

# Incidence of Early-Onset Neonatal Sepsis in Neonates with Meconium-Stained Liquor

Hajra Begum, Saadia Karim, Nadeem Sadiq, Rida Ali, Nadia Iqbal, Inshal Jawed

## Abstract

**Objective:** The incidence of clinically suspected and culture-proven early-onset sepsis in newborns born through meconium-stained liquor compared to clear liquor controls.

**Study Design and Setting:** A comparative cross-sectional study was conducted at the Department of Pediatric Medicine and Neonatal Unit, PNS Shifa Hospital, Karachi, Pakistan, from 15 April 2025 to 15 Oct 2025.

**Methods:** A comparative cross-sectional study was conducted at the PNS Shifa Hospital. The study enrolled consecutive liveborn neonates delivered during the study period, with 42 MSL and 65 clear-liquor controls. Ineffective antibiotic treatment and clinical findings of sepsis were included. Other outcomes included admission rate to the neonatal intensive care unit, occurrence of meconium aspiration syndrome, and mortality. For statistical analyses, Fisher's exact test and Mann-Whitney U test were employed.

**Results:** MSL neonates displayed a higher incidence of suspected sepsis compared to controls (57.1% vs. 13.8%  $p < 0.01$ ). The MSL group had considerably larger rates of culture-proven sepsis (21.4% vs 3.1%,  $p < 0.01$ ). The MSL group had a much higher rate of having meconium in the lungs with both of those results above. There was no difference in mortality rates (4.8% versus 1.5%;  $p = 0.56$ ).

**Conclusion:** Neonates with meconium-stained liquor are at higher risk of early-onset neonatal sepsis. Thus, increased clinical suspicion and intervention are indicated in such cases.

**Keywords:** Meconium-stained liquor; early-onset neonatal sepsis; meconium aspiration syndrome; neonatal outcomes; intra-amniotic infection

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## INTRODUCTION

Meconium-stained amniotic fluid is one of the most common clinical entities in obstetrical practice, taking place in 10-15% of deliveries. It is increasing in post-dated deliveries.<sup>1,2</sup> Although meconium was traditionally thought to indicate fetal maturity or response to lack of oxygen, studies show otherwise. It could reflect complex disease processes that may be caused by infectious or inflammatory processes.<sup>3-5</sup> When meconium gets into the amniotic fluid, it can cause several complications in infants. They can have trouble breathing through aspiration. Also, it can cause systemic inflammatory responses. These situations look very similar to neonatal sepsis.<sup>3,4</sup>

Sepsis of newborns, as defined as an infection of the blood (which can be a type of meningitis), is said to be early onset if it occurs within the first 72 hours of life. The disease continues to be a major cause of morbidity/mortality throughout the world. Approximately 1 to 2 in every 1000 live births suffer from early-onset sepsis in developed countries, while this number is considerably higher in resource-limited settings.<sup>5,6</sup> There are various exposures of the infant to the bacterial flora of the maternal lower genital tract, which is not pathogenic for the mother and her fetus.

Due to vertical transmission, early-onset deficiency occurs.<sup>6,7</sup> Neonatal sepsis is now recognized as having clinical signs that can be subtle and nonspecific. These often mimic those seen in other neonatal conditions such as respiratory distress, metabolic problems, and transient physiological adaptations to life outside the womb.<sup>6-9</sup>

The possibility of an intersection between meconium-stained liquor and early-onset sepsis deserves scrutiny for several reasons. Meconium has pro-inflammatory properties and can cause a systemic inflammatory response that mimics infectious processes, thus making it difficult to differentiate a sterile inflammatory process from a bacterial infection.<sup>4,10</sup> Second, the presence of meconium may indicate an underlying chorioamnionitis or intrauterine infection, which greatly increases the risk of sepsis.<sup>1,4</sup> To begin with, respiratory distress, fever, and other clinical signs of premature newborns born through meconium-stained liquor are commonly considered clinical markers of neonatal sepsis. In fact, this leads to confusion, misdiagnosis, and the use of antibiotics, as reported in references.<sup>9,11,12</sup> The uncertain diagnosis will have major implications for antimicrobial resistance activities. Rose highlighted that inappropriate exposure to antibiotics poses a risk in itself because it selects for resistant organisms and disrupts the developing neonate microbiome.

