

The Apgar Score: A Predictor of Clinical Adverse Outcomes during the Neonatal Period



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Article Info	A B S T R A C T		
Article type:	Introduction: The Apgar score, assessing newborns' health at birth, indicates adverse conditions and the		
Research article	ed for medical attention. This study investigates its predictive value for neonatal outcomes.		
Article History:	Material & Methods: This retrospective cohort study involved 207 neonates in Ilam city hospitals (2015-2016). It compared two groups: 69 neonates with Apgar scores <7 (exposed) and 138 with scores \geq 7 (unexposed) at birth. Neonates were followed through the neonatal period, and outcomes were compared. Statistical analysis used SPSS Statistics software.		
Received: Dec. 09, 2023	Results: At the fifth minute, the exposed group had higher rates of resuscitation need (51% vs. 26.7%,		
Revised: Feb. 13, 2024 Accepted: Apr. 04, 2024 Published Online: Apr. 16, 2024	p=0.01), re-admission (51% vs. 31.1%), and mortality (60% vs. 12.2%, p=0.03) compared to the unexposed group. Relative risks for the exposed group were 3.8 (resuscitation), 6.1 (NICU admission), 2.94 (re-admission), and 2.5 (mortality) at the first minute, and 2.9, 2.7, 2.3, and 19.9, respectively, at the fifth minute.		
Correspondence to:	Conclusion: Apgar scores <7 increase the risk of adverse neonatal outcomes including NICU		
Salman Daliri Health Deputy, Shiraz University of Medical Sciences,	admission, resuscitation, and higher mortality rates. The Apgar score serves as a valuable predictor of adverse neonatal outcomes.		
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Introduction

Apgar score is used to assess the clinical conditions of infants at birth. The Apgar score is determined, based on five clinical indicators of the baby, including body appearance and color, pulse rate, respiration rate, physical activity, and irritability. Given that, if the baby has defects or disorders in the organs and functioning of the body at birth, delaying the use of special medical procedures can lead to death or irreversible complications. As a result, using Apgar scoring method could accurately and quickly identify the clinical conditions of the infant during the first minutes after birth and, if necessary, applying relevant special care interventions (1-3).

The low Apgar score in the first minutes indicates the need for recovery and special care interventions. After providing special medical care, the evaluation of the Apgar score at 5, 10, and 20 minutes is usual and necessary so that, if a low Apgar score persists, the likelihood of injuries from the infant's inconsistency, or severe consequences, such as severe physical and neurological damages, and even death will be alerted. In this case, the need for the promotion of urgent medical services and interventions is inevitable (2).

Different factors such as congenital anomalies, preterm delivery, cesarean delivery, abnormal fetal presentation, multiple pregnancy, and placenta abruption can affect the Apgar score during pregnancy (4-9). These factors may cause disturbances in the growth and activity of different organs such as the respiratory, cardiovascular, and musculoskeletal systems, leading to a decrease in the Apgar score. A low Apgar score indicates the likelihood of multiple complications, including respiratory failure, heart failure, congenital defects, or even newborn death. Various worldwide studies have shown that babies with Apgar scores of less than 7 were more likely to have intrauterine growth retardation, require rehabilitation, admission to the Neonatal Intensive Care Unit (NICU), and ultimately, face death (10).

In some studies, an Apgar score less than 7 resulted in a 4.8-fold increase in neonatal mortality (11). While the low Apgar score at birth is associated with adverse clinical outcomes in the future, the rate of this association and the type of complications, particularly during the neonatal period, remain unclear, necessitating further studies.

Due to the lack of previous studies on the association of some undesirable clinical outcomes, including respiratory failure, the need for recovery operations, hospitalization in the NICU, and neonatal death during the neonatal period with the Apgar score in Iran, this study aimed to probe the relationship between the Apgar score and adverse clinical outcomes up to the end of the neonatal period in Ilam city between 2015 and 2016, using a cohort study. retrospective Determining the correlation between the Apgar score and adverse clinical outcomes enables health workers to address relevant issues and provide appropriate medical services to prevent or reduce the effects of these outcomes.

