# **REVIEW ARTICLE**

# PREGNANCY OUTCOMES IN MOTHERS WITH COMMUNITY-ACQUIRED PNEUMONIA.

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### Abstract

**Background:** Pneumonia is the most common cause of fatal non-obstetric infections in pregnant women. We looked at articles reporting pneumonia and pregnancy in the past 10 years to see the effect on pregnancy and on foetal outcomes.

**Materials and Methods:** A comprehensive article review was done using databases such as ClinicalKey, MEDLINE, PubMed, ScienceDirect, Wiley Online Library, and ProQuest with appropriate keywords: "Pneumonia in pregnancy", "neonatal outcomes in pneumonia" and "viral pneumonia". The selection criteria were restricted to observational studies published in English between 2011 to April 2020. Articles (n=12) on pregnancy and perinatal outcome were identified. Due to the heterogeneous articles, a narrative review was done.

**Results:** Mothers with community acquired pneumonia has a higher risk of having a LSCS performed as seen in many articles and noted to have OR of 1.7 in the largest review. There was also a high risk for premature deliveries.

**Conclusion:** Pneumonia in pregnancy resulted in higher incidence of LSCS in mothers and poses a risk of prematurity for foetuses.

Keywords: COVID-19, pneumonia, pregnancy outcome, LSCS, prematurity

#### Introduction

We embark on this review after noting observation from colleagues working in Public hospitals that they noted an increase in community-acquired pneumonia among pregnant mothers. This was just before the announcement of COVID-19 as a pandemic and before the pandemic hits Malaysian shore. Pneumonia contributes to one of the fatal non-obstetric infections in pregnant women.<sup>[1]</sup> The changes during pregnancy, both physiological and immunological, make pregnant women more vulnerable to bacterial and viral infections. This predisposes them towards a more severe course of pneumonia, which may result in unwanted outcomes such as maternal and foetal morbidity and mortality.<sup>[2]</sup>

However, besides this being common knowledge, we feel that there is often a delay in the announcements or awareness steps concerning pregnant women. This can be seen for example in the advocating of vaccination for pregnant women. The government have different policies concerning pregnant women, not based on scientific knowledge but on mainly, fear of the unknown. Vaccine companies are reluctant to do research involving pregnant women and because of that pregnant women are left alone with no protection against the microorganisms. <sup>[3]</sup>

Besides common types of pneumonia, the outbreak of severe acute respiratory syndrome (SARS) and the emergence of the Middle East respiratory syndrome (MERS), has received worldwide attention as important pathogens of the respiratory tract. <sup>[4]</sup> The World Health Organization (WHO) recently had announced the pandemic outbreak of the Novel Coronavirus. The presence of this disease, COVID-19, in pregnant women raises concerns, as other cases of pneumonia of different etiologies were frequently associated with adverse outcomes. <sup>[5]</sup>

Several studies have shown that pregnancies complicated by pneumonia results in unfavourable pregnancy and neonatal outcomes and other confounding factors such as comorbid conditions may play a part. Thus, this has raised concern on the importance of identifying the pregnancy and perinatal outcomes of reported cases of Community-Acquired Pneumonia (CAP) of different aetiologies in pregnancy. However, this review only attempts to look at the maternal and perinatal outcome in general. We feel that pregnant patients with pneumonia should be given priority in medical attention due to their vulnerability and since two lives or even more may be at risk.

#### **Materials and Methods**

This is a narrative review of 12 research articles on pregnant women with Community-Acquired Pneumonia (CAP) and their pregnancy and perinatal outcomes. This study design was chosen because the articles were too heterogeneous to permit a systematic review of qualitative studies or a theoretical qualitative meta-synthesis.

#### Inclusion and Exclusion Criteria

Articles were eligible for review if they met the following criteria: (i) Pregnant women diagnosed with Community-Acquired pneumonia (CAP) caused by either bacteria or viruses, with reported data about pregnancy and in case of delivery, reported outcomes. (ii) Observational studies (iii) Articles published in English in peer-reviewed and indexed journals between 2011 to 2020.

Exclusion criteria for our studies were as follows: (i) Article that does not report on the pregnancy and/or perinatal outcomes of pregnant women with pneumonia. (ii) Pre-print or pre-proof articles. (iii) Case reports (iv) Studies with sample size less than five.

#### Search Methods for Identification of Studies

The following databases were screened to detect eligible articles: Clinical Key, MEDLINE, PubMed, Wiley Online Library and ProQuest. The appropriate keywords used were: "pneumonia in pregnancy", "neonatal outcomes in pneumonia" and "viral pneumonia". The references of the retrieved articles was also checked for additional relevant articles.