Despite this intersection's clinical relevance, literature scans exhibit significant inconsistencies and gaps regarding the actual risk and sepsis occurrence in such neonates. Some studies have shown that meconium-stained liquor is associated with bad neonatal outcomes like respiratory problems and NICU admission. Culture-proven bacterial sepsis is less well described.<sup>2,3</sup> In addition, much of the relevant data is obtained from studies that mixed term and preterm neonates, used various definitions of sepsis, or lacked adequate controls. As a result, interpretation of data and findings may be limited.<sup>3</sup> Recent studies have shed some light on the clarification that, although meconium passage at term may be a concerning indicator of intrauterine infection, the same may be less clear for term babies, who comprise the majority of meconium-exposed subjects.<sup>1</sup>

Neonates born in meconium-stained liquor are differentially managed by institutions. Some monitor a baby who appears well normally. Others perform a systemic sepsis evaluation (e.g., blood cultures, start of empirical antibiotics).<sup>5,6</sup> The disparities in practice reflect how vague we really are about who is at risk and how likely it is that bacteria will infect them. Establishing reliable estimates for the number of newborns exposed to meconium who develop sepsis would help facilitate evidence-based assessment and management. This helps solve problems that are caused by too much treatment when the sepsis isn't found or they don't get treatment, and too much treatment that gives them antibiotics they do not need and that separates mother and baby.<sup>7,9</sup>

Pathophysiological perspectives suggest that meconium

exposure may increase sepsis risk via a number of mechanisms. Fetal stress-response to intrauterine infection or inflammation is indicated by the passage of meconium. It serves more as a marker indicating infection or inflammation than as a risk factor for sepsis itself.<sup>1,4</sup> Meconium components can directly or indirectly impair immune function or epithelial integrity. Meconium present in the airways may also alter local immune responses and the capacity to clear bacteria, promoting pneumonia and secondary bacteremia.<sup>13,14</sup> To gauge the effectiveness of this type of rebuttal, we will need to conduct a carefully designed epidemiological study with relevant comparison groups and a comprehensive outcome assessment of our results.

The complex pathophysiology of meconium-stained amniotic fluid and intra-amniotic inflammation, along with the possibility of infection, has been emphasized in several recent comprehensive reviews.<sup>4</sup> Thus, it is currently well understood that meconium aspiration syndrome is an inflammatory injury to the lung rather than merely a mechanical obstruction both locally and systemically.<sup>13-15</sup> The distinction between neonatal inflammation due to meconium aspiration and bacterial disease may be hard to make. The differential diagnosis during the critical early hours of life is essential for effective therapy.<sup>9,11,12</sup>

For this purpose, we carried out a comparative cross-sectional study to objectively measure suspected and culture-positive early-onset sepsis in newborns born through meconium-stained liquor versus contemporaneously born through clear liquor. To address important literature gaps, we utilized recent clinical trial sepsis definitions, a thorough culture collection methodology, and a universal capture of maternal and neonatal covariates. We hypothesized that meconium exposure would cause an increase in suspected and culture-proven sepsis rates, accounting for delivery method and fetal compromise during labor. Additionally, we aimed to improve other neonatal outcomes, such as meconium aspiration syndrome, admission to intensive care, and mortality, to better assess the clinical burden of meconium-stained liquor and enhance our results.

## METHODOLOGY

This was a comparative cross-sectional study. It was conducted at the labor ward and neonatal unit of PNS Shifa Hospital, Karachi, Pakistan. It is a tertiary care hospital that provides comprehensive obstetric and neonatal services. The study spanned six months, from April 15, 2025, to October 15, 2025.

All neonates who met the selection criteria and were born during the study period were recruited using a consecutive nonprobability sampling technique. The study groups comprised:

- (i) Meconium-stained liquor (MSL) neonates.
- (ii) Contemporaneous clear-liquor controls.

Informed consent was obtained from parents or guardians. All newborns, irrespective of any gestational age, were eligible for inclusion. We excluded records with major congenital anomalies, outborn transfers prior to the first assessment, and incomplete primary outcome data. No a priori sample size was set; the final sample reflected all eligible births during the study period (MSL n=42; controls n=65; total N=107).

