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Determinants of neonatal hypoglycemia among neonates admitted at Hiwot Fana Comprehensive Specialized University Hospital, Eastern Ethiopia: A retrospective cross-sectional study

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Abstract

Objective: The study aimed to assess the magnitude and determinants of neonatal hypoglycemia among neonates admitted to the Neonatal Intensive Care Unit at Hiwot Fana Specialized University Hospital, Eastern Ethiopia.

Methods: An institutional-based cross-sectional study was conducted among 698 randomly selected neonates at Hiwot Fana Comprehensive Specialized Hospital from 1 January 2018 to 31 December 2020. By looking at the charts, data were gleaned from the medical records. Data were entered into Epi-Data version 3.1 and analysis was performed using SPSS version 22. Bivariable and multivariable logistic regression analyses were conducted to identify determinant factors of neonatal hypoglycemia. Association was described using an adjusted odds ratio along with a 95% CI. Finally, a p-value <0.05 in the adjusted analysis was considered to declare a statistically significant association.

Results: Out of 698 neonates, 148 (21.2%; 95% CI: 18.3, 24.5) neonates had hypoglycemia. Preterm birth (AOR = 3.06; 95% CI: 1.02, 9.17), hypothermia (AOR = 2.65; 95% CI: 1.22, 5.75), neonatal sepsis (AOR = 2.61; 95% CI: 1.03, 6.59), diabetic mother (AOR = 2.34; 95% CI: 1.03, 5.33), and delay in initiation of breastfeeding for more than 1 h (AOR = 3.89; 95% CI: 1.17, 12.89) were identified as determinant factors of neonatal hypoglycemia.

Conclusion: The magnitude of neonatal hypoglycemia was quite common among neonates. Neonatal hypoglycemia was found to be predicted by preterm birth, hypothermia, neonatal sepsis, maternal diabetes mellitus, and delay in starting nursing. We therefore strongly suggest health-care workers work in the postnatal unit to manage and control these and other determinant factors of hypoglycemia to prevent the occurrence of neonatal hypoglycemia.

Keywords
Neonatal hypoglycemia, newborn, Harar

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Introduction

Neonatal hypoglycemia is a preventable cause of neurological sequelae. It is crucial in developing nations where neonatal mortality accounts for between 50% and 60% of all infant fatalities.[1] It is the most prevalent metabolic issue among newborns in their early years and a significant contributor to neonatal death overall.[2] After delivery, the source of glucose changes to intermittent feeds which were initially supplied by the mother continuously.[3] The lack of maturity

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of gluconeogenesis and the ketogenesis process among newborns also contributes to transient lower blood glucose concentrations.[4]

In healthy newborns, transient asymptomatic hypoglycemia appears to be normal throughout the transitional extrauterine life, but persistent or recurrent severe hypoglycemia can cause serious neonatal morbidity.[3] Prolonged, extremely low glucose concentrations have been associated with brain injury, as many infants with this degree of hypoglycemia experience irreversible brain damage.[5] It has been associated with long-term, adverse neurodevelopmental outcomes[6] including cerebral palsy, intellectual difficulties (learning problems), developmental delays (mental problems), seizures (epilepsy), and neurological dysfunction or disability.[2,7–9]

The presence of several factors and the existence of numerous comorbid illnesses are the primary causes of the prolonged duration of stay for neonates in the Neonatal Intensive Care Unit (NICU) of developing nations.[10,11] Different studies across the world indicated that the magnitude of neonatal hypoglycemia differed among newborns with diverse determinant factors. The overall incidence of neonatal hypoglycemia has been estimated to be 1–5 per 1000 live births with a higher incidence in at-risk populations. It is 52% for newborns with small gestational age, 48% for newborns born to diabetic mothers, and 54% for preterm newborns.[12] Preterm newborns had an approximately 34% incidence of hypoglycemia.[13]

