COVID-19: Is It Rare in Neonate?
Maksudur Rahman¹, Nishat Jahan², Liton Chandra Saha¹, Kinkar Ghosh³,
Kanta Chowdhury⁴, Md. Mahbubul Hoque⁴, M Monir Hossain⁴, Mahfuza Shirin¹,
MAK Azad Chowdhury⁴

Abstract
Background: The Global pandemic COVID-19 affects mainly adult population with serious devastating effects in some of them, particularly those with chronic comorbidities. It is less common in children and rare in neonates.

Objectives: The aim of study was to identify the COVID-19 in neonates so that we can give proper emphasis on neonatal COVID-19.

Methods: This cross sectional study was conducted from April 2020 to August 2020 at Dhaka Shishu (Children) Hospital in Bangladesh. Neonates with suspected COVID-19 were tested for SARS-CoV-2 virus by RT-PCR and positive cases were included in the study. Data were collected and statistical analysis was done by SPSS version 26.

Results: Out of 1714 admitted neonates, 32 (2%) cases were COVID-19 positive. Male were 21 (67%) and female were 11 (33%). Majority of the cases (28,88%) were at term. Twelve (38%) cases were from Dhaka and 20 (62%) cases came from outside Dhaka. Only 4(13%) cases were found positive for SARS-CoV-2 virus by RT-PCR within 3 days, among them 2 (6%) cases were within 24 hours of age. Nine cases (28%) were RT-PCR test positive within 4-7 days and 19 cases (59%) were RT-PCR positive within 8-28 days. Most of the cases belonged to neonatal medicine (24,75%) and 8(25%) cases were associated with surgical diseases. Sepsis was present in 17(53%) cases, perinatal asphyxia in 8(25%) and pneumonia in 6(19%) cases. Fourteen cases were discharged after improvement, 12 were referred to COVID-19 designated hospital, 2 cases were transferred to corona unit and 4 cases died.

Conclusion: In this study a good number of neonates were affected with COVID-19. Perinatal asphyxia, sepsis and pneumonia were common association with COVID-19. So for proper management and prevention of transmission of this disease, it should be properly addressed in neonates.

Keywords: COVID-19, neonate.

1. Associate Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Bangladesh.
2. Registrar, Department of Neonatal Medicine, Dhaka Shishu (Children) Hospital, Bangladesh.
3. Epidemiologist, Dhaka Shishu (Children) Hospital, Bangladesh.
4. Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Bangladesh.

Correspondence to: Dr. Maksudur Rahman, Associate Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Sher-e-Bangla Nagar, Dhaka- 1207, Bangladesh. Cell: 01715315462, Email: maksuddr@gmail.com
Received: 26 September 2020; Accepted: 25 November 2020
**Introduction**

There was an outbreak of viral pneumonitis in Wuhan, Hubei, China in December 2019. This global pandemic disease is caused by a novel beta coronavirus species, the 2019 novel coronavirus (2019-nCoV). It was finally renamed as SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) and the disease was named as COVID-19 (coronavirus disease 2019).

The disease is less common in children and rare in neonate. The first case in neonate with covid-19 was found in china on first February 2020. Then 3 cases of neonatal COVID-19 were identified in china up to February 2020. In Iran first neonatal case was also identified in the month of February.

Due to enhance surveillance of COVID-19 and availability and accessibility of rapid genetic amplification assays, a growing number of pediatric cases with COVID-19 was confirmed in Wuhan and other areas. Now the number of neonates with COVID-19 are increasing in different areas of the world.

The SARS-CoV-2 causes variety of clinical symptoms especially in respiratory system like mild upper respiratory tract infection, pneumonia, severe pneumonia. Sometime this infection rapidly spreads causing acute respiratory distress syndrome (ARDS), shock and death. Most of the children are asymptomatic and have mild clinical manifestations unlike adults. Neonates with COVID-19 have less clinical manifestations.