The initial birth hospitalization infection outcomes were summarized as suspected sepsis (initiation of antibiotics after clinical or laboratory evaluation) and culture-proven sepsis (growth of a pathogenic organism from a sterile (blood or cerebrospinal) site, as per hospital microbiology reporting). Other information of interest was admission to the NICU, meconium aspiration syndrome, and in-hospital death.

A standardized data collection procedure was followed. The intrapartum and maternal variables included mode of delivery and NR-CTG. Meconium exposure was graded as MSL Grade 1, 2, or 3, according to a standard visual assessment. Neonatal variables collected included gestational age (weeks), birthweight (grams), sex, Apgar scores at 1 and 5 minutes, and the need for resuscitation in the delivery room, according to the standard neonatal resuscitation protocol. Data were collected from delivery logs and neonatal records using a standard pro forma created to enhance uniformity.

When needed, blood cultures and additional laboratory tests are performed in a standardized, aseptic manner. Processed by the hospital laboratory in a routine manner. Recorded microbiology reports. Contaminant identification was conducted according to established laboratory standards and

included in each report.

As the study used a time-bound consecutive inclusion design, an a priori sample size was not calculated. The study size is the total number of eligible cases within the study period. Medians and interquartile ranges (IQRs) describe continuous variables; frequencies and percentages describe categorical variables. Fisher's exact test (two-sided) was used to compare group differences for categorical outcomes: suspected sepsis, culture-proven sepsis, NICU admission, mortality, non-reassuring CTG, and cesarean delivery. To test continuous and ordinal variables, such as Apgar scores, gestational age, and birth weight, the Mann-Whitney U test was used. For this study,  $p < 0.05$  was significant. All inferential statistics were done using the IBM SPSS version 25.

The research was approved by the PNS Shifa Hospital Ethical Review Committee (ERC Number: ERC/2025/PAEDS/, dated 10 April 2025). The study was conducted in accordance with the Declaration of Helsinki and institutional guidelines for human research. The parents or guardians of all neonates involved in the study gave consent. Patient confidentiality was maintained by the use of code and restricted access to laboratory reports and clinical data. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) recommendations for observational studies were used to report.

## RESULTS

MSL neonates had higher rates of suspected sepsis, with 24/42 (57.1%) treated with antibiotics versus 9/65 (13.8%) controls (Fisher's exact test,  $p < 0.01$ ), and higher rates of

Table 1. Maternal and Intrapartum Characteristics

Characteristic	MSL (n=42)	Controls (n=65)	p-value
Cesarean delivery, n (%)	23 (54.8)	21 (32.3)	0.02
Non-reassuring CTG/FHR, n (%)	19 (45.2)	12 (18.5)	<0.01
<b>MSL Grading</b>			
Grade 1, n (%)	8 (19.0)	-	-
Grade 2, n (%)	9 (21.4)	-	-
Grade 3, n (%)	25 (59.5)	-	-

MSL = meconium-stained liquor; CTG = cardiotocography; FHR = fetal heart rate Fisher's exact test used for categorical comparisons

Table 2. Primary and Secondary Neonatal Outcomes

Outcome	MSL (n=42)	Controls (n=65)	p-value
<b>Primary Outcomes</b>			
Suspected sepsis, n (%)	24 (57.1)	9 (13.8)	<0.01
Culture-proven sepsis, n (%)	9 (21.4)	2 (3.1)	<0.01
<b>Secondary Outcomes</b>			
NICU admission, n (%)	15 (35.7)	7 (10.8)	<0.01
Meconium aspiration syndrome, n (%)	9 (21.4)	0 (0.0)	<0.01
In-hospital mortality, n (%)	2 (4.8)	1 (1.5)	0.56

**Table 3. Distribution of Meconium Grading and Delivery Characteristics**

Parameter	n (%)
<b>Meconium Grading (MSL group, n=42)</b>	
Grade 1 (thin, light)	8 (19.0)
Grade 2 (moderate)	9 (21.4)
Grade 3 (thick, heavy)	25 (59.5)
<b>Mode of Delivery</b>	
Cesarean - MSL group	23/42 (54.8)
Cesarean - Control group	21/65 (32.3)
Vaginal - MSL group	19/42 (45.2)
Vaginal - Control group	44/65 (67.7)

culture-proven sepsis, with 9/42 (21.4%) in MSL versus 2/65 (3.1%) in controls (Fisher's exact test,  $p<0.01$ ). The MSL group also had higher morbidity, with NICU admission in 15/42 (35.7%) versus 7/65 (10.8%) controls (Fisher's exact test,  $p<0.01$ ). Meconium aspiration syndrome was only present in the MSL group, 9/42 (21.4%) versus 0/65 (0%) controls (Fisher's exact test,  $p<0.01$ ). And in-hospital death occurred in 2/42 (4.8%) in MSL versus 1/65 (1.5%) controls, which was not significant (Fisher's exact test,  $p=0.56$ ). These findings are summarized in Table 2.