The neonatal-related predictors of neonatal hypoglycemia were preterm birth, low birth weight, small for gestational age, infection, birth asphyxia, hypothermia, and delay in commencement of nursing for more than 2 h postnatal.[2,10] Neonatal hypoglycemia was determined by maternal factors such as pre-eclampsia, eclampsia, and gestational or maternal diabetes mellitus (DM). Shreds of evidence from different sources indicate that comprehending this neonatal hypoglycemia determining factors aids in the identification of hypoglycemic neonates, and may also assist in the early and effective prevention of the sequelae of neonatal hypoglycemia.[10,14]

For program managers, and policymakers to properly plan, administer, and evaluate programs for the reduction of neonatal mortality related to hypoglycemia and other disorders, it is necessary to identify the factors that determine the morbidity and mortality of neonatal hypoglycemia. Additionally, it aids in enhancing newborn care and ensuring that neonates live healthy lives. There are not enough epidemiological studies on the determinant of neonatal hypoglycemia in Eastern Ethiopia, though. Therefore, this study aimed to assess the magnitude and determinants of neonatal hypoglycemia among neonates admitted to the NICU at Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH) in Eastern Ethiopia.

Material and methods

Study period and setting

The study was conducted in NICU at HFCSUH. HFCSUH is a specialized university hospital that provides service to more than 5 million people in the catchment region, the eastern part of Ethiopia. It is currently the sole teaching comprehensive hospital in Eastern Ethiopia. Every year over 1800 newborns are brought into the NICU at HFCSUH.

Ethical considerations

The Helsinki Declaration of Medical Research Ethics was followed during the study's execution.[15] The Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University's College of Health and Medical Sciences granted ethical clearance. Legally appointed representatives (hospital administrators and the head of the medical record office) provided voluntary, written, and signed consent and were approved by the Institutional Review Board of Haramaya University (IHRERC) with a reference number (IHRERC/012/2020). The confidentiality of the data was kept and used for the study purpose only.

Study design and population

An institutional-based retrospective cross-sectional study design was carried out. All newborns who were admitted to and received care at the HFCSUH NICU between 1 January 2018 and 31 December 2020, G.C. were the source population. Using a medical record's serial number as a starting point, computer-generated random numbers were used to choose the study population.

Inclusion and exclusion criteria

Included all newborns with issues admitted to the NICU at HFCSUH. Neonatal patients with incomplete (inadequate) information medical records, those referred to other facilities (institutions), and those discharged against medical advice were all disqualified from the study.

Sample size determination and sampling technique

A single population proportion formula was used by taking the magnitude of neonatal hypoglycemia in the NICU at Saint Paul's Hospital Millennium Medical College, Addis Ababa ($p = 25\%$),[16] the margin of error of 3%, and using 95% confidence level (CI) to compute the sample size. The final sample size became 727 after accounting for the non-retrieval rate of 10%. Six thousand four hundred forty-three newborns were admitted to the NICU at HFCSUH between 1 January

2018 and 31 December 2020, G.C., according to data from the medical record office. The sample frame was created for those study populations using their Medical Registration Number, which was retrieved from their medical records. A simple random sampling procedure (computer-based) was used to choose the study participants from the sampling frame ($N = 6443$).

Measurement and data collection tools

After reviewing relevant literature, a semi-structured data extraction tool[2,10,17,18] was developed to obtain information on sociodemographic characteristics of mothers and neonates, antepartum-related factors, neonatal and intrapartum-related factors, and the treatment given to newborn through chart review. Four BSc nurses gathered the data under the supervision of 1 MSc nurse.

Operational definition

Neonatal hypoglycemia: neonatal hypoglycemia was defined as a random blood sugar concentrations of <40 mg/dl for any postnatal age.[19]

Hypothermia: an axillary temperature of less than 36.5°C and recorded on the medical record.[20]

Preterm birth: infants born alive before 37 full completed weeks of pregnancy.

Post-term birth: an infant who was born after 42 weeks were completed.