As increasing the publications, it is found that newborns are susceptible to this disease from COVID-19 positive mother and community, and viruses are detected for a prolonged period; therefore, newborns might play a role in community transmission.

So it is important to see the incidence of neonatal COVID-19, so that management of the disease can be taken more appropriately and transmission to heath personnel as well as family members can be prevented.

**Materials and Methods**

This cross sectional study was conducted from April 2020 to August 2020 at Dhaka Shishu (Children) Hospital (DSH), one of the largest children hospital in south Asia. An isolated corona unit was started at the middle of July in this hospital. Appropriate written consent was taken before each intervention from the parents of neonates. All neonates who were admitted at this hospital for different reasons were assessed for any suspicion of COVID-19. Clinical suspicions were made by baby born to suspected or confirmed COVID-19 mother, exposed to relatives infected with COVID-19, related with cluster outbreak and with abnormal clinical course such as respiratory distress, fever, not responded with conventional treatment and abnormal chest X-ray. Neonates with suspected COVID-19 were tested for SARS-CoV-2 and it is our hospital protocol to do RT-PCR before going for any operation. Nasal swab was taken with a swab stick by heath technologist with all aseptic precautions and wearing PPE (Personal protective instrument). The Swab stick, named COPAN FLOQSwabs (503CS01; COPAN Diagnostics, Brescia, Italy) was introduced into nose at a length similar to half way between ear lobule to same side ala nasi of nose. Then proximal broken swab stick was put into a tube (Falcon tube) filled with 1 mL of 1X RNA shield (D7005; Zymo, Irvine, CA). Finally, RT-PCR (Reverse transcription-polymerase chain reaction) was done for detection of nucleic acid of virus. The method used for this test was real time PCR for SARS-CoV-2 using the TaqPath COVID-19 RT-PCR Kit (A7817; Thermo Fisher Scientific, Waltham, MA). All tests were done in a government approved laboratory.

Then all the positives cases were evaluated and cases were either discharged who had features of improvement or referred to COVID-19 designated hospital or transferred to corona unit of Dhaka Shishu (Children) Hospital. The discharged neonates were given proper counselling for breastfeeding, isolation care of baby and also isolation for attendants.

In this study main outcome variable was number of test positive cases for SARS-CoV-2. Data regarding gender, birth weight, gestational age, resident, and associated diseases were collected. The data were entered and analyzed using Statistical Package of Social Science SPSS, version 26. The descriptive statistics such as frequencies, percentages were calculated to summarize nominal and ordinal data, while mean and standard deviation to describe numerical variables.

**Results**

During this study period total 1714 neonates were admitted. Among them 32(2%) cases were COVID-19 positive (Fig 1).
Among the cases male were 21(67%) and female were 11 (33%). Male and female ratio was 1.9:1. Term baby was 28(88%) and preterm was 4(12%). Mean weight was 2698±294 g. Twelve (38%) cases were from Dhaka and 20(62%) cases were from outside of Dhaka (Table I).

Table I

| Distribution of cases according to gender, gestational age, weight and resident (N=20) |
|---------------------------------------------|----------------|---------------|
| Male                                       | 21            | 67            |
| Female                                     | 11            | 33            |
| Term                                       | 28            | 88            |
| Preterm                                    | 4             | 12            |
| Weight in g (mean±SD)                       | 2698±294      |               |
| Dhaka (capital)                             | 12            | 38            |
| Outside Dhaka                              | 20            | 62            |

Only 4 (13%) cases were positive for SARS-CoV-2 virus by RT. PCR within 3 days, among them 2 (6%) cases were within 24 hours of age. Nine (28%) cases were test positive within 4-7 and 19(59%) cases were positive within 8-28 days (Table II).

