Determinants of Low APGAR score in Newborns Delivered at Lemlem Karl General Hospital, Northern Ethiopia, 2018: A Case Control Study

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Abstract

BACKGROUND: The Apgar score is a method to quickly summarize the health of newborn children. It establishes a simple and clear classification of newborns, which could be used to predict survival and to compare methods of resuscitation and perinatal experience across hospitals and obstetric practices. Low Apgar score is associated with various immediate and long-term adverse health outcomes of newborns. Hence; in order to decrease the risk/complications, identifying the determinant factors of low Apgar is crucial to act on the modifiable risk factors. This study is aimed to investigate the determinant factors of a low Apgar score in newborn children.

METHOD: The study was conducted in Lemelem Karl general hospital; northern Ethiopia. An institutional-based unmatched, case-control study was implemented. Data were retrieved from medical charts of 662 newborns' mothers who gave birth in the hospital from Sep 2014 to Sep 2017. Among these, 221 of them were cases (charts of mothers whose newborns' fifth minute Apgar score was <7) and 441 of them were controls (charts of mothers whose newborns' Apgar score was 7 and above). Data was collected using a pretested and structured checklist using systematic sampling and data was entered & analyzed using SPSS version 20. Binary and multivariable logistic regression was done to determine the association and statistical significance was declared at P-value of ≤0.05.

RESULTS: This study revealed that low Apgar score was significantly associated with antepartum hemorrhage *[Adjusted odss ratio (AOR) 3.509; 95% confidence interval (CI) 1.526-8.067), P= 0.003],* pregnancy-induced hypertensive disorders *[AOR 2.69; 95% CI (1.351-5.357), P= 0.005]*, prolonged second stage of labor *[AOR 2.63; 95% CI (1.399-4.944), P= 0.003]*, Cesarean delivery *[AOR 2.005; 95%CI (1.223-3.287), P= 0.006],*meconium-stained liquor *[AOR 6.955; 95% CI (3.721-13.001), P<0.001]*, and low birth weight *[AOR 4.38; 95% CI (2.216-8.657), P<0.001]*.

CONCLUSION: Result from this study showed a remarkable linkage of low Apgar score with antepartum hemorrhage, pregnancy-induced hypertensive disorders, meconium-stained liquor, and low birth weight. Therefore, meticulous antenatal care and labour management service are recommended to prevent low Apgar score and the concomitant neonatal death.

Background

The first minutes after birth are crucial for newborn's adaptation to extra-uterine life [1]. The Apgar score comprises five components Color, Heart Rate, Reflexes, Muscle Tone, and Respiration; each assigned a score of 0, 1, or 2. The score is reported at 1st and 5th minutes after birth for all infants, and at 5-minute intervals thereafter until 20 minutes for infants with a score of less than 7 [2]. Apgar score can be classified as reassuring, moderately abnormal and low if the score is 7–10, 4–6, and 0–3 respectively in the term and late-term infants [3].

Low 1st minute Apgar score has not been found to correlate with future outcomes, such as negative neurological outcomes, and is poor sensitivity markers for asphyxia. However, low 5th minute Apgar

score is associated with increased mortality in premature newborns [4–8], and also associated with various types of future developmental and cognitive problems [9].

Since it is the only form of evaluation in developing countries, where laboratory tests may not be available, the low cost of the Apgar score is useful in identifying children who need additional care, even in the absence of laboratory data [10].

Globally, 5.9 and 2.7 million under-five children and neonates died in 2015 respectively [11]. In Sub-Saharan Africa, the under-five and neonatal mortality rates were 83 & 29, deaths per 1,000 live births. The seven countries with an under-five mortality rate above 100 are all located in sub-Saharan Africa [11].

In Ethiopia 1 in every 35 children dies within the first month, 1 in every 21 children dies before celebrating the first birthday, and 1 of every 15 children dies before reaching the fifth birthday [12].

Concerning the magnitude of low Apgar score (LAS), studies conducted in Portugal, Brazil, Denmark, Iran, Indonesia, and Sweden showed prevalence's of 3.8%, 0.4%, 0.7%, 3.3%, 5.4%, and 0.7% respectively [13–18]. A previous study conducted in Ghana showed that the prevalence of LAS was 1.9% [19]. According to the study conducted in Gondar University referral hospital, North West Ethiopia in 2013, the proportion of LAS was 13.8% [20].