Materials and methods

This study aimed to investigate the Apgar score as a predictor indicator of adverse clinical outcomes among neonates in Ilam city from the beginning of 2015 to the end of 2016. To achieve this, the maternity wards of Shaheed Mostafa Khomeini and Kowsar hospitals in Ilam city were visited, and the Apgar scores of newborn infants were reviewed. All newborns with an Apgar score less than 7 were selected as the exposed group. Simultaneously, two neonates with an Apgar score of ≥ 7 , born at the same or close date, were considered as the unexposed group, and the necessary information was obtained from their records. In total, 207 neonates were enrolled in the study, with 69 cases classified as the exposed group and 138 newborns as the control (unexposed) group at the first minute. Among the 69 exposed neonates at the first minute, 24 showed improvement at five minutes. Consequently, 45 neonates were considered as the

exposed group and 90 neonates as the control (unexposed) group at five minutes from birth. Data collection was conducted from neonatal records in the obstetrics, gynecology, and Neonatal Intensive Care Unit (NICU) wards where applicable. Subsequently, to investigate potential outcomes during the neonatal period (28 days after birth), all necessary data were collected from relevant health centers. In cases where additional information was needed, the parents of the infants were contacted.

A researcher-designed questionnaire, validated for its accuracy and consistency, was employed to gather the necessary data. This questionnaire encompassed details such as the Apgar score, birth weight, requirement for resuscitation, NICU hospitalization, respiratory distress syndrome, necrotizing enterocolitis, among others. Approximately 10% of the questionnaires, totaling 20, were administered through interviews and subsequently assessed for validity and reliability using Cronbach's alpha. Following the computation, Cronbach's alpha yielded a score of 76%, indicating satisfactory validity and reliability of the questionnaire.

This study received approval from the Ethics Committee of Ilam University of Medical Sciences (Ethics code: ir.medilam.rec.1394.11).

To ensure comparability between the exposed and unexposed groups in terms of certain newborn characteristics, selection procedures were conducted simultaneously. When an infant was born with a low Apgar score, two infants born on the same date and in the same hospital were selected as controls. This approach aimed to match neonates based on birth timing, location, and the availability of specialized medical services at delivery.

The inclusion criteria for this study were: live birth in the hospital, Apgar score recorded at one and five minutes, residency in Ilam, and availability of required information for the infant from birth up to 28 days thereafter. Neonates not meeting these criteria were excluded.

Descriptive statistical methods were utilized to estimate the mean and frequency of data. Relative risk was calculated by comparing the incidence of risk in the exposed group to that in the unexposed group. The collected data were entered into SPSS software version 18 for statistical analysis, with a significance level set at 0.05 or less.

Results

A total of 207 neonates participated in the study. Among them, 49 required restoration operations, 51 were admitted to the Neonatal Intensive Care Unit (NICU), 13 were diagnosed with necrotizing enterocolitis, and 13 neonates experienced respiratory distress syndrome. Unfortunately, neonatal death occurred in 40 infants by the end of the 28th day.

Based on the Apgar score at one minute, 69 neonates were classified in the exposed group, while 138 neonates were in the unexposed group. Comparing the exposed and unexposed groups, the mean birth weight and frequency of preterm birth were 2731 ± 877 vs. 2772 ± 704 grams and 23.6%vs. 22.2%, respectively. Clinical outcomes observed until the end of the neonatal period, based on the one-minute Apgar score, revealed that the mean duration of hospital admissions in the NICU was 12.73 (24.6%) days for the exposed group and 3.75 (6.2%) days for the unexposed group (p<0.01). The need for resuscitation was 42.4% vs. 15.9%, and readmission to other hospital wards was 45.5% vs. 21.7% for the exposed and unexposed groups, respectively (p<0.02). The mortality rate in the exposed group was 28.6%, compared to 14.5% in the unexposed group (p<0.03). Additionally, the mean days of initiating breastfeeding for the exposed and unexposed groups were on the third and first days, respectively (Table 1). Overall, the need for resuscitation operations and neonatal death were higher in the exposed group compared to the unexposed (Figures group 1 and 2).



Figure 1. Proportion of the Need for Resuscitation Operations Based on the Apgar Score in the First Minute of Birth.



Figure 2. Proportion of Outcomes Occurring During the Neonatal Period Based on the Apgar Score in the First Minute at Birth.