Table II

| Days at which test positive for SARS-CoV-2 by RT-PCR (N=20) |
|-------------------------------------------------------------|
| Age of the cases (day) | Number of cases | Percentage of cases |
|------------------------|-----------------|---------------------|
| 1-3                    | 4               | 13                  |
| 4-7                    | 9               | 28                  |
| 8-28                   | 19              | 59                  |

SARS = severe acute respiratory syndrome; COV-2 = corona virus 2; RT-PCR = reverse transcription-polymerase chain reaction.

Most of the diseases associated with COVID-19 belonged to neonatal medicine department (24,75%) and 8 (25%) cases were associated with surgical diseases. In neonates two or more diseases coexisted in same cases. Sepsis was present in 17(53%) cases with COVID-19. Perinatal asphyxia was present in 8(25%) and pneumonia in 6(19%) cases (Table III). Among 32 positive cases, 14 cases were discharged after improvement, 12 cases were referred to COVID-19 designated hospital and 2 cases were transferred to corona unit of DSH, which was finally discharged with advice. Four cases died at our hospital (Table IV).

Discussion

This cross sectional study was conducted from April 2020 to June 2020 at Dhaka Shishu (Children) Hospital. All admitted neonates with COVID-19 were taken as cases. During this study period total 1714 neonates were admitted. Among them 32 (2%) cases were COVID-19.

The first case of COVID-19 was detected in Bangladesh at 8th March 2020 who was adult.11 We started RT-PCR for COVID-19 at this hospital in the month of April in this year.

Worldwide the incidence of covid19 in children is very few in contrast to adult and it is rare in neonates.12 The first children affected by COVID-19 was in china on January, 2020.13 Liu et al14 showed in their study that the incidence of COVID-19 in paediatric age group was 1.6% among the hospitalized children with respiratory tract infection. Another study conducted by Tu et al15 showed that the incidence of COVID-19 in children was 0.6% among the confirmed cases of all age group. In the month of February several study showed that neonates were also affected by COVID-19.3,16 The first neonate with COVID-19 was identified in first February 2020 which was published by Wang et al.3 Then 3 neonates with COVID-19 were identified in that month which was published by Choi et al.1 At that time in different countries neonates were also affected with COVID-19. In Iran first case of neonatal COVID-19 was found in this month.6 Different publications on neonates with COVID-19 showed that the number of neonate with COVID-19 is increasing in the world.1,6 But still it is very few unlike adult.7 The cause of less neonatal COVID-19 may be the presence of less number of ACE2 receptor in their respiratory tract and their more stronger innate immunity than adult.17,18 Surprisingly we see more
| Name of the Diseases | Admission age of cases (day) | Number of cases | Percentage of cases# |
|----------------------|------------------------------|-----------------|----------------------|
| Term, Perinatal Asphyxia HIE II<sup>a</sup> with Pneumonia<sup>c</sup> | 1 | 3 | 9 |
| Perinatal Asphyxia | 4 | 15 | |
| HIE II<sup>a</sup> with sepsis<sup>b</sup> | 22 | 4 | 13 |
| Perinatal Asphyxia HIE III with sepsis<sup>b</sup>, Term, IUGR, Jaundice | 6 | 1 | 3 |
| Neonatal Jaundice with sepsis<sup>b</sup> | 5 | 4 | 13 |
| Pneumonia<sup>c</sup> with sepsis<sup>b</sup> | 20 | 2 | 6 |
| Term AGA with EONS | 8 | 2 | 6 |
| Term AGA with LONS | 20 | 4 | 13 |
| *Pneumonia<sup>c</sup> with CHD with syndromic Baby | 20 | 1 | 3 |
| *Congenital Heart disease | 23 | 1 | 3 |
| AKI | 8 | 1 | 3 |
| PUV with B/L TEV | 15 | 1 | 3 |
| *Occipital Encephalocele | 2 | 1 | 3 |
| Myelomylengoele | 5 | 4 | 13 |
| ARM with sepsis<sup>b</sup> | 5 | 1 | 3 |
| *ARM | 22 | 1 | 3 |
| Hypertrophic pyloric stenosis | 17 | 1 | 3 |

