Innovative Journal of Pediatrics
Volume 31 · Issue 4 · e112780

OPEN PEER REVIEW

Clinical Findings, Laboratory Assessment, and Outcomes of 44 Infants Born to Mothers with Confirmed or Suspected COVID-19: A Multicenter Cohort Study

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SUBMITTED	REVISED	ACCEPTED	DOI
9 Jan 2021	14 Jul 2021	26 Jul 2021	10.5812/ijp.112780

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 1 Feb 2021 – 6 Mar 2021

Mirhadi Mousavi Reviewer

MINOR REVISION 1 Feb 2021

Hello. You have put a lot of effort into the study, which deserves thanks, but the following suggestions are recommended:
- The keywords are not based on MeSH.
- The conclusion isn't fully consistent with the findings; please rewrite it based on the definitive findings of the study.
- The methods are not appropriate or well described;
Neonatal sampling criteria and reasons for the second visit should be specified.
Of the 15 symptomatic infants admitted, only two had a positive PCR. How did you determine that the other neonates' problems and symptoms were related to COVID?
- It is suggested that the characteristics of mothers and newborns be presented in two separate tables.

Gaurav Gupta Reviewer

MINOR REVISION 6 Mar 2021

1. Data from pregnant women with suspected COVID and COVID-positive women are merged.
2. There should be segregation of data according to pregnant women with suspected and confirmed COVID.
3. Symptoms in infants may be due to comorbidities in pregnant women rather than COVID positivity in women.
4. So symptomatic infants should be stratified according to comorbidities and COVID positivity.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Reviewers

Thank you for the opportunity to revise our manuscript, Clinical findings, laboratory assessment, and outcomes of 44 infants born to mothers with confirmed or suspected COVID-19: a multicenter cohort study.

We appreciate the careful review and constructive suggestions. We believe that manuscript is substantially improved after marking the suggested edits.

Following this letter are the editor and reviewer comments with our responses. Changes made in the manuscript are marked in highlights. The revision has been developed in consultation with all coauthors.

Reviewer 1

-1.keywords are not based on the mesh: *we changed it based on the mesh.*

-2. The conclusion isn't appropriate exactly to findings; please rewrite based on the definitive findings of the study: *we have re-edited it precisely; thank you for your attention*

-3. The methods are not appropriate and well described
Neonatal sampling criteria and causes on the second visit should be specified

According to AAP guidelines published on April 2, 2020, recommended testing newborn of M-positives 24 hours after birth and an optional second test if clinically required, prior to discharge. And due to our country protocols in that period, we had to check the RT-PCR during the first 48 hours of birth. The second time depended on the neonatologist's clinical suspicion because all the other diagnoses had ruled out; we had to test the COVID-19 RT-PCR again.

4.Of the 15 symptomatic infants admitted, only two had a positive PCR; how did you find other neonates' problems and symptoms related to Covid?

Due to the persistence of manifestations and ruling out the other causes, we assumed it might be probable.

-5. It is suggested the characteristics of mothers and newborns should be in two separate tables.

We have written the characteristics of the mothers in a separate table. Table-1.

Reviewer 2:
1.suspected Covid pregnant women and covid positive women data is merged

As mentioned beforehand, thirty-five pregnant women had confirmed COVID-19 with a positive RT-PCR test; Four mothers were clinically suspected by their chest CT, which had a suggestive pattern of SARS-COV2.

The four mothers did not have positive RTPCR. This test has false-negative results. At the first of the epidemic, we accepted mothers with the covid-19 pattern as suspected positive but not confirmed.

2. there should be segregation of data according to suspect and confirmed pregnant women:

AS mentioned in the article, we highlighted that four pregnant women had a suggestive pattern of sars-cov2 in the CT. Therefore, they were assumed and treated as a confirmed covid-19 disease.

3. symptomatic infant may be due to comorbidities in pregnant women rather than covid positivity in women.