LAS is a major contributory factor for the high magnitude of neonatal and infant mortalities as it is evidenced by several studies that have been undertaken around the globe [4–8]. The complications of LAS immensely affect the health of newborns. Consequently, it is a major challenge to developing countries like Ethiopia to attain the desired neonatal health indices. This might be attributed to the socio-economic factors, the quality of newborn care and the heath care setting. Moreover, LAS is associated with various types of cognitive and developmental problems, neonatal respiratory distress, orotracheal intubation, need for neonatal intensive care unit (NICU), hypoxic-ischemic-encephalopathy, psychosis, childhood cancers, infantile seizures, pneumothorax, reduced vision, neonatal sepsis and asphyxia [5, 9, 14, 21–26].

Globally, the academic community has extensively explored the determinant factors of LAS. However, few researches have been conducted to identify the determinant factors of LAS in the study area and in Ethiopia. Hence, there is a need to carry out research to pinpoint the determinant factors of LAS. On the other hand, identifying the determinant factors of LAS will be useful in designing guidelines to prevent contributing factors and reduce the costs imposed on the health care system and to provide community health.

Methods

An institutional-based retrospective unmatched case control study was conducted from September 2017 to January 2018 to assess the determinant factors of a low Apgar score in newborns delivered at Lemlem Karl general hospital using a medical chart review.

The hospital is located in Maichew town, 662 km north of Addis Ababa, the capital city of Ethiopia and 120 km south of Mekelle, the capital city of Tigray regional state. The hospital has 132 beds and it is estimated that around 1000 women give birth annually in the hospital.

The sample size was calculated using Open Epi Data statistical software. A 2:1 ratio of controls to cases, 95% confidence level and power of 80% was assumed. Taking proportion of grand multiparity among exposed which is 12.09 and 5.4% among non - exposed [27], it yielded a total sample size of 662 (221 charts of mothers whose newborns' 5th minute Apgar score is < 7 (cases) and 441 charts of mothers whose newborns' 5th minute Apgar score is ≥ 7 (controls)).

Charts of mothers who gave birth in Lemlem Karl General Hospital from September 11, 2014, to September 10, 2017, which were selected using systematic sampling were reviewed in this study. All neonates born after 34 completed weeks of gestation in the hospital were included in the study. Newborns whose fifth minute Apgar score < 7 were regarded as cases and newborns whose fifth minute Apgar score ≥ 7 were taken as a control group. Newborns with gross congenital anomalies incompatible with life, neonates born via elective cesarean section (CS), deliveries of unknown gestational age (unknown last normal menstrual period and no ultrasound estimation), twin pregnancy, neonates born to mothers with pre-existing medical disease and newborns who had not been given an Apgar score at fifth minutes of birth and incomplete records (if at least 3 variables were missed) were excluded from the study.

Data were retrieved from the sampled mothers' chart using a structured checklist which was developed after reviewing variables discussed in various literatures to enable the researchers to collect data on socio-demographic status, obstetric factors, and fetal factors.

Prior to the data collection, the checklist was reviewed by senior researchers for its validity. Four graduated midwives with previous experience in data collection were employed as data collectors and two MSc in Clinical Midwifery students were recruited as supervisors. Three days of training on data collection was provided. The collected data were checked by supervisors every day for its completeness and the principal investigator monitored the overall tasks. The checklist was pretested in 10% of the calculated sample size in the same hospital on charts of mothers who visited this hospital prior to the study period. After this pretest was undertaken, two explanatory variables (educational status and annual income) were omitted from the checklist.

The data were checked for completeness, then coded, entered, and analyzed using Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics were used to compute frequency, percentile, mean and median of different variables. A Binary regression model was employed to test the association between the dependent and independent variables.Low Apgar score was the dependent variable. Socio-demographic and fetal factors such as sex, gestational age, fetal presentation, and birth weight are independent variables. Moreover, obstetric factors such as parity, gestation, the onset of labor, duration of labor, mode of delivery, augmentation of labor, pregnancy-induced hypertensive disorders, antepartum hemorrhage, meconium-stained liquor, premature rupture of membrane, duration of the premature rupture

of the membrane are independent variables. All variables with P-value ≤ 0.25 in the binary regression were included in the multivariable analysis. The magnitude of the association was measured using odds ratio at 95% confidence interval and statistical significance was declared at P-value of ≤ 0.05.