The selection criteria were limited to English articles published between 2011 to April 2020 to ensure the relevancy of the review and it was during this time that the COVID-19 pandemic has not been declared. Our primary focus of the review is on the pregnancy and perinatal outcomes of Community-Acquired Pneumonia (CAP) of various aetiologies in pregnant women hence, period of gestation at diagnosis, the clinical features, and severity of pneumonia, comorbidities, and complications during pregnancy were excluded.

#### **Data Extraction and Analysis**

Three researchers independently evaluated and assessed the list of titles, abstracts, and full text screening of articles to minimize risk of bias. Data retrieved from the selected articles were analysed descriptively and narratively reviewed. However, the studies included in this review also have limitations that should be acknowledged. The most important of these are that most studies have small sample size. Of 12 selected articles, five were case series, and three retrospective studies had less than 30 sample size.

Many studies provided insufficient sociodemographic information about their research participants. Only 6 studies acknowledge study limitations and recruitment biases. <sup>[6, 7, 8, 9, 10, 11]</sup> Only one article in our review provides large sample size and reliable data collection. <sup>[6]</sup> Therefore, this article provides most of the reference in this review.

In common with other narrative reviews of qualitative studies, we do not seek to assess the ways that participant selection may have influenced results. Because this is not a systematic review and few articles were found, evaluations of methodological quality were not used to exclude papers from the study. All studies were recruited at clinical sites with the help of health professionals except for one study that uses a nationwide population-based study. <sup>[6]</sup> Although only one study represented a community-acquired infection, other studies were considered as well because of the availability of the pregnancy and perinatal outcomes data. A summary of tables with findings for respective studies was tabulated and narratively reviewed.

#### **Ethical consideration**

Ethical approval was not required for this review. All the findings obtained from the research articles will be kept and handled confidentially, in accordance with applicable laws and/or regulations. When publishing or presenting the study results, the subjects' identity will not be revealed without their consent.

#### Results

Our literature search uncovered 12 observational studies, including eight from China, and one from Taiwan, Turkey, Saudi Arabia, and Brazil, respectively (Table 1). Table 2 summarized the mean maternal age, the pregnancy, and perinatal outcomes of all 12 articles.

# Pregnancy Outcomes of Pregnant Women with Pneumonia

Many of the patients diagnosed with pneumonia had undergone caesarean section. It is interesting to know what was the indication that made obstetricians decide to perform surgery rather than allow for vaginal delivery. Was it because the neonates were affected by the disease that necessitated Caesarean section to be performed? Was it purely obstetrical or was it because of the possibility of vertical transmission?

We looked at the largest study in article 1 and found that pregnant mothers with pneumonia were more likely to have caesarean delivery than women without pneumonia. After adjustments were made for co-morbidities and confounders, the odds ratio of having caesarean section was 1.77 (95% CI, 1.58-1.98) times more than the normal population. However, the indication for Caesarean section was unfortunately not studied and this may be due to the limitation of data available since the data is from pooled nationbased data and not from hospital data.

A retrospective study was done in article 3 revealed that out of 30 pregnant women with pneumonia, 23 (77%) of them had caesarean delivery, in comparison, six (16%) cases of the control group. However, this study was undertaken in mothers with severe pneumonia following the criteria based on Infectious Diseases Society of America/American Thoracic Consensus Guidelines Society on the Management of Community-Acquired Pneumonia in Adults (Clinical Infectious Diseases 2007), in which the mother may have one out of two major criteria i.e. on mechanical ventilation or in sepsis or having two minor criteria. The termination of pregnancy was made as soon as possible if the patient suffered from severe hypoxemia or combined obstetric complications to avoid foetal distress Therefore the decision made was due to the mother's deteriorating condition.

In article 6, out of five cases, two patients underwent caesarean delivery due to foetal tachycardia during pregnancy and gestational diabetes respectively. This mode of delivery was mainly determined by obstetric factors and not affected by the coexistence of COVID-19 infection.

Article 4 retrospectively reviewed the medical records of nine pregnant women infected with COVID-19 and found all of them were reported to undergo Caesarean section. All the indications for the Caesarean section were reported. These indications include severely elevated alanine aminotransferase (ALT) or aspartate transaminase (AST), a patient with two histories of previous Caesarean delivery, preeclampsia, foetal distress, two histories of stillbirth, and prelabour rupture of membranes (PROM). Another indication for caesarean delivery is uncertainty about the risk of intrapartum mother-to-child transmission if vaginal delivery is performed. Article 10 also showed a similar indication of Caesarean delivery where four cases had caesarean delivery due to uncertainty of vertical transmission to the newborn. This raised a concern especially in symptomatic pregnant women, assuming a high level of viremia after the onset of the symptom. Another indication for caesarean delivery in article 10 was preeclampsia and severely elevated ALT.