So symptomatic infants should have stratification according to comorbidities and covid positivity

We had 19 pregnant women with comorbidity (high blood pressure/hypothyroidism/PROM/ GDM), and all of these mothers had positive COVID-19 RTPCR. We had six neonates with positive RTPCR in these 17 women, and just one of these neonates had positive COVID-19 RTPCR in the first 48 hours of life with a mother who had hypothyroidism.

2 Revision 1

0 comments

No public comments in this round.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

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Dear Reviewers

Thank you for the opportunity to revise our manuscript, Clinical findings, laboratory assessment, and outcomes of 44 infants born to mothers with confirmed or suspected COVID-19: a multicenter cohort study.

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Reviewer 1

-1. The abstract result needs to summarize:

We summarized the results in the abstract.

-2. Analysis and results revision is recommended. The analysis is not appropriate to the study purpose then the conclusion is not appropriate.

As you know, It's a cohort study that we performed it at the beginning of the COVID-19 pandemic (March 20, 2020) and our purpose was to describe the symptoms and complication of neonates who were born from mothers with covid-19 pneumonia. As a result, out of 44 neonates, 15 neonates (34.1%) were symptomatic **at birth**, and during the observation, more neonates became symptomatic. Finally, **27/44** (61.3%) neonates became symptomatic, and 17/44 remained asymptomatic.

Then, in part of the analysis description, we had to write the results out of 44 neonates (all the neonates) and somewhere we described symptoms out of 27 ***symptomatic neonates****. And we mentioned in the table for example* ***(21/27)****respiratory distress.*

It is part of article

Statistical Analysis

The study aimed to evaluate neonates' clinical features and laboratory data born to mothers with COVID-19 (positive test or suspected with chest CT), looking for a relationship between the positive RTPCR test result of neonates and the type of clinical features and the percentage of neonates with COVID-19 infection who were born to infected mothers. To conduct a comprehensive analysis, all categorical data were manifested as frequency (%), showing

continuous data as mean ± SD. The statistical analyses were fulfilled with the IBM SPSS ver. 18.0 Statistics for windows.

3. All neonate's symptoms can not directly correlate with covid infection due to only 9 neonates.

Due to the persistence of manifestations and ruling out the other causes during the pandemic period and negative results of RTPCR of covid-19 in that time (it was the beginning of the pandemic and we did not have precise tests , also the colleagues who performed the test did not have excellent skills in doing a test), we assumed it might be probable.

با سلام و احترام خدمت اساتید گرامی

همان طور که مستحضر هستید این مطالعه جزو اولین مطالعات بین بیمارستانی در اوایل دوران پاندمی کرونا بوده است.

هدف ما از این مطالعه کوهورت توصیف علایم بالینی و ازمایشات و یافته های گرافی نوزادان متولد از مادران کووید مثبت بوده است و با توجه به این مساله که علایم نوزادان (از جمله علایم تنفسی یا تغییردرجه حرارت و یا سایر علایمی که در متن ذکر شده است) با سایر علل قابل توجیه نبوده است و علاوه بر این موضوع این نوزادان از مادران مبتلا به ویروس کرونا متولد شده اند و با توجه به احتمال منفی کاذب تست نازوفارنژیال کووید ، ما ارتباط این علایم را با ویروس کرونا متصور شدیم. همچنین با توجه به انجام این طرح در اوایل آغاز دوران پاندمی کرونا ویروس و احتمال مهارت و دانش کم در انجام دادن تست نازوفارنژیال کووید-19 احتمال منفی بودن تست پی سی ارنیز وجود داشته است. به نظر می رسد در مجموع علی رغم تعداد کم تست های مثبت کروناویروس در نوزادان می توان به دلیل وجود احتمال بالای منفی کاذب تست پی سی ار کووید-19 و رد کردن سایر علل ، علایم را به کل نسبت داد.

3 Revision 2

0 comments

No public comments in this round.