Results

Socio-demographic characteristics of the study participants

A total of 662 charts of newborns' mothers (221 cases and 441 controls) were reviewed in this study. The mean (± SD) age of mothers was 28(± 6) and 27 (± 5) years among cases and controls respectively. Socio-demographic characteristics of the study participants are listed in Table 1.

Table 1
Socio-demographic characteristic of mothers, Lemlem Karl general hospital, northern Ethiopia; 2018. (N = 662)

Variables	Categories	Fifth Minute ApgarScore		Total
		Cases N (%)	Controls N (%)	N (%)
Age of mothers	<=19	10(4.5)	25(5.7)	35(5.3)
	20–34	188(85.1)	385(87.3)	573(86.6)
	>=35	23(10.4)	31(7.0)	54(8.2)
Residence	Urban	120(54.3)	243(55.1)	363(54.8)
	Rural	101(45.7)	198(44.9)	299(45.2)

Obstetric characteristics of mothers among cases and controls

This study revealed that proportion/percentage/magnitude of prolonged second stage of labor PSSL among mothers of the cases was 15.8% which is higher than among mothers of the controls, 6.1%. Additionally, 7.2% of mothers among cases and 3.2% of mothers among controls were diagnosed with antepartum hemorrhage (APH) in the current pregnancy. More than one-fifth (21.7%) mothers of the cases and (5.7%) mothers of the controls were diagnosed with the pregnancy-induced hypertensive disorder (PIHD). The obstetric characteristic of mothers among cases and controls is shown in Table 2.

Table 2
Obstetric characteristics of mothers among cases and controls, Lemlem Karl general hospital, northern Ethiopia, 2018 (N = 662)

Variables	Categories	Fifth Minute Apgar Score		Total N (%)
		Cases N (%)	Controls N (%)	
Parity	Primipara	102(46.2)	188(42.6)	290(43.8)
	Multipara	96(43.4)	220(49.9)	316(47.7)
	Grandmultipara	23(10.4)	33(7.5)	56(8.5)
APH	Yes	16(7.2)	14(3.2)	30(4.5)
	No	205(92.8)	427(96.8)	632(95.5)
Pregnancy induced hypertensive disorder	Yes	48(21.7)	25(5.7)	73(11.0)
	No	173(78.3)	416(94.3)	589(89.0)
Premature Rupture of membrane (PROM)	Yes	28(12.7)	30(6.8)	58(8.8)
	No	193(87.3)	411(93.2)	604(91.2)
Duration of the PPROM	< 12 hours	11(39.3)	12(40.0)	23(39.7)
	>=12 hours	17(60.7)	18(60.0)	35(60.3)
Onset of labor	Spontaneous	184(83.3)	412(93.4)	596(90.0)
	Induced	37(16.7)	29(6.6)	66(10.0)
Prolonged second stage of labor	Yes	35(15.8)	27(6.1)	62(9.4)
	No	186(84.2)	414(93.9)	600(90.6)
Meconium stained liquor	Yes	50(22.6)	18(4.1)	68(10.3)
	No	171(77.4)	423(95.9)	594(89.7)
Augmentation of labor	Yes	25(11.3)	44(10.0)	69(10.4)
	No	196(88.7)	397(90.0)	593(89.6)
Mode of delivery	Spontaneous Vaginal Delivery	99(44.8)	313(71.0)	412(62.2)
	Operative Vaginal Delivery	39(17.6)	47(10.7)	86(13.0)
	Caesarean Delivery	69(31.2)	73(16.6)	142(21.5)
	Vaginal Breech Delivery	14(6.3)	8(1.8)	22(3.3)

Characteristics of Newborns

Of all study subjects, nearly half (48.4%) of cases and more than half of the controls (51.7%) were females. Furthermore, regarding the gestational age (GA) three-fourth (78.3%) of cases and the majority (89.8%) of controls were terms. The characteristics of newborns are shown in Table 3.