HIE: Hypoxic Ischemic Encephalopathy; IUGR: Intra Uterine Growth Retardation; AGA: Appropriate for Gestational Age; EONS: Early Onset Neonatal Sepsis; LONS: Late Onset Neonatal Sepsis; CHD: Congenital Heart Disease; AKI: Acute Kidney Injury; PUV: Posturetral Valve; B/L: Bilateral; TEV: Telipes Equenovarus, ARM: Anorectal Malformation; *late preterm; <sup>a</sup> perinatal asphyxia 8 cases, <sup>b</sup> sepsis 17 cases, <sup>c</sup> pneumonia 6 cases. # percentage expressed in round figure.
number of neonates with COVID-19 (2%, 20 cases) in this study. The neonatal COVID-19 is increasing. It may be due to increase community transmission, and household contact including mother. Though the transmission of SARS-CoV-2 virus through placenta and breast milk is still unidentified.19-21

Among the cases with COVID-19 male were 21 (67%) and female were 11 (33%). Male and female ratio was 1.9:1. Term baby was 28 (88%) and preterm was 4 (12%). Mean weight was 2698±294 g. It was found that in this study male was predominantly affected by COVID-19. The cause of this finding is still unknown. In this study it was found that term and normal weight neonates were affected more. But regarding gender and gestational age, no statistical comparison was done. In one study, it was found that there was no significant sex predominance in children.5 In this study Twelve (38%) cases with covid19 lived in Dhaka and 20 (62%) cases in outside of Dhaka. This implies that only in Dhaka (capital of Bangladesh) affected cases were more as a single city than rest of the districts. In another study it was found that COVID-19 affected cases were more in city.5

In our study only 4 (13%) cases were positive for SARS-CoV-2 virus by RT-PCR within 3 days, among them 2 (6%) cases were within 24 hours of age. Nine (28%) and 19 (59%) cases were test positive within 4-7 days and 8-28 days respectively. It may imply that most of the cases were affected from community or from family members. In one study it was found that children were affected from community or household contact.16

It was found in this study that most of the diseases associated with COVID-19 belonged to neonatal medicine department (24.75%) and only 8 (25%) cases were associated with surgical diseases. In neonates two or more diseases coexisted in the same case. Sepsis was present in 17 (53%) cases with COVID-19. Perinatal asphyxia was present in 8 (25%) and pneumonia in 6 (19%) cases.

This hospital is not a COVID-19 designated hospital and all patients were out born. An isolated corona unit was started at the middle of July in this hospital, initially all patients were admitted in another hospital and later referred to this hospital. Newborns with any conditions or diseases was admitted. In this study it was not found whether associated conditions like sepsis and pneumonia were caused by COVID-19 or these conditions were associated with neonatal COVID-19. Several study showed COVID-19 presented with respiratory distress, sepsis like manifestation etc.5,10

In this study among 32 positive cases, 14 cases were discharged after improvement, 12 cases were referred to COVID-19 designated hospital and 2 cases were transferred to our corona unit which was finally discharged with advice. Four cases died at our hospital. In this study exposer history could not be evaluated properly.

We have found significant number of neonates with COVID-19 in this study. These neonates may be a source of transmission of this disease. So, we should give proper emphasis on test, tracing and management of neonatal COVID-19 like adult.

Conclusion
In this study a good number of neonates were affected with COVID-19. Perinatal asphyxia, sepsis and pneumonia were common association with COVID-19. So for proper management and prevention of transmission of this disease, it should be properly addressed in neonates.

Acknowledgements
The authors are grateful to the microbiology department and CHRF (Child Health Research Foundation) who has provided facilities to carry out the research work.

Conflict of interest
There was no conflict of interest.