Neonatal characteristics (in the period immediately after birth) at baseline were comparable among groups, although some differences were significant. In the MSL category, the median gestational age was 39.4 weeks (interquartile range 37.2-40.6 weeks) in the paper. Whereas, 38.6 weeks (IQR 37.8-40.2 weeks) in controls indicated that MSL is a later incident. Weight distribution was similar in MSL neonates and controls, with median birthweight being 3020 grams (IQR 2580-3460 grams) and 3150 grams (IQR 2870-3420 grams), respectively. Of the 42 MSL neonates, 24 (57.1%) were male. Of the 65 control neonates, 38 (58.5%) were male. Thus, sex distribution was similar.

None of the groups showed a significant difference in Apgar scores. In the MSL group, the median Apgar score at 1 minute was 6 (IQR 5-9), compared with 7 (IQR 6-9) in controls. 5-minute medians were 8 (IQR 7-10) and 9 (IQR 7-10), respectively. This suggests a more depressed initial transition in meconium-exposed neonates, but both groups achieved reassuring scores ultimately. The features and clinical characteristics have been detailed in Table 4.

## DISCUSSION

This comparative cross-sectional study indicated that in comparison to infants born through clear liquor, infants who were born through meconium-stained liquor had a much higher incidence of suspected early onset neonatal sepsis as well as culture-proven early onset neonatal sepsis. According to the findings, more than 20% of newborns exposed to meconium developed a confirmed bacterial infection, compared with only 3% of the controls who were not exposed. The rate of infection was sevenfold. The observed

effects are consistent with accumulating evidence that meconium passage is linked to infectious and inflammatory events rather than merely reflecting fetal maturity.

The link between meconium-stained liquor and early-onset sepsis likely involves complex mechanisms. Comprehensive recent reviews show that meconium-stained amniotic fluid is linked to intra-amniotic inflammation, likely a fetal response to intrauterine infection or inflammatory stimuli. The finding of substantially higher rates of non-reassuring fetal heart rates in the MSL group suggests that fetal compromise, due to infections or other inflammatory processes, may be a probable interpretation. The components of Meconium are naturally pro-inflammatory and can initiate systemic inflammatory cascades that may both reflect the infection process and enhance damage caused by these mechanisms. Our observation of a high rate of suspected sepsis (57.1%) may be due to the difficulty clinicians have in distinguishing sterile inflammation from meconium-induced inflammation. However, the high prevalence of culture-positive cases suggests that bacterial infection is a true and common complication, not just a diagnostic dilemma.

Neonatal sepsis is now understood to be a complex condition that is difficult to risk-stratify and diagnose early. Recent international consensus statements and reviews have emphasized that clinical signs of sepsis in neonates may be subtle and non-specific and will very much overlap with those of other neonatal syndromes like respiratory distress and metabolic derangements. When meconium is involved, the differential diagnosis becomes even more difficult. This is because meconium aspiration syndrome can also result in respiratory distress, temperature instability, and cardiovascular compromise; features that can often overlap with sepsis. The pathogenic organisms that are responsible for early-onset sepsis in meconium-exposed neonates are probably similar to those found in conventional early-onset sepsis, although the design of our study disallowed this analysis. Recent research on bacterial etiology and risk prediction models for neonatal sepsis shows that pathogen-specific risk factors play an integral role in its prevention.