Table 3
Characteristics of newborns delivered at Lemlem Karl general hospital, northern Ethiopia, 2018. (N = 662)

Variables	Categories	Fifth Minute Apgar Score		Total
		Cases N (%)	Controls N (%)	N (%)
Sex	Female	107(48.4)	228(51.7)	335(50.6)
	Male	114(51.6)	213(48.3)	327(49.4)
Gestational Age	Late Preterm (34–36 + 6 weeks)	41(18.6)	29(6.6)	70(10.6)
	Term	173(78.3)	396(89.8)	569(86.0)
	Post term	7(3.2)	16(3.6)	23(3.5)
Fetal presentation	Breech	23(10.4)	11(2.5)	34(5.1)
	Vertex	196(88.7)	427(96.8)	623(94.1)
	Non-Vertex*	2(0.9)	3(0.7)	5(0.8)
Birth weight	Low birth weight	52(23.5)	24(5.4)	76(11.5)
	Normal birth weight	166(75.1)	413(93.7)	579(87.5)
	Macrosomia	3(1.4)	4(0.9)	7(1.1)

*= Brow presentation and Shoulder presentation

Determinant factors for low Apgar score

This study encompassed 14 independent variables. Both bivariate and multivariable logistic regression analyses were done to see the association of the independent variables and LAS. Low Apgar score is significantly associated with the age of mothers, parity, antepartum hemorrhage (APH), pregnancy-induced hypertensive disorder (PIHD), premature rupture of membrane (PROM), the onset of labor, the prolonged second stage of labor (PSSL), meconium-stained liquor, mode of delivery, gestational age (GA), fetal presentation, and fetal birth weight in the bivariate analysis. However, in the multivariate logistic regression analysis APH, PIHD, PSSL, MSL, mode of delivery, and fetal birth weight was associated with the low Apgar score.

Accordingly, the odds of having LAS among neonates born to mothers with PSSL were 2.6 times *[AOR 2.63; 95% CI (1.399–4.944), P = 0.003]*, higher compared to their counterparts. Moreover, the likelihood of

encountering LAS was 3.5 times *[AOR 3.509; 95% CI 1.526–8.067), P = 0.003]* higher among neonates born to mothers those who diagnosed with APH.In this study, the higher odds of developing LAS were also observed among neonates born to mothers with PIHD *[AOR 2.69; 95% CI (1.351–5.357), P = 0.005]*, than newborns born to mothers without PIHD. Likewise, the odds of exhibited low AS among neonates with low birth weight was 4.38 times *[AOR 4.38; 95% CI (2.216–8.657), P < 0.001]*,higher compared to those of their counterparts.The logistic regression table indicating the association of all independent variables with the dependent variable is shown in Table 4.

Table 4
Bivariate and multivariate analysis of determinant factors of low Apgar score, Lemlem Karl General Hospital, northern Ethiopia, 2018 (N = 662)

Variables	Cases no(%)	Controls no(%)	Odds ratios (95% CI)		P-Value
			Unadjusted	Adjusted	
Age of mothers(Yrs.)					
20–34	188(85.1)	385(87.3)	1	1	-
<=19	10(4.5)	25(5.7)	0.819(0.385–1.741)	0.711(0.279–1.865)	0.604
≥35	23(10.4)	31(7.0)	1.519(0.862–2.678)	1.646(0.728–3.724)	0.148
Residence					
Urban	120(54.3)	243(55.1)	1	-	-
Rural	101(45.7)	198(44.9)	1.033(0.747–1.429)	-	0.845
Parity					
Multipara	96(43.4)	220(49.9)	1	1	-
Primipara	102(46.2)	188(42.6)	1.243(0.885–1.747)	1.120(0.723–1.734)	0.209
Grandmultipara	23(10.4)	33(7.5)	1.597(0.891–2.864)	1.595(0.723–1.734)	0.116
Antepartum hemorrhage					
Yes	16(7.2)	14(3.2)	2.380(1.140–4.971)	3.509(1.526–8.067)*	0.003
No	205(92.8)	427(96.8)	1	1	-
Pregnancy induced hypertensive disorder					
Yes	48(21.7)	25(5.7)	4.617(2.759–7.726)	2.69(1.351–5.357)*	0.005
No	173(78.3)	416(94.3)	1	1	-

*: Significantly associated

1: Reference group

n (number), % (Percent)