In article 2, five of 12 patients were reported to have undergone caesarean delivery as soon as the diagnosis of severe pneumonia was made. Article 12 reported 131/233 cases of pregnant women with influenza A (H1N1) infection had caesarean delivery meanwhile article 5, 7, and 9 reported more than half pregnant women with COVID-19 pneumonia underwent caesarean delivery, no indications were reported in these studies. Case series of influenza H1N1 2009 infection in pregnancy by article 8 reported seven patients underwent caesarean delivery, however, this study also did not mention the indication for caesarean delivery.

#### Perinatal outcome of neonates born to women with pneumonia

Most of the articles reviewed reported preterm birth as their adverse perinatal outcome (1, 2, 4, 5, 5)8, 9, 10, 11, and 12). Article 1 by Yi-Hua Chen et.al. shows that 180 women with pneumonia had a higher prevalence of preterm births (12.3% vs 7.1%, P < 0.001) than women without pneumonia. The odds ratio (OR) of preterm birth was greater than 1 (1.71, 95% CI, 1.42 - 2.05) which indicates the outcome is more likely to occur in neonates born to mothers with pneumonia. A similar finding was seen in article 2 and preterm was the leading adverse outcome in newborns. Of seven deliveries of neonates born to mother with pneumonia, six (85.7%) were delivered preterm. Article 4 reported four preterm births (all beyond 36 weeks). Although the findings were similar to other studies, the researchers in this study claimed that COVID-19 pneumonia was not the cause of the premature birth because one patient had severe pre-eclampsia, one had a history of two stillbirths, one had a history of two caesarean sections and irregular contractions, and one had a premature rupture of membrane for 12 hours and

suspected intrauterine infection. Article 5 recorded three cases of preterm births (27.3%) out of 11 deliveries. However, the researchers mentioned that it was because of the belief that antiviral treatment was needed as early as possible in the disease course, thus, these patients were delivered early via caesarean section at 34-36 weeks.

In article 8, four (16%) preterm deliveries (23 -32 weeks of gestation) out of 25 pregnant women with H1N1 2009 influenza were recorded. Article 9 reported three cases of the neonatal respiratory syndrome after birth, among which two were premature (<35 weeks) babies from mothers with confirmed COVID-19 and one was a full-term baby from a normal mother. Recent studies on neonates born to mothers with COVID-19 in article 10 recorded four preterm deliveries (57.1%) out of seven case series. While among five pregnancies with MERS-CoV infection during pregnancy that was reported in article 11, one neonate (20%) was born preterm and was surgically delivered at 24 weeks due to maternal deterioration and death after four hours after birth. The baby was not tested for MERS-CoV infection thus vertical transmissibility was not able to be concluded.

Article 12 compared the gestational outcomes in cases of pregnant women with influenza A (H1N1) (died) and control (recovered) reported 64 preterm births (27.4%) in total, in which 34 was from cases who died and 30 from controls who recovered. There were no reported preterm deliveries in articles 6 and 7. In both the studies, neonates were born term with good birthweight and APGAR score.

From 57 newborn babies, including two cases of twins in article 9, 20 babies (born from confirmed and from normal mothers) that were subjected to SARS-CoV-2 examination by throat swab samples 24 hours after birth tested negative. Despite the limitations of not taking throat swabs for all the newborns were highlighted, their study did not show any evidence of vertical transmission in neonates born to mothers with COVID-19. A more detailed study on vertical transmission by article 4 that tested the amniotic fluid, cord blood, breast milk, and neonatal throat swab at birth showed that SARS-CoV-2 was negative in all the samples, suggesting no intrauterine foetal infections as a result of COVID-19 infections during the late stage of pregnancy. No newborns showed any signs of perinatal COVID-19 infection.

