Relationship Between COVID-19 Lockdown and Epidemiology of Neonatal Sepsis

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Background: We compared the hospital-based epidemiology of neonatal sepsis after the coronavirus disease 2019 lockdown (LD) versus historical epochs and the LD period versus phases of unlocking.

Methods: This retrospective cohort study was conducted in a level 3 neonatal unit. We compared neonates born in three 24-week periods—Group LD: 22 March 2020 to 5 September 2020—the reference group, Group pre-LD: 29 September 2019 to 14 March 2020, and Group temporally corresponding to LD in 2019 (corres-LD): 24 March 2019 to 7 September 2019. We also studied linear trends from LD phase 1.0 until Unlock 4.0. The key outcome was culture-positive sepsis.

Results: There were 1622, 2744 and 2700 subjects in groups LD, pre-LD and corres-LD, respectively. The incidence of any culture-positive sepsis in pre-LD was higher than LD [odds ratio (95% CI) = 1.61 (1.02–2.56)]. This was mainly due to a statistically significant reduction in Acinetobacter baumannii sepsis, with incidence rate differences of pre-LD versus LD [0.67 (95% CI: 0.37–0.97), P = 0.0001] and corres-LD versus LD [0.40 (95% CI: 0.16–0.64), P = 0.0024]. Groups pre-LD and corres-LD had higher proportion of multi-drug resistant (MDR)/extreme drug resistance/pan drug resistance sepsis than LD [77%, 77% and 44%, respectively (P values of both groups vs. LD = 0.01)]. From LD 1.0 to Unlock 4.0, there were fewer episodes of MDR sepsis (Fmeasure = 0.047). On multivariable analysis, group pre-LD (vs. reference group LD), male sex, birth weight and Apgar score independently predicted culture-positive sepsis.

Conclusions: LD favorably impacted the epidemiology of neonatal sepsis in a hospital setting, with less A. baumannii and MDR sepsis, which persisted during unlocking.

Key Words: SARS-CoV-2, Acinetobacter baumannii, septicemia, multi-drug resistant, newborn

The government of India announced a public curfew on March 22, 2020, severe restrictions on March 23–24 and a stringent lockdown (LD) starting from March 25, 2020. The LD was extended until May 31, followed by unlocking in 1-month phases, during which restrictive measures were eased.

As expected, there were fewer neonates delivered in our center from March 22, 2020 onwards. A few months into the pandemic, we observed a decrease in episodes of culture-positive sepsis. In the absence of formal analysis of data, we were unsure about the validity of this observation and whether it was a consequence of fewer admissions, behavioral changes, administrative measures or a combination thereof. Improvements in the pattern of neonatal sepsis may hold useful lessons for a future non-pandemic situation.

Hence, we studied neonates delivered in 3 time periods, each lasting 6 months—the first starting with the LD in 2020, the second immediately prior to the LD and the third in 2019, temporally identical to the LD. We investigated trends across the phases of locking and unlocking. We hypothesized that the LD was associated with a lower incidence of neonatal sepsis, especially MDR sepsis and that unlocking was associated with a partial reversal of the same.

METHODS

We conducted a retrospective cohort study on neonates delivered in our hospital in three 24-week periods (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/E680):

Group LD: 22 March 2020 to 5 September 2020.
Group pre-LD: prior to the LD: 29 September 2019 to 14 March 2020.
Group temporally corresponding to LD in 2019 (corres-LD): 24 March 2019 to 7 September 2019.

Group LD was the reference group. We included Group corres-LD to control for the possible impact of seasonal variations on demographics and sepsis.

To study the effect of stringency of measures, we included all liveborn infants delivered from 22 March 2020 to 30 September 2020 (see Figure, Supplemental Digital Content 1; http://links.lww.com/INF/E680). A composite objective measure of restrictions is the Government Stringency Index, ranging from 0 to 100, with 100 representing maximum stringency. This part of the study included the following phases:

| Phase of LD/Unlocking | Duration (mm/dd/yyyy) | Government Stringency Index |
|-----------------------|------------------------|-----------------------------|
| LD phases 1 and 2     | March 22, 2020–May 3, 2020 | 96.3–100                    |
| LD phases 3 and 4     | May 4, 2020–May 31, 2020  | 79.17–91.94                 |
| Unlock 1.0            | June 1, 2020–June 30, 2020 | 75.46–76.39                 |
| Unlock 2.0            | July 1, 2020–July 31, 2020 | 74.07–77.78                 |
| Unlock 3.0            | August 1, 2020–August 31, 2020 | 79.63                       |
| Unlock 4.0            | September 1, 2020–September 30, 2020 | 73.81–81.02 |

The time period of LD/unlocking was almost identical to Group LD, except that the former extended to 30 September 2020, whereas the latter ended on 5 September 2020. Detailed descriptions of the containment measures can be accessed elsewhere.