SVD: Spontaneous vaginal delivery

CS: Cesarean section

Variables	Cases no(%)	Controls no(%)	Odds ratios (95% CI)		P-Value
			Unadjusted	Adjusted	
Premature Rupture of membrane (PROM)					
Yes	28(12.7)	30(6.8)	1.988(1.155–3.420)	1.669(0.850–3.278)	0.013
No	193(87.3)	411(93.2)	1	1	-
Duration of PROM					
< 12 hours	11(39.3)	12(40.0)	1	-	-
≥ 12 hours	17(60.7)	18(60.0)	1.030(0.359–2.953)	-	0.956
Onset of labor					
Spontaneous	184(83.3)	412(93.4)	1	1	-
Induced	37(16.7)	29(6.6)	2.857(1.705–4.787)	1.858(0.924–3.738)	< 0.001
Prolonged second stage of labor					
Yes	35(15.8)	27(6.1)	2.885(1.697–4.907)	2.630(1.399–4.944)*	0.003
No	186(84.2)	414(93.9)	1	1	-
Meconium stained liquor					
Yes	50(22.6)	18(4.1)	6.871(3.897–12.117)	6.955(3.721–13.001)*	< 0.001
No	171(77.4)	423(95.9)	1	1	
Augmentation of labor					
Yes	25(11.3)	44(10.0)	1.151(0.684–1.935)	-	-
No	196(88.7)	397(90.0)	1	-	0.596
Mode of delivery					

*: Significantly associated

1: Reference group

n (number), % (Percent)

SVD: Spontaneous vaginal delivery

CS: Cesarean section

Variables	Cases no(%)	Controls no(%)	Odds ratios (95% CI)		P-Value
			Unadjusted	Adjusted	
SVD	99(44.8)	313(71.0)	1	1	-
Operative Vaginal	39(17.6)	47(10.7)	2.623(1.622–4.244)	1.568(0.868–2.835)	0.136
CS	69(31.2)	73(16.6)	2.988(2.005–4.455)	2.005(1.223–3.287)*	0.006
Vaginal Breech	14(6.3)	8(1.8)	5.533(2.255–13.576)	2.679(0.597–12.024	0.198
Sex of neonates					
Female	107(48.4)	228(51.7)	1	-	-
Male	114(51.6)	213(48.3)	1.140(0.825–1.576)	-	0.426
Gestational Age					
Term	173(78.3)	396(89.8)	1	1	-
Late Preterm (34–36 + 6 weeks)	41(18.6)	29(6.6)	3.236(1.947–5.378)	1.354(0.666–2.750)	< 0.001
Post term	7(3.2)	16(3.6)	1.001(0.405–2.478)	0.981(0.333–2.894)	0.998
Fetal presentation					
Vertex	196(88.7)	427(96.8)	1	1	-
Breech	23(10.4)	11(2.5)	4.555(2.177–9.530)	2.080(0.590–7.330)	< 0.001
Non-vertex	2(0.9)	3(0.7)	1.452(0.241–8.762)	2.019(0.313–13.036)	0.684
Fetal birth weight					

*: Significantly associated

1: Reference group

n (number), % (Percent)

SVD: Spontaneous vaginal delivery

CS: Cesarean section

Variables	Cases no(%)	Controls no(%)	Odds ratios (95% CI)		P-Value
			Unadjusted	Adjusted	
Normal birth weight	166(75.1)	413(93.7)	1	1	-
Low birth weight	52(23.5)	24(5.4)	5.391(3.217–9.032)	4.380(2.216–8.657)*	< 0.001
Macrosomia	3(1.4)	4(0.9)	1.866(0.413–8.428)	2.655(0.474–14.876)	0.267
*: Significantly associated					
1: Reference group					
n (number), % (Percent)					
SVD: Spontaneous vaginal delivery					
CS: Cesarean section					

Discussion

This study has indicated that low Apgar score has an important determinant factor. One of the main findings of this study was the association of LAS with APH in which low Apgar score was more than three times more likely to encounter in neonates born to mothers who were diagnosed APH in the index pregnancy *[AOR 3.509; 95% CI (1.526–8.067), P = 0.003]*. This result is correspondent with the studies done in Nigeria and India ([AOR, 3.03; 95% CI (1.12–8.19); P = 0.028])[28, 29]. Nevertheless, a study conducted in Brazil contradicts this study as it claimed that APH has no significant association with LAS [14]. This can be owing to difference in sample sizes, and socio-economic factors.