The relative risk (RR) of the need for resuscitation and admission to the NICU among the compared groups based on the one-minute Apgar score was 4 and 6.58, respectively (p<0.01). Additionally, the RR for other clinical events during the neonatal period, such as the rate of hospitalization and mortality rate, were 2.94 (p<0.02) and 2.5, respectively (p<0.03). However, there was no significant correlation between the Apgar score of infants and the incidence of jaundice, respiratory distress syndrome, and necrotizing enterocolitis (Table 1).

Variable		Exposed N (%)	Non-exposed N (%)	Relative risk (CI 95%)	P value
Desuscitation	No	40 (57.6)	116 (84.1)	1	-
Resuscitation	Yes	29 (42.4)	22 (15.9)	3.8 (1.22-12.9)	0.01
	No Resuscitation	18 (24.96)	96 (69.5.86)	1	-
Type of resuscitation	Oxygen Therapy	25 (36.8)	15(10.9)	8.8 (2.77-36.6)	< 0.01
	Ventilation	7 (10.5)	15(10.9)	2.5 (0.18-10.5)	0.56
	Chest compressions	11 (15.8)	2 (1.45)	29.3 (4.7-72.8)	< 0.01
	Drug therapy	1 (1.44)	8(5.8)	0.7 (0.19-25.5)	0.59
	Tracheal intubation	7 (10.5)	2 (1.45)	18.7 (2.07-49.8)	< 0.01
Admission to	No	36 (51.5)	120 (87)	1	-
the NICU	Yes	33 (48.5)	18 (13)	6.1 (1.9-14.34)	< 0.01

Table 1. Comparison of Clinical Outcomes During the Neonatal Period Between Exposed and Unexposed Groups Based on the First Minute Apgar Score.

Hospitalized days in the	No NICU	38 (54.5)	112 (81.2)	1	-
	1	2 (3)	4 (2.2)	1.47(0.85-24.05)	0.4
	2 to 7	10 (14.5)	18(13)	1.6 (0.45-7.66)	0.52
NICU	>7	19 (28)	4 (2.2)	14 (1.86-33.4)	< 0.01
TT 1. 11 .1	No	38 (54.5)	108 (78.3)	1	-
Hospitalization	Yes	31 (45.5)	30 (21.7)	2.94 (1.07-8.8)	0.02
Neonatal weight	≥500	49 (70.4)	113 (81.9)	1	-
gain (gr)*	<500	20 (29.6)	24 (18.1)	1.92 (0.54-6.9)	0.24
Ioundiaa	No	34 (48.5)	56 (40.6)	1	-
Jaunuice	Yes	35 (51.5)	82 (59.4)	0.72 (0.27-1.9)	0.35
Necrotizing	No	61 (87.9)	133 (96.4)	1	-
enters colitis	Yes	8 (12.1)	5(3.6)	3.5 (0.45-18.2)	0.19
Respiratory	No	65 (93.9)	124 (93.5)	1	-
distress	Yes	4 (6.1)	9(6.5)	0.84 (0.12-7.3)	0.68
Consequences for neonates	Recovery	39 (57.1)	98 (71)	1	-
	Hospitalization	10 (14.3)	20(14.5)	1.26 (0.6-8.09)	0.3
	death	20 (28.6)	20(14.5)	2.5 (1.04-9.45)	0.03
Day of starting breast feeding **	1	29 (42.4)	125 (90.6)	1	-
	2 to 5	23 (33.3)	9 (6.5)	11(2.29-35.2)	< 0.01
	>5	17 (24.2)	4 (2.9)	18.3(1.8-47.4)	< 0.01
TPN	No	40 (72.7)	133 (96.4)	1	-
	Yes	19 (27.3)	5(3.6)	12.6 (1.3-39.6)	< 0.01

*By the end of 28 days, **Time to start breastfeeding

Among the 69 neonates with an Apgar score less than 7 at one minute, the Apgar score of 24 neonates improved by the fifth minute. Subsequently, 45 neonates with an Apgar score less than 7 at the fifth minute were categorized as the exposed group, while 90 neonates were classified as the unexposed group. Within the exposed group, 23 neonates (51%) required resuscitation at birth, with the most common intervention being oxygen therapy. Among these, 23 (51%) were transferred to the NICU for further treatment, and 11 of them were hospitalized for more than 7 days. Additionally, 23 (51%) of these infants were readmitted to the hospital one or more times until the end of the 28th day. Unfortunately, 27 (60%) infants from this group succumbed before the end of the neonatal period (Table 2).