We recorded demographic data, admission to the NICU and/or HDU, duration of hospital stay, the final outcome and sepsis data during hospital stay. Antibiotic resistance was defined as “no MDR,” MDR, extreme drug resistance (XDR) and pan drug resistance (PDR) in Group LD, we performed a COVID-19 GeneXpert test in all laboring mothers and isolated the neonates from their mothers and other neonates until the mother was reported negative. We recorded the number of neonates thus isolated, and the number of neonates and mothers whose test was positive.

We used χ² test, Fisher exact test, Mann-Whitney U or Student t test as appropriate. We calculated incidence rate ratios of episodes of culture-positive, A. baumannii and antibiotic-resistant sepsis. We compared the phases of LD/unlocking by tests for linear trends [χ² for linear trends, Jonckheere-Terpstra or Analysis of Variance for trends, as appropriate] and without linear trends for linear trends, Jonkheere-Terpstra or Analysis of Variance for linear trends [1.77 (95% CI: 1.13–2.85)], but not when corres-LD was compared with group LD. There were significant differences in etiologic organisms between the groups. Of note, there were no episodes of A. baumannii sepsis in Group LD, whereas there were 19 (24%) and 11 (20.7%) episodes in groups pre-LD and corres-LD, respectively. TheIRR of A. baumannii sepsis in group pre-LD or corres-LD versus LD could not be calculated as the denominator was zero. Hence the incidence rate differences were calculated which were statistically significantly different for pre-LD versus LD [0.67 (95% CI: 0.37–0.97)] and corres-LD versus LD [0.40 (95% CI: 0.16–0.64)].

There were significantly more episodes caused by MDR/XDR/PDR organisms in group pre-LD and corres-LD compared with LD. The IRR of episodes caused by organisms that were MDR or worse when comparing group pre-LD versus LD [3.08 (95% CI: 1.64–6.29)] and group corres-LD versus LD [2.14 (95% CI: 1.11–4.48)] were statistically significant. Significantly more culture-positive episodes were treated with colistin in group pre-LD compared with Group LD. Almost all isolates of A. baumannii were MDR/XDR/PDR. The difference in MDR/XDR/PDR organisms between the phases was primarily driven by the difference in A. baumannii. There were no significant differences in the proportion of non-A. baumannii MDR organisms (as a percentage of all sepsis) between LD, pre-LD and corres-LD.

In group LD, 425 neonates were briefly isolated from their mothers and other neonates until their mothers’ COVID-19 report was available. One-hundred-eight severe acute respiratory syndrome coronavirus-2–positive mothers were isolated from other patients in a dedicated COVID building along with their neonates. Eight of these neonates were detected to be severe acute respiratory syndrome coronavirus-2 positive.

When comparing the phases of LD and unlocking, there were significant differences in gestational age and birth weight across phases, but no significant linear trends (Table 3). The proportion of subjects with any episode of culture-positive sepsis declined from LD phase 1.0 to unlock phase 4.0 but was not statistically significant. The difference in the proportion of etiologic organisms did not show a linear trend. There were progressively fewer episodes of MDR sepsis (P_trend = 0.047).

The candidate predictors in the multivariable analysis did not show multi-collinearity, hence all were included in the model. The Group (ie, LD, pre-LD and corres-LD), male sex, birth weight and Apgar score independently predicted the occurrence of any episode of culture-positive sepsis (Table 4). The prediction accuracy was 97.9% (assuming cases with >50% predicted probability were true sepsis) and the C-statistic was 0.85 (95% CI: 0.81–0.89).