With that being said, the researchers did address the possibility of their limitations on the sample size, the stage of pregnancy at the onset of COVID-19 infection, and failure to collect samples of vaginal mucosa or shedding in birth canals which could affect their findings. They were unable to ascertain the possibility of vertical transmission in the first or second trimester. Interestingly, this study mentioned a case of a neonate born to a pregnant woman with COVID-19 pneumonia and was tested positive for SARS-CoV infection few days (36 hours) after birth. This case was not included in the study as it was detected beyond their study period (Jan 20 – Jan 31, 2020). However, a few loopholes like delayed neonatal throat swab samples collection (30 hours after birth) and the absence of direct testing of intrauterine tissue samples (amniotic fluid, cord blood, or placenta) has made the researchers unable to conclude whether or not intrauterine infection occurred in this particular case. None of the foetuses born to mothers with H1N1 influenza in articles 8 or 12 have any evidence of infection.

#### Discussion

Anatomical, physiological, and immunological changes occur in pregnant women to ensure that the foetus or foetuses they carry will be adequately nourished, protected, and given the best environment for growth. <sup>[12]</sup> However, these conditions too will put mothers at a higher risk of being infected with microorganism in the event of a pandemic or when there is a possibility of exposure to infection.

Over the years, the world has seen a plethora of micro-organisms affecting human beings and therefore affecting pregnant women too. In recent years, infections such as Zika, Ebola, SARS, MERS, and currently COVID-19 causes concern among obstetricians and paediatricians alike on to what extent the pregnancy and the foetus can be affected.

In this review of 12 articles, we noted that many of the articles reported a higher risk of mothers undergoing LSCS although we did not get details whether they were done electively or as an emergency. From the indications cited by some articles, we knew that some of the indications were purely obstetric causes (for example due to two previous caesarean section, GDM), whereas some cited pre-eclampsia, PPROM, foetal distress, foetal tachycardia. [8, 13] It is not known for sure whether they are related to pneumonia. Some, as in article 4 were due to mothers' deteriorating condition due to pneumonia. However, some cited the indication for surgery was due to fear or possibility of vertical transmission from mother to baby as the baby travels through the birth canal. <sup>[11]</sup> It is noted that some infections for example HIV, HSV affect the baby as they pass through the birth canal and delivery by caesarean section is advocated to reduce the chance of transmitting the virus to the baby.

But not all microorganism infects the foetus while in the birth canal and therefore it is important to ascertain which organism causes vertical transmission and which ones do not. More research needs to look at the amniotic fluid, the placenta, the throat swab of the baby at delivery, and the umbilical cord. In this review, only one article looked at the amniotic fluid, cord blood and neonatal throat swab and noted the specimens were negative for COVID-19. <sup>[8]</sup> It would also be worthwhile to look at the levels of antibodies passed from the mother to foetus and whether they can provide some protection for the newly born babies.

The largest data reported that after adjusting for co-morbidities and other confounders, they noted that mothers with pneumonia were 1.73, 1.71, 1.35, 1.77, 3.86, and 3.05 times more likely than unaffected mothers to have LBW, preterm birth,

SGA, CS, low Apgar scores, and preeclampsia/eclampsia, respectively. However, there were no cases of maternal death noted. <sup>[6]</sup> This may be because most of the infections were bacterial in origin and hence responded better to treatment.

There were 4 maternal deaths reported which looked only at severe pneumonia, however, the organism was not mentioned.<sup>[14]</sup>

The strength of this article is that we were able to get the largest community-based data hence, this article was reliable as it represents nationwide population.

This research was subjected to several limitations. First, the complete reliance on the previously published research and the availability of these studies using the methods outlined. The second limitation concerns the limited access to only free full-text articles which may result in a possible lack of reliable studies for review. Researchers' fluency in only the English language was also a limitation thus, our review list was limited to only English- published articles. Further research that includes articles published in other languages may be appropriate. This can further increase the total series and accuracy of this review. Some of the articles did not report on the type of microorganism.

#### **Conclusion and Recommendations**

In conclusion, pneumonia in pregnancy predisposes mothers to a higher risk of caesarean section. Some mothers affected with severe pneumonia succumb to the disease. Preterm deliveries were seen as an adverse perinatal outcome in most cases.

With pregnancy itself being an immunocompromised condition and susceptible to respiratory pathogens, pregnant mothers are at risk of severe morbidity and mortality. Thus, pregnant women, who predominantly are more susceptible should follow standard guidelines in maintaining self-care and hand hygiene.

There are substantial implications of this research. As the world ages, we are finding ourselves exposed to a more and more virulent form of microorganisms and we may be facing few more pandemics in the future. The increased risk of adverse pregnancy and perinatal outcomes in pregnant women with pneumonia warrants higher surveillance among this population to ensure prompt medical interventions are given. Pregnant mothers should be given priority in access to earlier medical treatment. Pregnant mothers should receive treatment just like normal adults and pregnancy should not deter the physicians from providing the best for the patients.