The relative risk of the need for resuscitation and admission to the NICU among the compared groups based on the five-minute Apgar score was 2.9 and 2.7, respectively (p<0.01). Additionally, the incidence rate of death in the exposed group was significantly higher than in the unexposed group (p<0.03). Neonates in the exposed group exhibited less favorable conditions in terms of weight gain (RR=0.4) compared to the unexposed group, although this difference was not statistically significant (p=0.3). Further details of the comparisons based on the five-minute Apgar score provided in Table 2. are

Table 2. Comparison of Clinical Outcomes During the Neonatal Period Between Exposed and Unexposed Groups Based on the Fifth Minute Apgar Score.

Variable		Exposed 45N (%)	Non-exposed 90N (%)	Relative risk (CI 95%)	P value
Resuscitation	No	22 (49)	66 (73.3)	1	-

	Yes	23 (51)	24 (26.7)	2.9 (0.62-12.6)	0.16
	No Resuscitation	12 (26.7)	30 (33.3)	1	-
	Oxygen Therapy	13(28.9)	22 (24.4)	1.5 (0.46-19.59)	0.25
	Ventilation	5(11.1)	20(22.2)	0.6 (0.3-21.9)	0.70
Type of resuscitation	Chest	5 (11.1)	10 (11.1)	1.2 (0.44-27.7)	0.28
resubertation	Drug therapy	5 (11.1)	4 (4.4)	3.12 (0.69-28.5)	0.20
	Tracheal intubation	5 (11.1)	4 (4.4)	3.12 (0.69-28.5)	0.20
Admission to the	No	22 (49)	65 (71.9)	1	-
NICU	Yes	23 (51)	25 (28.1)	2.7 (0.57-11.5)	0.19
Hospitalized	No NICU	19 (40.9)	65 (72.2)	1	-
days in the	1	4 (11.1)	3 (2.2)	4.56 (0.7-29)	0.80
	2 to 7	11 (24)	11 (12.3)	3.42 (0.56-20.6)	0.26
NICO	>7	11 (24)	11 (12.3)	3.42 (0.56-20.6)	0.25
Hospitalization	No	22 (49)	62 (68.9)	1	-
Hospitalization	Yes	23 (51)	28(31.1)	2.31 (0.48-9.65)	0.26
Neonatal weight	≥500	18 (40)	20 (22.2)	1	-
gain (gr)*	<500	27 (60)	70(77.8)	0.4 (0.12-10.9)	0.33
Isundice	No	17 (37.5)	41 (46.4)	1	-
Jaunaice	Yes	28 (62.5)	49 (54.4)	1.4 (0.3-6.4)	0.50
Necrotizing	No	34 (75)	85 (94.4)	1	-
enters colitis	Yes	11 (25)	5 (5.6)	5.5(0.83-23.37)	0.11
Respiratory	No	34 (75)	87 (96.5)	1	-
distress	Yes	11 (25)	3 (3.5)	9.4 (1.08-37.4)	0.04
Consequences	Recovery	9 (20)	73 (81.1)	1	-
for neonates	Hospitalization	9 (20)	6 (6.7)	12.2(2.52-49.5)	0.04
	death	27 (60)	11 (12.2)	19.9 (1.3-79.25)	0.03
Day of starting breast feeding **	1	4 (8.3)	66 (73.3)	1	-
	2 to 5	28 (62.5)	14 (15.6)	33(5.74-58.8)	< 0.01
	>5	13 (29.2)	10 (11.1)	21.5 (6.2-64.4)	< 0.01
TPN	No	22 (49)	80 (88.9)	1	-
	Yes	23 (51)	10 (11.1)	8.4 (1.64-32.28)	0.02

*By the end of 28 days, **Time to start breastfeeding

There was a notable disparity in the relative risk associated with Apgar scores less than 7 at 1 and 5 minutes for various clinical outcomes, including resuscitation operations such as oxygen therapy, chest compression, and tracheal tube insertion, as well as admission to the NICU and prolonged stays exceeding seven days in this unit, total parenteral nutrition (TPN), time taken to initiate breastfeeding, and neonatal death (p<0.01). These differences are detailed in Table 3.

Table 3. Comparison of Relative Risk for Selected Clinical Outcomes Between Apgar Scores at 1 and 5 Minutes During the Neonatal Period (28 Days).