To better understand A. baumannii, which had disappeared in group LD, we pooled data of the first episode of Gram-negative sepsis from groups pre-LD and corres-LD and compared A. baumannii versus other Gram-negative sepsis (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/E681). On univariable analysis, A. baumannii sepsis was associated with male sex, lower gestational age, lower birth weight and more concurrent births in the week the subject was born. In a multivariable logistic regression analysis to predict A. baumannii sepsis among all cases with Gram-negative sepsis in the full study population (see Table, Supplemental Digital Content 3, http://links.lww.com/INF/E682), the only independent predictor was the number of concurrent births.
DISCUSSION

The number of live births in group LD was only 60% of the numbers in group pre-LD and corres-LD. The reduced number of live births in group LD was probably due to difficulties encountered by patients in traveling to our hospital during the LD and the fear of contracting COVID-19 at our hospital. Many mothers may have preferred to deliver in a hospital closer to home. Neonates in group LD had better Apgar scores and were discharged with better outcomes. Greater proportions in group LD were admitted in theNICU and HDU, and at a younger postnatal age. There was an overall reduction in culture-proven sepsis following the LD primarily driven by a striking reduction in A. baumannii sepsis and sepsis due to MDR/XDR/PDR organisms. This led to lower usage of colistin.

Continuous variables are presented as mean (SD) or median (1st, 3rd quartile) and are compared using the ANOVA test or Kruskal-Wallis test. Categorical variables are compared using the Chi-Square test or Fisher’s exact test. Two-sample t test was used to compare mean values of two groups with normal distribution of continuous data. The odds ratio (OR) and 95% confidence interval (CI) were computed for the binary variables. The significance level was set at 0.05. The outcomes in group LD were compared to controls using logistic regression, and the statistically significant differences were indicated by OR and 95% CI. The data were analyzed using IBM SPSS (version 24) and Stata (version 16).

**Table 1.** Comparison of Demographic, Admission, and Discharge Data Between 3 Groups

| Variable | LD Period: Group "LD" (N = 1622) | Pre-LD Period: Group "Pre-LD" (N = 2744) | Corresponding Period In 2019: Group "Corres-LD" (N = 2700) | P Value: Group "LD" vs. "Pre-LD" (Reference Group = "LD") | P Value: Group "LD" vs. "corres-LD" (Reference Group = "LD") |
|----------|----------------------------------|----------------------------------------|--------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Gestational age, weeks | Median (1st, 3rd quartile) | 37.0 (34.0, 38.0) | 37.0 (35.0, 38.0) | 37.0 (34.0, 38.0) | 0.1 | 0.022 |
| Mean (SD) | 35.77 (3.2) | 35.90 (3.1) | 35.92 (3.1) | | 0.2 | 0.049 |
| Gestation categories* | Extremely preterm (<28 weeks) | 44 (2.7) | 68 (2.5) | 65 (2.4) | | |
| Very preterm (28–<32 weeks) | 125 (7.7) | 220 (8.0) | 230 (8.5) | | |
| Moderate to late preterm (32–<37 weeks) | 574 (35.4) | 880 (32.1) | 844 (31.3) | | |
| Term (37–41 weeks) | 877 (54.1) | 1572 (57.3) | 1554 (57.6) | | |
| Post-term (>41 weeks) | 2 (0.1) | 4 (0.1) | 7 (0.3) | | |
| Birth weight, grams, median | <1000 g | 59 (3.6) | 129 (4.7) | 123 (4.6) | 0.3 | 0.5 |
| 1000–1499 g | 154 (9.5) | 236 (8.6) | 277 (10.3) | | |
| >1499 g | 809 (49.9) | 1324 (48.3) | 1318 (48.8) | | |
| >4200 g | 1 (0.1) | 4 (0.1) | 3 (0.1) | | |
| Apgar score at 5 min | Male | 883 (54.4) | 1418 (54.0) | 1426 (52.8) | 0.9 | 0.5 |
| Female | 737 (45.4) | 1259 (45.9) | 1268 (47.0) | | |
| Ambiguous | 2 (0.1) | 4 (0.1) | 6 (0.2) | | |
| Appropriate for gestational age* | AGA | 999 (64.5) | 1713 (63.3) | 1670 (61.9) | 0.3 | 0.2 |
| SGA | 513 (33.1) | 944 (34.9) | 971 (36.0) | | |
| LGA | 37 (2.4) | 50 (1.8) | 57 (2.1) | | |
| Age transferred to NICU, d, median | <1000 g | 7 (5.8) | 7 (6.8) | 7 (6.8) | | |
| 1000–1499 g | 74.2 (1.6) | 7.29 (1.6) | 7.23 (1.5) | | |
| Admitted in NICU* | 177 (10.9) | 184 (6.7) | 213 (7.9) | <0.001 | 0.005 |
| Admitted in HDU* | 297 (18.3) | 313 (11.4) | 265 (9.8) | <0.001 | 0.005 |
| Age transferred to NICU, d, median | 2 (1.3) | 3 (2.5) | 3 (2.5) | <0.001 | <0.001 |
| Age transferred to HDU, d, median | 7 (4.13) | 8 (5.14) | 10 (5.17) | 0.003 | <0.001 |
| Duration of hospital stay among <32 weeks gestation, d, median | 20 (4.39) | 10 (2.30) | 12 (3.29) | 0.001 | 0.005 |
| Final outcome | N = 1622 | N = 2744 | N = 2694 | 0.028 | 0.13 |
| Discharged home | 1553 (95.7) | 2583 (94.1) | 2541 (94.3) | | |
| Died | 67 (4.1) | 145 (5.3) | 142 (5.3) | | |
| LAMA or DOR | 1 (0.1) | 2 (0.1) | 4 (0.1) | | |
| Transferred elsewhere | 1 (0.1) | 14 (0.5) | 7 (0.3) | | |