References
1. Choi S, Kim W, Kang Ji, Kim H, Cho E. Epidemiology and clinical features of coronavirus disease 2019 in

Table IV
Outcome of Neonates with COVID-19 (N=32)

| Variable                        | Number (Percentage) |
|---------------------------------|---------------------|
| Discharged with advice          | 14 (44)             |
| Transferred to corona Unit*     | 2 (6)               |
| Referred to COVID-19 designated hospital | 12 (38) |
| Death                           | 4 (12)              |

*which finally discharged with advice; # percentage expressed in round figure.
2. Rose D, Piersigilli F, Ronchetti MP. Novel coronavirus disease (COVID-19) in newborns and infants: what we know so far. *Ital J Pediatr* 2020;46:56. DOI: 10.1186/s13052-020-0820-x.

3. Wang S, Guo L, Chen L, Liu W, Cao Y, Zhang J, et al. A case report of neonatal 2019 coronavirus disease in China. *Clinical Infectious Diseases* 2020;XX(XX):1-5. DOI: 10.1093/cid/ciaa225(1,5,25).

4. Zhang ZJZ, Yu XJ, Fu T, Liu Y, Jiang Y, Yang BX, et al. Novel coronavirus Infection in newborn babies under 28 days in China. *European Respiratory Journal* 2020;55(6):2000697. DOI: 10.1183/13993003.00697-2020.

5. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020;145(6): e20200702. DOI: https://doi.org/10.1542/peds.2020-0702.

6. Aghdam MK, Jafari N, Eftekhari K. Novel coronavirus in a 15-day-old neonate with clinical signs of sepsis, a case report. *Infectious Diseases* 2020;6:427-29.

7. Zeng M. 2019 novel coronavirus disease in children: an insight and the next steps forward. *Pediatr Med* 2020;3:1.

8. Piersigilli F, Carkeek K, Hocq C, Grambezen B, Hubinont C, Chatzis O, et al. OCOVID-19 in a 26-week preterm neonate. *Lancet Child Adolesce Health* 2020;4:476-78.

9. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr* 2020;174:722-25.

10. Lu Q, Shi Y. Coronavirus disease (COVID 19) and neonate: What neonatologist need to know. *J Med Virol* 2020;92:564-67.

11. COVID-19 pandemic in Bangladesh. Available at https://en.wikipedia.org/wiki/COVID-19_pandemic_in_Bangladesh. Accessed on 8/7/2020.

12. World Health Organization. Report of the WHO-China joint mission on COVID-19, 16-24 February 2020. Geneva (Switzerland): World Health Organization; 2020.

13. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514-23.

14. Liu W, Zhang Q, Chen J, Xiang R, Song H, Shu S, et al. Detection of COVID-19 in children in early January 2020 in Wuhan, China. *N Engl J Med* 2020;382:1370-71.

15. Tu WX, Tang HL, Chen FF. Epidemic update and risk assessment of 2019 novel coronavirus - China, January 28, 2020. *China CDC Weekly* 2020;2:83-86.

16. The Society of Pediatrics, Chinese Medical Association; the Editorial Board, Chinese Journal of Pediatrics. Recommendations for the diagnosis, prevention and control of the 2019 novel coronavirus infection in children (first interim edition). *Zhonghua ErKeZaZhi* 2020;58:E004.

17. Turner AJ, Hiscox JA, Hooper NM. ACE2: from vasopeptidase to SARS virus receptor. *Trend Pharmacol Sci* 2004;25:1-4.

18. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.

19. Fornari F. Vertical transmission of COVID-19-a systematic review. *J Pediatr Perinatal Child Health* 2020;4:7-13.

20. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;9:51-60.

21. Karimi-Zarchi M, Neamatzadeh H, Dastgheib SA, AbbasiH, Mirjalili SR, Behforouz A, et al. Vertical transmission of coronavirus disease 19 (COVID-19) from infected pregnant mothers to neonates: A review. *Fetal and Pediatric Pathology* 2020;3:246-50.