Vaccination should be the way forward to reduce complications to mother and baby. More research and funds on vaccination in pregnant women should be done and it is not acceptable anymore for drug companies to put a blanket rule saying pregnant women are contraindicated without scientific evidence.

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#### **Conflict of Interest**

The authors report no conflict of interest.

Author	Title	Study	Study	Pregnancie	
		Location	design	s (n)	
1. Yi-Hua Chen (2012) – Article 1 <sup>[6]</sup>	Pneumonia and pregnancy outcomes: a Nationwide population-based study	Taiwan	Cross- sectional	1462	
2. Ping Ping Tang (2018) – Article 2 <sup>[7]</sup>	Characteristics and pregnancy outcomes of patients with severe pneumonia complicating pregnancy: a retrospective study of 12 cases and a literature review	China	Retrospec tive Cohort	12	
3. Jing Huang (2016) – Article 3 <sup>[14]</sup>	The Termination of Gestational Weeks and Methods of Delivery of Severe Pneumonia in Pregnancy	China	Retrospec tive	30	
4. Huijun Chen (2020) -Article 4 <sup>[8]</sup>	Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records	China	Retrospec tive review	9	
5. Dehan Liu (2020) – Article 5 <sup>[13]</sup>	Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis	China	Retrospec tive	15	
6. Siyu Chen (2019) – Article 6 <sup>[15]</sup>	Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia	China	Retrospec tive	5	
7. Nan Yu (2020) – Article 7 <sup>[9]</sup>	Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study	China	Retrospec tive	7	
8. S,ebnem O"zyer (2011) – Article 8 <sup>[16]</sup>	Pandemic influenza H1N1 2009 virus infection in pregnancy in Turkey	Turkey	Retrospec tive	25	
9. Hui yang (2020) – Article 9 <sup>[10]</sup>	Clinical features and outcomes of pregnant women suspected of coronavirus disease 2019	China	Retrospec tive	13	
10. Pu Yang (2020) – Article 10 <sup>[11]</sup>	Clinical characteristics and risk assessment of newborns born to mothers with COVID-19	China	Retrospec tive	7	
11. Abdulla Assiri (2016) – Article 11 <sup>[17]</sup>	Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases from Saudi Arabia	Saudi Arabia	Case Series	5	
12. Ana Freitas Ribeiro (2018) – Article 12 <sup>[18]</sup>	Severe influenza A(H1N1) in pregnant women and neonatal outcomes, State of Sao Paulo, Brazil, 2009	Brazil	Case Control	233	

## Table 1. General characteristics of the included studies

*\*N/A*= *Not available* 

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Case	1	2	3	4	5	6	7	8	9	10	11	12
Maternal characteristics												
Mean age	N/A	27	28.9	29.9	32	28.8	32	26.2	30.2	N/A	30.8	25.7
Pregnancy outcomes												
C-section	812	5	20	9	10	2	7	7	9	7	1	131
Miscarriage	N/A	1	0	0	N/A	0	0	2	0	0	0	8
Maternal death	N/A	2	4	0	N/A	0	N/A	0	N/A	N/A	2	42
Perinatal outcome												
Preterm	180	6	N/A	4	3	0	0	4	2	4	1	64
Low birth weight	143	N/A	30	2	N/A	0	0	2	0	1	0	37
(LBW)												
Small for	303	N/A	0	0	N/A	0	0	0	0	0	0	19
gestational age												
(SGA)												
Low APGAR	10	2	N/A	0	0	0	0	0	N/A	0	0	0
score												
Congenital	13	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Anomalies												
Intrauterine death	N/A	1	N/A	0	0	0	0	0	0	0	1	N/A
(IUD)												
Neonatal death	N/A	1	N/A	0	0	0	0	0	0	0	1	20

Table 2. Pregnancy and Perinatal Outcomes

\*Miscarriage: Death before 24 weeks.

*†Preterm: <37 completed weeks* 

*‡LBW: <2500g* 

§SGA: Birthweight below the 10th percentile for babies of the same gestational age //LGA: Birthweight more than the 90th percentile for babies of the same gestational age ¶Low APGAR: Lesser than 7 at the 1<sup>st</sup> and 5<sup>th</sup> minutes

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\*\*Congenital anomalies: Hydrocephaly, Anencephaly, Microcephaly, Meningomyelocele, Encephalocele and Spina Bifida

*††UD: Death after 24 weeks.* 

*‡‡Neonatal death: Death after delivery.* 

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