*Figures in brackets are percentages of the total subjects in the respective period.
AGA indicates appropriate for gestational age; DOR, discharged on request; LAMA, left against medical advice; LGA, large for gestational age; OR, odds ratio; SGA, small for gestational age.

Any episode of culture-positive sepsis. It was reassuring to find that there was no increase in the incidence of culture-proven sepsis with progressive unlocking. There were no clinically meaningful differences in the average gestation between the three groups, although there was a statistically significant difference between LD and corres-LD. Our observation is contrary to previous reports, where the incidence of preterm births has declined during the pandemic. More neonates were admitted to the NICU and HDU after the LD possibly because the decrease in absolute number of live births made it easier to find a vacant bed in our NICU or HDU. The lower postnatal age of transfer to these areas supports the latter possibility. Similarly, the relatively longer hospital stay in the LD group can be attributed to the greater availability of vacant beds and hence less pressure on the physicians to discharge patients before schedule from the hospital.
The decrease in hospital deliveries coupled with an increase in the need for NICU/HDU care has not been reported before. However, a 57% decrease in children’s emergency visits has been documented during the peak of the pandemic.18–21 Like us, Goldman et al found that the acuity of sickness and admission rate among children was higher during the peak compared with preceding epochs. In a recent meta-analysis, Chmielewska et al did not observe significant differences in the mode of delivery, births <32 weeks gestation, perinatal asphyxia, low-birth-weight status, NICU admissions or neonatal deaths between the pandemic and pre-pandemic periods.5 The incidence of preterm births <37 weeks gestation was significantly lower only among high-income countries. This meta-analysis did not evaluate neonatal sepsis.

The improvement in the epidemiology of neonatal sepsis in our study may be partly explained by earlier transfer of neonates to the NICU and HDU than what was possible prior to the LD. This