In addition low Apgar score was found to be significantly associated with PIHD *[AOR 2.69; 95% CI (1.351–5.357), P = 0.005]*, in this study. This finding is in line with the studies done in Sweden and India; which showed a statistically significant association between PIHD and LAS [30, 31]. This could be ascribed to the fact that PIHD may cause problems with placenta. The placenta may bleed or it may begin to separate from the wall of the uterus. Placenta insufficiency may also occur, a state in which the placenta fails to support appropriate fetal development because it cannot deliver the necessary amount of oxygen or nutrients to the fetus. If any of these complications occurs, fetal distress may develop ultimately leads to LAS.

Another finding of this study was the association of LAS with PSSL. This study revealed that neonates born to mothers with PSSL were nearly three times more likely to have LAS than their counterparts *[AOR 2.63; 95% CI (1.399–4.944), P = 0.003]*. This is in line with studies done in Brazil, Sweden, and the USA [14, 18, 32, 33]. This might be due to the fact that in the prolonged second stage of labor, there is a higher chance of cesarean delivery or manipulative vaginal deliveries and a chance of fetal distress, which could further affect the Apgar score.

This study also revealed that newborns born via cesarean delivery were about 2 times more probable to have a LAS than neonates born via spontaneous vaginal delivery. This finding is consistent with the studies done in Brazil, Sweden, and Australia [34–36]. This could be due to the lack of fetal chest compression during cesarean delivery which facilitates lung clearance from secretions and fluids. Similarly, drugs used for anesthesia during CS can also decrease uterine and placental circulation then it causes fetal hypoxemia which further leads to fetal morbidity including LAS [37].

Newborns of mothers with MSL during labor are almost seven times more likely to have LAS than newborns of the reference group *[AOR 6.955; 95% CI (3.721–13.001), P < 0.001]*. This study is agreeable with studies done in Australia *[AOR 3.1; 95% CI (2.0-4.61), P < 0.01]*, [36]. Notwithstanding this, a study from Brazil failed to support this result in which they reported there was no association of meconium-stained liquor with a LAS [14]. This could primarily be due to the quality of obstetrical care services being provided. Moreover, it could be also due to the fact that the Brazilian finding was reported from a relatively small sample size.

Moreover, this study also revealed newborns born with low birth weight were 4 times more likely to have LAS *[AOR 4.38; 95% CI (2.216–8.657), P < 0.001]*. This finding is similar to a study done in North West Ethiopia [20]. This could be explained by the fact that small babies might suffer from difficult birthing and might develop difficulty in cardiopulmonary transition and perinatal asphyxia which predisposes the newborns to various complications including LAS.

Conclusion

This study concluded that low Apgar score is significantly associated with obstetric factors like antepartum hemorrhage, pregnancy-induced hypertensive disorders and prolonged second stage of labor. Cesarean delivery also tremendously increased the odds of a low Apgar score. On top of this, meconium stained liquor and low birth weight were found to be a major determinant factors for a low Apgar score. Therefore, it is better for health care providers to keep their strength on early detection and management of newborns with LAS.

Abbreviations

AOR
Adjusted Odds Ratio
APH
Antepartum Hemorrhage
LAS
low Apgar score
CI
Confidence Interval
COR

Crude odds Ratio
CS
Cesarean Section
MRN
Medical Record Number
MSc
Master's Degree in Science
MSL
Meconium Stained Liquor
NICU
Neonatal Intensive Care Unit
PIHD
Pregnancy Induced Hypertensive Disorders
PROM
Premature Rupture of Membrane
PSSL
Prolonged Second Stage of labor
SPSS
Statistical Package for Social Sciences

Declarations

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Ethics approval and consent

Ethical clearance for the study was obtained from the Institutional Review Board of Mekelle University and a letter of permission was written from the chief executive director of Lemlem Karl General Hospital to Gyn– Obs ward head and HMIS office. Furthermore, confidentiality was not breached as the checklist developed is anonymous and does not identify mothers' personal information.

Author's contributions

MMG: Developed the proposal, analyzed data, and wrote the report and the manuscript. **MWG** and **BGG**: Organized overall process. **TAH, GAG**, **M-AMR, KGT, NBY** and **HKM**: Contributed in proposal writing, data

collection and analysis. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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