Yes : 43	Yes: 15	Yes : 1	Yes : 5	NA
<b>APGAR at 1 &amp; 5 mins</b>	1 min: 8.5 (7-10 5 min: 9.5 (8-10)	1 min: 10 (NA:3)	1 min: 8-9 5 min: 9-10	NA	10 (time unspecified)	For n=18 1 min: 7 5 min: 9	9-10 (94.1%)	1 min: 8 5 min: 9
<b>Neonatal outcome</b>	Small for date: 1 Large for date: 1	All survived	All survived	Death: 2	Death: 1	Respiratory distress: 1 Dysplastic kidneys: 1	Death : 0	Death : 0
<b>Neonatal RT-PCR for SARS-CoV-2</b>	Negative: 8	Negative :10 NA:3	Negative: 2 Positive : 1 NA: 4	Negative: 46 NA: 9	Negative: 25 NA: 7	Negative : 18 NA: 25	Negative: 17	NA

\*NA: Data Not Available

**Table 2:** Information of the included articles in the systematic review

	Study author	Author background	Date of article	Study design	Study area (country)
13	David A. Schwartz et al	USA	March, 17 2020	Review, Case Series	China
14	Yangli Liu et al	China	February 27, 2020	Report, Case Series	China
15	Nan Yu et al	Wuhan, China	March 24, 2020	Retrospective single centre study	China
16	Dashraath P et al	Singapore	March 17, 2020	Review, Case Series	Singapore
17	E. Mullins et al	UK	March 10, 2020	Rapid review	UK
18	Breslin N et al	USA	April 9, 2020	Retrospective Review, Case series	USA
19	Khan (2020)	Wuhan, China	March 27, 2020	Case series	China
20	Liu D. (2020)	China	March 7, 2020	Review, Case Series	China

Neonatal death was observed only in 3 occasions from all the extracted data.

The maternal complications (e.g. mechanical ventilation) or the foetal complications (e.g. still birth, foetal distress etc.) were found to be negligible (Table 1). The rate of premature births was variable across the studies and it ranged from 2.32% to 78.18%.<sup>14,17</sup> The neonatal death proportion only 1.62% from all the studies. The neonatal testing data showed that 68.1% of the results turn out to be negative and only 1 neonate had a positive result from all the data. Rest of the test results cannot be extracted from the articles.

#### 4. Conclusion

The fate of a COVID-19 pregnancy was observed to be much similar to a non-infected one from the current systematic review. The outcomes of the pregnancies were also comparable to uninfected ones. The possibilities of vertical transmission were almost nil. The rates of premature births were found higher. However, lack of sufficient research, inclusion of only last trimester of pregnancy and rapid progression of the current pandemic warrants further triangulation in the topic for obtaining valid conclusions.

#### 5. Limitations

Few data pertaining to some aspects of pregnancy and its outcome were not available. The pandemic is continuing and the data are updating thus the observations and their interpretations need to be looked with caution. The data of infection in first and second trimester were not included for the analysis.

#### 6. Source of Funding

None.

#### 7. Conflict of Interest

None.

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**Hardika J Khanpara** Assistant Professor

### Author biography

**Donald S Christian** Associate Professor

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