### TABLE 2. Comparison of Sepsis-Related Data Between 3 Groups

| Variable | LD Period: Group “LD” (N = 1622) | Immediate Previous Period: Group “Pre-LD” (N = 2744) | Corresponding Period in 2019: Group “Corres-LD” (N = 2700) | P Value: Group “LD” vs. “Pre-LD” (Reference Group = “LD”) | P Value: Group “LD” vs. “Corres-LD” (Reference Group = “LD”) |
|----------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Number of patients with any episode of culture-positive sepsis | 25 (1.5) | 68 (2.5) | 51 (1.9) | 0.038 [OR, 1.61 (95% CI: 1.02–2.56)] | 0.4 [OR, 1.23 (95% CI: 0.76–2.00)] |
| Number of episodes of culture-positive sepsis* | N = 25 | N = 68 | N = 51 | 0.6 | 0.4 |
| 1 episode | 23 (92) | 59 (88.6) | 49 (96.1) | 0.6 | 0.4 |
| 2 episodes | 2 (8) | 7 (10.3) | 2 (3.9) | 0.6 | 0.4 |
| 3 episodes | 0 (0) | 2 (2.9) | 0 (0) | 0.6 | 0.4 |
| Total number of episodes of culture-positive sepsis | 27 | 79 | 53 | ... | ... |
| Cumulative duration of hospital stay, person-days | 17,210 | 28,387 | 27,432 | 0.004 [IRR, 1.13–2.85] (95% CI: 0.76–2.04] | 0.19 [IRR, 1.23 (95% CI: 0.76–2.04)] |
| Incidence rate of culture-positive sepsis (episodes/1000 patient-days) | 1.57 | 2.78 | 1.93 | ... | ... |
| Number of episodes with specific organisms† | N = 27 | N = 79 | N = 53 | 0.0001 [IR difference, 0.67 (95% CI: 0.16–0.64)] | 0.0024 [IR difference, 0.40 (95% CI: 0.16–0.64)] |
| E. coli | 4 (14.8) | 11 (13.9) | 9 (16.9) | 0.03 | 0.049 |
| K. pneumoniae | 3 (11.1) | 3 (3.8) | 4 (7.5) | 0.03 | 0.049 |
| A. baumannii | 0 (0) | 19 (24.0) | 11 (20.7) | 0.03 | 0.049 |
| S. aureus | 0 (0) | 5 (6.3) | 0 (0) | 0.03 | 0.049 |
| S. epidermidis | 4 (14.8) | 15 (18.9) | 14 (26.4) | 0.03 | 0.049 |
| Other CONS | 7 (25.9) | 16 (20.2) | 8 (15.1) | 0.03 | 0.049 |
| E. coli/fecalis | 1 (3.7) | 1 (1.3) | 0 (0) | 0.03 | 0.049 |
| Miscellaneous | 8 (29.6) | 9 (11.4) | 7 (13.2) | 0.03 | 0.049 |

†Percent expressed of all episodes of sepsis.
‡Percent expressed of total number of episodes of culture-positive sepsis.
*Percent expressed of number of patients with any episode of culture-positive sepsis.