Variable	Relative Risk (CI 95%) in minute 1	Relative Risk (CI 95%) in minute 5	P value
Resuscitation	3.8 (1.22-12.9)	2.9 (0.62-12.6)	0.03
Oxygen therapy*	8.8 (2.77-36.6)	1.5 (0.46-19.59)	< 0.01

Ventilation	2.5 (0.18-10.5)	0.6 (0.3-21.9)	0.9
Chest compression*	29.3 (4.7-72.8)	1.2 (0.44-27.7)	<0.01
Drug therapy	0.7 (0.19-25.5)	3.12 (0.69-28.5)	0.25
Tracheal intubation	18.7 (2.07-49.8)	3.12 (0.69-28.5)	0.01
Admitted to the NICU	6.1 (1.9-14.34)	2.7 (0.57-11.5)	0.01
1 days in the NICU	1.47 (0.85-24.05)	4.56 (0.7-29)	0.32
2 to 7 days in the NICU	1.6 (0.45-7.66)	3.42 (0.56-20.6)	0.92
> 7 days in the NICU *	14 (1.86-33.4)	3.42 (0.56-20.6)	< 0.01
Hospitalization	2.94 (1.07-8.8)	2.31 (0.48-9.65)	0.02
Neonatal weight gain	1.92 (0.54-6.9)	0.4 (0.12-10.9)	0.96
Jaundice	0.72 (0.27-1.9)	1.4 (0.3-6.4)	0.94
Necrotizing enter colitis	3.5 (0.45-18.2)	5.5 (0.83-23.37)	0.98
Respiratory distress *	0.84 (0.12-7.3)	9.4 (1.08-37.4)	< 0.01
Breastfeeding on day 2 to 5	11 (2.29-35.2)	33 (5.74-58.8)	1
Breastfeeding on >5 days	18.3(1.8-47.4)	21.5 (6.2-64.4)	1
TPN	12.6 (1.3-39.6)	8.4 (1.64-32.28)	1
Death *	2.5 (1.04-9.45)	19.9 (1.3-79.25)	< 0.01

*Significant difference

Discussion

This retrospective cohort study aimed to assess the relationship between neonatal Apgar score and adverse clinical outcomes at the end of the neonatal period in Ilam city. According to the findings of this study, newborns with an Apgar score less than 7 showed a significantly higher need for resuscitation and hospitalization in the NICU compared to those with an Apgar score greater than 7. Among various types of resuscitation operations, oxygen therapy had the highest incidence, while drug therapy had the lowest ratio. In a study by Abbot et al., 100% of neonates with an Apgar score less than 7 received oxygen therapy at birth, 97% underwent ventilator ventilation, 96% were intubated, 63% had chest compressions, and 57% received medical interventions (12). Kilander found that 19% of neonates required resuscitation, with 80% receiving ventilation and the remaining 20% being intubated (13). In a study by Chen et al. (2020) conducted on 11 million babies, an Apgar score > 7 was

associated with adverse clinical outcomes in infants, including the need for a ventilator, seizures, and neonatal death. Furthermore, a lower Apgar score was associated with an increased risk of adverse clinical outcomes (14). Cnattingius et al. (2020) demonstrated that an Apgar score of less than 7 significantly increases the infant mortality rate (15). Generally, studies conducted worldwide have consistently shown that the Apgar score serves as a predictive factor for adverse clinical outcomes during the neonatal period, corroborating the findings of the present study. These consequences are observed across different races and geographic locations and impact all infants. Consequently, there is a critical need for neonatologists and obstetricians to prioritize this score at birth and ensure the provision of necessary measures and equipment to care for high-risk babies and mitigate resulting mortality rates.

Nonetheless, the Apgar score is typically determined based on five clinical indicators. Consequently, any

dysfunction in these bodily organs can lead to a decrease in the Apgar score. Infants with an Apgar score less than 7 often require resuscitation operations due to impaired respiratory and cardiac function. Depending on the severity of the condition, more advanced interventions may be necessary. Following successful resuscitation, infants are often transferred to the Neonatal Intensive Care Unit (NICU) for intensive care and further treatment. This process can result in tangible and intangible costs for both health systems and families and may even lead to the unfortunate outcome of newborn mortality.