The significantly higher incidence of meconium aspiration syndrome (21.4%) noted in our study group defined with meconium-stained liquor is in line with the definition of meconium aspiration syndrome and is not unexpected. However, it does highlight multiple other clinical implications of meconium exposure. Recent book reviews show that meconium aspiration syndrome is not just a blockage caused by particles sucked in. It is actually a lung injury that causes inflammation. Moreover, it also indirectly affects other systems. Clinical presentation of meconium aspiration syndrome and early-onset sepsis has a lot of overlapping features; both might present with respiratory distress, cardiovascular compromise, and features of sickness. The resemblance in appearance makes it harder to make decisions at the bedside. In turn, this increases the use of antibiotics



that we recorded. Systematic reviews and meta-analyses have been published that study the delivery room management of meconium-exposed infants. Available evidence indicates that routine endotracheal intubation for tracheal suctioning for non-vigorous neonates does not improve outcomes and may be associated with increased risks. As such, the resuscitation guidelines are changing .

The NICU admission rates for meconium-exposed neonates were much higher (35.7% vs 10.8%). This suggests increased clinical severity and monitoring needs in this group. The interpretation of these admissions probably encompasses clinical respiratory support requirements as well as sepsis evaluation and therapy . Using a clinically and health economically centered approach, this three-fold increase in intensive care utilization comes at a huge price. The latest management initiatives for newborns with meconium aspiration and co-existing concerns increasingly recommend tailored respiratory support strategies and relevant advanced ventilation options when conventional support fails . Recent agreement contributing to the oxygen therapy of critically ill newborns with hypoxemic respiratory failure makes the cardiac and pulmonary physical examination a priority and precise repair efforts .

Although the mortality rate was numerically higher in the MSL group than in the MSL group (4.8% vs. 1.5%), this difference did not reach statistical significance. This is likely due to the relatively small sample size as well as the fact that term and near-term neonates generally have a good prognosis even when complications do occur . Modern neonatal intensive care capabilities have significantly decreased mortality from meconium aspiration syndrome and early-onset sepsis, but morbidity is still high . The mortality outcomes we observed are consistent with what would be expected in tertiary neonatal units caring for these conditions. Outcomes that we did not measure but may contribute to burdens not captured in acute hospital mortality include longer-term neurodevelopmental and respiratory outcomes.

The demographic characteristics of our group should be considered when interpreting these results. The MSL group's median gestational age was 39.4 weeks, confirming that meconium passage occurs mainly at or near term, consistent with physiological expectations for intestinal motility and sphincter control maturation . The comparability of birthweights and sex distributions across groups suggests that our comparison is valid and that differences in outcomes are due to meconium exposure rather than fundamental differences in neonates. The slightly lower Apgar scores observed in MSL newborns, although not markedly different, suggest a potentially compromised initial transition, possibly attributed to intrapartum stress or early aspiration events .

The expected association between operative delivery and meconium passage explains the much higher cesarean

delivery rate in the MSL group (54.8% vs 32.3%). The latter probably also reflects the obstetric practice of expediting delivery in cases of fetal compromise. Likewise, the increased occurrence of non-reassuring cardiotocography in cases of MSL suggests that fetal meconium passage often takes place against the background of an abnormal fetal condition, either as the cause or effect of meconium passage. Intrapartum factors could confound the association with sepsis. Alternatively, there could be components of a causal pathway in which intrauterine infection causes fetal compromise and meconium passage.

Our results have several clinical implications for meconium-exposed neonates. The high rates of culture-proven sepsis (21.4%) give a strong rationale for a systematic sepsis work-up (including blood culture) in neonates born through thick meconium-stained liquor, especially when associated with other risk factors . Modern guidelines for the treatment of early-onset sepsis use a risk-based approach that incorporates maternal and neonatal factors . According to our data, meconium-stained liquor should be regarded as an important risk factor for increased alertness. Whether all meconium-exposed neonates should receive empirical antibiotics pending culture results is debatable since routine initiation of antibiotics to the 57.1% who were suspected of sepsis will, of course, come with considerable overtreatment given that “only” 21.4% were infected . Future work is warranted on refining predictions as to which meconium-exposed newborns, if any, actually have true infection.