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| Variables | Lockdown Phases 1 and 2 (N = 387) | Lockdown Phase 3 and 4 (N = 252) | Unlock Phase 1 (N = 310) | Unlock Phase 2 (N = 339) | Unlock Phase 3 (N = 296) | Unlock Phase 4 (N = 266) | P Value of Linear Trends* | P Value Without Linear Trends† |
|-----------|---------------------------------|---------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|-----------------------------|
| Number of live births per day, mean (SD) | 8.9 (2.8) | 9.0 (3.2) | 10.3 (3.2) | 10.9 (4.3) | 9.6 (3.3) | 8.8 (3.0) | 0.7 | 0.067 |
| Gestational age, weeks, median (1st, 3rd quartile) | 37 (35, 38) | 37 (34, 38) | 36 (34, 38) | 36 (34, 38) | 37 (34, 38) | 37 (34, 38) | 0.6 | 0.028 |
| Gestation categories‡ | <28 weeks | | | | | | |
| Extremely preterm (<28 weeks) | 8 (2.1) | 10 (4.0) | 10 (3.2) | 8 (2.4) | 7 (2.4) | 7 (2.7) | 0.3 | 0.059 |
| Very preterm (28–<32 weeks) | 17 (4.4) | 22 (8.7) | 28 (9.0) | 31 (9.1) | 23 (7.8) | 26 (10.0) | | |
| Moderate to late preterm (32–41 weeks) | 130 (39.7) | 82 (32.5) | 120 (38.7) | 128 (37.8) | 104 (35.1) | 76 (29.1) | | |
| Post-term (>=41 weeks) | 0 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |
| Birth weight, grams, median (1st, 3rd quartile) | | | | | | | | |
| <1000 g | 10 (2.6) | 12 (4.8) | 13 (4.2) | 14 (4.1) | 9 (3.0) | 12 (4.6) | 0.3 | 0.056 |
| 1000–1499 g | 22 (5.7) | 31 (12.3) | 37 (11.9) | 32 (9.4) | 26 (8.8) | 27 (10.3) | | |
| 1500–2499 g | 153 (39.7) | 79 (31.3) | 133 (42.9) | 114 (33.6) | 106 (35.8) | 99 (37.9) | | |
| 2500–4200 g | 199 (51.7) | 130 (51.6) | 127 (41.0) | 179 (52.8) | 155 (52.4) | 123 (47.1) | | |
| >4200 g | 1 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |
| Birth weight categories‡ | | | | | | | | |
| <1000 g | 10 (2.6) | 12 (4.8) | 13 (4.2) | 14 (4.1) | 9 (3.0) | 12 (4.6) | 0.3 | 0.056 |
| 1000–1499 g | 22 (5.7) | 31 (12.3) | 37 (11.9) | 32 (9.4) | 26 (8.8) | 27 (10.3) | | |
| 1500–2499 g | 153 (39.7) | 79 (31.3) | 133 (42.9) | 114 (33.6) | 106 (35.8) | 99 (37.9) | | |
| 2500–4200 g | 199 (51.7) | 130 (51.6) | 127 (41.0) | 179 (52.8) | 155 (52.4) | 123 (47.1) | | |
| >4200 g | 1 (0.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | | |
| Antimicrobial resistance‡ | | | | | | | | |
| Not MDR or worse | 221 (61.2) | 169 (68.1) | 185 (63.4) | 210 (64.8) | 194 (67.6) | 176 (66.0) | 0.9 | 0.4 |
| MDR | 10 (2.8) | 2 (0.8) | 8 (2.7) | 7 (2.2) | 9 (3.1) | 5 (1.9) | | |
| XDR | 8 (2.1) | 8 (2.1) | 8 (2.1) | 8 (2.1) | 8 (2.1) | 8 (2.1) | 0.4 | 0.02 |
| Admitted in NICU‡ | 36 (9.3) | 26 (10.3) | 37 (11.9) | 39 (11.5) | 34 (11.5) | 13 (11.3) | 0.3 | 0.9 |
| Age transferred to NICU, d, median (1st, 3rd quartile) | | | | | | | | |
| 2 (2, 2.75) | 2 (1, 2.25) | 2 (1, 2.25) | 2 (1, 2.25) | 2 (1, 2.25) | 2 (1, 2.25) | 2 (1, 2.25) | | |
is reflected in fewer episodes of sepsis in the labor room stabilization unit. The changes can also be attributed to behavioral factors. Unfortunately, we do not have data that can quantify these behavioral changes, so our observations are necessarily anecdotal and subjective. Prior to the LD, healthcare workers (HCW) and family members were expected to wash hands at entry to all patient care areas and HCWs were expected to follow hand hygiene measures at the 5 moments of hand hygiene prescribed by the World Health Organization but wearing a face mask was not mandatory. During the LD, compliance to hand hygiene measures increased substantially and there was universal usage of face masks by HCWs and family members. Before the LD, housekeeping measures included regular disinfection of equipment and surfaces, but during the LD these were followed more assiduously, with disinfection of high-touch surfaces such as doorknobs, telephones, etc. performed at least twice in every nursing shift. Instructions for disinfection of mobile phones were provided to all HCWs. Patients were distributed across more areas because those awaiting COVID reports were isolated in a separate 12-bedded isolation ward for mothers and a 6-bedded isolation ward for neonates, and proven cases were managed in a separate building. HCWs working in the isolation wards with suspected or proven cases of COVID-19 donned N-95 masks, caps, goggles, impervious gowns, shoe covers and gloves. There were no changes in the water sources or frequency of surveillance cultures for MDR organisms in the unit. Academic activities and meetings went online, and HCWs practiced social distancing.