Reviewing the events occurring during the neonatal period (28 days) revealed that the rate of neonatal death in neonates with an Apgar score less than 7 was significantly higher than in other neonates. However, there was no difference between the incidence of respiratory distress syndrome and birth weight gain between the two groups. In a study by Jeganathan et al., the incidence of fetal distress in neonates with an Apgar score less than 7 was higher than in those with an Apgar score greater than 7 (16). Another study found that an Apgar score less than 7 at the 5th minute was associated with higher of neurological abnormalities, visual rates impairment, and mortality during the neonatal period (17). Manríquez et al., compared the mean Apgar score between neonates who died and those who survived until the end of the neonatal period at one minute, with results of 3.7 vs. 8.7, respectively. For the fifth minute, the results were 5.2 vs. 9.4 in respective showing each group, significant differences (10).

A study conducted in Brazil demonstrated that an Apgar score less than 7 at 1 and 5 minutes increased neonatal mortality by 4.8 and 6.26 times, respectively (11). Additionally, in a study by Abbot et al., infants with an Apgar score less than 7 exhibited more birth defects, including respiratory failure, heart failure, and neonatal death (10-12). Forsblad et al. showed that low Apgar scores at 1, 5,

and 10 minutes were directly correlated with infant survival, indicating that lower Apgar scores were associated with lower survival rates (18). Razaz et al. (2019) investigated the effect of Apgar score changes between 7 and 9 at 5 and 10 minutes on clinical outcomes in neonates. Their findings revealed that any decrease in the Apgar score resulted in increased neonatal mortality, infection, hypoglycemia, and respiratory distress (19). Similarly, in another study by Thavarajah et al. (2017), an Apgar score of less than 7 was associated with increased respiratory distress, NICU admission, neonatal death, infection, nutritional disorders, low birth weight, and hypoglycemia (20), aligning with the findings of the current study.

The Apgar score of a newborn at birth serves as a predictor for the infant's clinical status, with lower scores on each index potentially indicating premature or latent adverse clinical outcomes. In the current study, early clinical adverse outcomes associated with the Apgar score at 1 and 5 minutes, including the need for resuscitation, NICU hospitalization, breastfeeding problems, mortality, and late effects such as re-admission to other hospital wards and neonatal death. were significantly identified. findings These are consistent with those of other studies, highlighting that low Apgar scores at 1 and 5 minutes could increase the likelihood of these clinical outcomes in neonates.

Study strengths included:

- 1. Conducting a cohort study, allowing for the observation of outcomes over time.
- 2. Follow-up of newborns up to 28 days, providing comprehensive data on neonatal outcomes.
- 3. Absence of pregnancy-related disorders in mothers, reducing potential confounding factors.
- 4. Identification of the association between low Apgar score at birth and adverse outcomes during

the neonatal period, providing valuable insights into clinical practice.

5. Relatively high sample size evaluated in the study, enhancing the statistical power and generalizability of the findings.

Study limitations included:

- 1. Incomplete information in some cases of infants and families, potentially leading to data inaccuracies or bias.
- 2. Inability to assimilate and control all confounding variables, which may affect the interpretation of results.
- 3. Non-compliance of some families to participate in the study, possibly introducing selection bias.
- 4. Migration of some families to other provinces, leading to loss to follow-up and potentially impacting the study's findings and conclusions.

Conclusion

Based on the findings of the present study, an Apgar score of less than 7 significantly increased the risk of adverse clinical outcomes, including the need for the requirement admission NICU. for to resuscitation, breastfeeding delays, and neonatal death. The lower Apgar score appears to be a crucial and potentially significant predictor of clinical outcomes during and after the neonatal period. Therefore, it is recommended that further studies be conducted with larger sample sizes in this field to better determine the role of the Apgar score in predicting these outcomes. This will contribute to a deeper understanding of the clinical implications and aid in the development of targeted interventions to improve neonatal care and outcomes.

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Conflict of interest

The authors declare no conflict of interest regarding this study.

Authors' contributions

AK: Data analysis and interpretation, approval of the final version to be published. **KA**: Data collection, writing the manuscript, approval of the final version to be published. **R N and AM**: Writing the manuscript, critical interpretation of content, approval of the final version to be published. **MMH**: Writing the manuscript, critical interpretation of content; approval of the final version to be published. **DS**: Data collection, writing the manuscript, approval of the final version to be published.

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