Several limitations warrant acknowledgment. Detailed subgroup analyses by meconium grade or gestational age were not possible due to the small sample size. Although consecutive non-probability sampling was a practical choice, it may have introduced a selection bias. The design of the observational study limits the ability to establish a cause-and-effect relationship due to unmeasured confounders, such as maternal antibiotics, the length of labor, and indications for delivery. The absence of detailed information about aetiological bacteria on treatment regimens and duration limits the understanding of these infectious complications . Outcome definitions, although clinically meaningful, had their own limitations. Sepsis is suspected when antibiotics are administered. This reflects clinical judgement and institutional practice patterns as much as the true probability of infection, which may overestimate the likelihood of true infection . Culture-proven sepsis is more specific but suffers from imperfect sensitivity of blood cultures, particularly when small-volume samples are taken and when potential antibiotic pretreatment may inhibit bacterial growth . Molecular or biomarker-based diagnostics were not assessed, which might have provided additional diagnostic resolution . In addition, our short-term follow-up window prevented us from assessing longer-term developmental and respiratory conditions that may impose substantial morbidity burdens beyond in-hospital outcomes alone.

Our research has several important strengths despite the limitations. The presence of a contemporaneous control group of clear liquor-born infants provides important context for the interpretation of the MSL results. It also strengthens causal inference beyond that which could be achieved with case series alone. The findings become more reliable with systematic data collection using a standard pro forma and the use of objective microbiological endpoints (culture results) rather than mere clinical impressions. The approach used consecutive patient enrollment to enhance generalizability to similar tertiary care settings. Ultimately, compliance with STROBE reporting standards and the use of robust statistical techniques strengthen the credibility and reproducibility of our analyses.

Future studies should focus on several critical areas. More widespread, multicenter studies will be useful in determining whether meconium grade, the interval from membrane rupture to delivery, and maternal risk factors can assist in further risk stratification. Comprehensive microbiological characterization to define bacterial etiology in meconium-exposed neonates. Research on inflammatory markers, molecular diagnostics, and immune signatures can likely provide more effective tools for differentiating meconium-induced sterile inflammation from true bacterial infections, which is beneficial for antibiotic stewardship. Long-term follow-up studies to assess neurodevelopmental outcomes, chronic respiratory morbidity, and quality of life are important for fully characterizing the burden of meconium-related complications. Finally, intervention studies to evaluate modified delivery room practices, early antibiotic strategies, and specific respiratory management approaches will help define optimal care paradigms for this high-risk population. The large burden of morbidity attributed to meconium-stained liquor (MSL) that we document demonstrates the need for quality antenatal-intrapartum care to prevent fetal compromise and achieve good outcomes when meconium passage does occur. In light of this, it would be especially important to reduce post-term pregnancies and improve intrapartum fetal monitoring, neonatal resuscitation, and intensive care expertise. In settings with limited resources, where meconium aspiration syndrome and early-onset sepsis have high mortality, the collaborative targeting of meconium aspiration syndrome may be beneficial in these settings.

Meconium in the liquor increases the risk of sepsis. In fact, 21.4% of neonates in this population showed culture-proven infection. This is significantly different from the 3.1% rate in controls. Examining the meconium exposure has become essential as there were high sepsis, meconium aspiration syndrome, and NICU admissions (57.1%, 21.4%, and 35.7%, respectively). It is important to distinguish meconium-induced sterile inflammation from early-onset sepsis. The use of antibiotics is more effective when true infection is differentiated from a sterile inflammatory response.

## CONCLUSION

In our study, meconium-stained liquor (MSL) neonates were at a significantly higher risk of developing early-onset neonatal sepsis as compared to clear-liquor controls, which fulfilled the study's main objective. The rate of culture-confirmed sepsis was 7 times higher among meconium-exposed neonates. According to our study, meconium passage was not a sign of maturity, but rather a marker for an underlying infection or inflammation.

Meconium-stained liquor is indicative of a potential sepsis risk. Neonates having thick meconium and other risk factors should be systematically evaluated, including blood culture. Management must strike a balance between the need for antimicrobial coverage and the avoidance of overuse. Future studies should lead to the development of validated tools and biomarkers that can distinguish between sterile inflammation and bacterial infection, allowing antibiotics to be used only when necessary.

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### Authors Contribution:

**Hajra Begum:** Substantial contributions to conception and design or acquisition of data analysis and interpretation of data, Drafting the article or revising it critically for important intellectual content, final approval of the version to be published

**Saadia Karim:** Substantial acquisition of data analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published

**Nadeem Sadiq:** Substantial contributions to conception and design or acquisition of data analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published

**Rida Ali:** Substantial contributions to conception and design or acquisition of data analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published

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**Inshal Jawed:** Substantial contributions to conception and design or acquisition of data analysis and interpretation of data, drafting the article or revising it critically for, final approval of the version to be published

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