*A. baumannii* is an important cause of neonatal sepsis in developing countries. The decrease in *A. baumannii* sepsis disproportionate to other Gram-negative sepsis in group LD is puzzling. The only independent risk factor we could identify was less overcrowding (see Table, Supplemental Digital Content 4, http://links.lww.com/INF/E683), but it is unclear why it should preferentially impact one species. *A. baumannii* is known to behave differently than other Gram-negative bacteria, characterized by more rapid acquisition of MDR, and resistance to desiccation and disinfectants. Compared with *E. coli* or *Klebsiella*, neonates with *A. baumannii* sepsis have lower birth weight. It is possible that infection control measures may have differential effects on *A. baumannii* sepsis and other Gram-negative sepsis. In a systematic review and network meta-analysis of 42 studies on adult ICU patients, compared with standard treatment alone, the addition of environmental cleaning to standard treatment plus antibiotic stewardship program or the addition of source control to standard treatment and environmental cleaning significantly reduced MDR *A. baumannii* sepsis. On the other hand, infection control strategies that mandatorily included antibiotic stewardship programs significantly reduced sepsis due to MDR extended-spectrum beta-lactamase producing Gram-negative infections. In a study from China, the authors reported the effect of relocation of the NICU and introduction of a care bundle designed to evaluate the effect of infection control measures on the decline of MDR sepsis or organism-wise sepsis and we were unable to quantify the infection control measures. Although augmentation in infection control measures was an important feature of the LD epoch, apart from infection control measures there were several other differences between the 3 epochs. Authors of a study on older patients in the United Kingdom reported differential effects of the pandemic on etiologic organisms: *Enterobacteriaceae* reached an all-time low and coagulase-negative *Staphylococcus* an all-time high.

**TABLE 4.** Multivariable Logistic Regression Model to Predict Patients With Any Episode of Culture-Positive Sepsis

| Variable                  | Regression Coefficient | aOR       | 95% CI of aOR     | P value |
|---------------------------|------------------------|-----------|-------------------|---------|
| Constant                  | −2.25                  |           |                   | 0.053   |
| Time period               |                        |           |                   |         |
| LD (reference group)      |                        |           |                   |         |
| Pre-LD                    | 0.81                   | 2.24      | 1.11–4.51         | 0.024   |
| Corres-LD                 | 0.51                   | 1.67      | 0.83–3.35         | 0.15    |
| Births in the week subject was born | −0.007 | 0.99 | 0.98–1.004 | 0.2     |
| Male sex                  | 0.81                   | 2.26      | 1.55–3.29         | <0.001  |
| Gestational age           | −0.05                  | 0.95      | 0.48–1.08         | 0.5     |
| Birth weight              | −0.002                 | 0.998     | 0.997–0.999       | <0.001  |
| Apgar score at 5 min      | 0.53                   | 1.69      | 1.46–1.96         | <0.001  |
| Appropriateness for gestation |                |           |                   | 0.2     |
| AGA (reference group)     | −0.4                   | 0.67      | 0.39–1.16         | 0.15    |
| SGA                       | 0.92                   | 2.5       | 0.64–9.73         | 0.19    |

AGA indicates appropriate for gestational age; aOR, adjusted odds ratio; LGA, large for gestational age; SGA, small for gestational age.
The absolute decline in MDR sepsis was not merely a consequence of overall decline in sepsis, as MDR sepsis as a proportion of all sepsis declined significantly in group LD. Our data shows that the decrease in MDR sepsis was driven by the decline in *A. baumannii*, which is frequently multi-drug resistant.

As early-onset neonatal sepsis is attributed to maternal risk factors that are unlikely to be altered by the pandemic, and late-onset neonatal sepsis is environmentally acquired, we expected to see a greater proportion of early-onset neonatal sepsis in group LD. We observed this difference, but it was not statistically significant.

It was interesting to note that there were no major differences from LD 1.0 to unlock 4.0. This could be due to the small sample sizes in each phase. The easing of restrictions may have had little impact on hospital functioning. It did not alter important predictors of sepsis, for example, gestational age, birth weight and appropriateness for gestational age. A closer look at the government stringency index shows that there was very little objective decline in the stringency of restrictions during the various phases of unlocking. We do not have data to quantify any change in behavior or infection control measures during the phases of unlocking.

In the multivariable analysis, Group pre-LD independently doubled the odds of an episode of culture-positive sepsis compared with group LD. Our analysis suggests that the overall changes after the LD were associated with less culture-positive sepsis rather than overcrowding specifically around the time of birth.

Groups LD and corre-LD covered virtually identical dates exactly a year apart whereas group pre-LD covered a different time of the year. Since the differences in most outcomes were larger between groups LD and pre-LD compared with groups LD and corre-LD, it suggests that seasonal differences may have accentuated the differences between Groups LD and pre-LD. We studied the incidence of sepsis, particularly *A. baumannii* sepsis, for 4 years prior to 2019, to evaluate the possibility that a downward sloping trend may have exaggerated the effect of the LD. However, no such trend could be observed from the year 2015 through 2018 (see Table, Supplemental Digital Content 4, http://links.lww.com/INF/E683).

The strengths of our study were a large sample size and two comparison groups. Being retrospective, it was prone to several biases. There may have been unmeasured differences in patient characteristics, clinical practices, and rigor of data collection between the time periods. We limited our observation to hospital stay and may have missed cases of sepsis after transfer or discharge. Our results may not be generalizable to centers with fewer resource constraints, and less MDR sepsis. Weekly births are a sub-optimal surrogate for overcrowding. We were unable to quantify behavioral changes and infection control measures following the LD and during unlocking. We do not have data about the harm caused to neonates whose mothers were not able to reach our center due to the pandemic. Improvement in sepsis parameters may have occurred at the expense of worse outcomes among those who delivered elsewhere.

**CONCLUSIONS**

From the limited experience accrued from our center, we conclude that the LD may be associated with a decrease in culture-proven neonatal sepsis, primarily due to *A. baumannii* sepsis and antibiotic-resistant sepsis in settings like ours. Efforts must be made to consolidate the gains achieved during the pandemic by reinforcing the desirable administrative and infection control practices.

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in Maryland, United States, and the infection control measures used to pre-
infected by imported rats from the Gambia. A case of imported monkeypox
cases in the United States were in an outbreak involving 47 persons
traveler returning from Nigeria. Before that case, the last confirmed monk-
since 2018. In the United States, a case was recently identified in Texas in a
remain rare, but are increasing: 7 international cases have been diagnosed
from this disease had been reported. Outside Africa, cases of monkeypox
keypox outbreak, as of October 2021, a total of 502 cases and 8 deaths
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Imported Monkeypox From International Traveler, Maryland, United
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Since the eradication of smallpox, monkeypox has assumed the role of the
most prominent orthopoxvirus affecting human communities. Formerly a
rare disease native to Africa, monkeypox is now endemic to countries in
western and central Africa, which have faced a resurgence of monkeypox
outbreaks over the past decade. Nigeria is in the midst of an ongoing mon-
keypox outbreak, as of October 2021, a total of 502 cases and 8 deaths
from this disease had been reported. Outside Africa, cases of monkeypox
remain rare, but are increasing: 7 international cases have been diagnosed
since 2018. In the United States, a case was recently identified in Texas in a
traveler returning from Nigeria. Before that case, the last confirmed mon-
keypox cases in the United States were in an outbreak involving 47 persons
across 6 states; those cases were associated with contact of prairie dogs
on his skin, followed by development of discrete vesicles on his forehead
on his skin, followed by development of discrete vesicles on his forehead
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23. Comment: Monkeypox has an overall case-fatality rate of up to 11%,
and increasing human populations have no immunity to poxvirus; therefore,
future progress in understanding monkeypox is critical. The World Health
Organization Research and Development Blueprint in 2018 classified mon-
keypox as an emergent disease requiring accelerated research, development
and public health action. Although the public health experience addressing
monkeypox in the United States has been limited, this case illustrates the
effectiveness of the basic principles of infection control; rapid identification
and isolation of the index patient; use of personal protective equipment by
HCWs; and thorough contact tracing, including monitoring for secondary
cases throughout the incubation period.
Although vaccination was not required in this case, public health
recommendations to prevent secondary disease transmission of monkey-
pox include the smallpox vaccine. The 2 Food and Drug Administration–
approved vaccines are ACAM2000 and JYNNEOS; this second vaccine is a
nonreplicating, live virus vaccine, licensed specifically for monkeypox
prevention. In addition to smallpox vaccine, vaccinia immune globulin is
available and can be used as prophylaxis for severely immunocompromised
patients when smallpox vaccine should be avoided. The Food and Drug
Administration–approved drugs to treat smallpox are tecovirimat and brin-
cidofovir, which can also be used to treat monkeypox, but there are no mon-
keypox-specific antiviral drugs for treatment or postexposure prophylaxis.
Multiple appearances beyond disease-endemic countries indicate that
monkeypox has become a relevant travel-related disease and physi-
cians should remain vigilant in diagnosing and preventing transmission of
this virus.