Low birth weight: a newborn that weighs less than 2500 g.

Neonatal sepsis: an infection occurs among newborns both early-onset neonatal sepsis and late-onset neonatal sepsis and is recorded on the medical records of the neonates.

Data quality assurance and management

Before real data was collected and the required modifications were made, the checklist was pretested on 36 medical records (5% of the sample total) at the Jegol General Hospital. Daily, supervisors, and the primary investigator evaluated the data for completeness, correctness, and clarity before entering it. The goal of the study, the sampling process, and the techniques for extracting data from medical records were all covered in training sessions for data collectors and supervisors.

Statistical analysis

The data that had been coded were put into Epi-data version 3.1 and analyzed using SPSS version 22. For descriptive analysis, data were compiled as proportions and frequency tables. To get the crude odds ratio (COR) and confidence interval (CI), binary logistic regression was performed. To identify independent predictors that were associated with outcome variables, a multivariable was used to discover variables with a p value of less than 0.25. In the multivariate analysis, variables with a p value under 0.05 were deemed to have a statistically significant association.

The Hosmer-Lemeshow statistic and Omnibus test were used to assess the model's goodness of fit.[21–24] Since the model is significant for the Omnibus test ($p < 0.001$) but not for the Hosmer-Lemeshow statistic ($p = 0.401$), it was deemed to be a good match. The variance inflation factor (VIF) and standard error (the multi-collinearity test) were used to examine the association between independent variables. All variables were observed with a VIF of <3 and a standard error of <2. A 95% CI and an adjusted odds ratio (AOR) were used to determine if there was a significant association between the independent and outcome variables. To declare a link between neonatal hypoglycemia and its determinant variables, a p-value of 0.05 was used.

Table 1. Sociodemographic characteristics of mothers of neonates admitted to NICU at HFCSUH, Eastern Ethiopia, 2021 ($n = 698$).

Variables	Categories	Frequency	Percentage (%)
Maternal age recorded	Yes	612	87.7
	No	86	12.3
Maternal age ($n = 612$)	15–24	236	38.6
	25–34	286	46.7
	35–49	90	14.7
Residence	Urban	333	47.75
	Rural	365	52.3
Neonatal age on admission in hour	0–24 h	482	69.1
	24–72 h	65	9.3
	72–169 h	51	7.3
	Greater than 169 h	100	14.3

Results

Sociodemographic characteristics

During the study period, 727 neonates were selected from the NICU of HFCSUH. Of these, 29 neonates were excluded due to incomplete charts. A total of 698 neonates' outcome status was included in the analysis. The male-to-female sex ratio among admitted neonates was 1.6:1. The majority (91.5%) of the neonates were born from singletons pregnancies, while the remaining newborns were born from multiple pregnancies. Neonatal age had a mean and SD of 1.6 and 1.1 h, respectively. Mothers were between the ages of 15–49 years (Table 1).

Obstetric-related factors

Of the total women who underwent ANC follow-up, 517 (74%) women had at least one visit whereas 138 (19.7%)

Table 2. Obstetric-related factors among mothers of neonates admitted to NICU at HFCSUH, Eastern Ethiopia, 2021 ($n = 698$).

Variables	Categories	Frequency	Percentage (%)
Party	Primiparous (1)	283	40.5
	Multiparous (2–4)	319	45.7
	Grand multiparous (⩾5)	96	13.8
Gestational age	Preterm	224	32.1
	Term	471	67.5
	Postterm	3	0.40
ANC follow-up	Yes	517	74
	No	181	26
Number of visits	1	517	74
	2–3	422	60.4
	4 and above	138	19.7
History of neonatal loss	Yes	55	7.9
	No	643	92.1
Presence of complications during pregnancy	Yes	205	29.4
	No	493	70.6
If yes, type of complications	Antepartum hemorrhage	77	37.6
	Pregnancy-induced hypertension	72	35.1
	Preterm labor	23	11.2
	Premature rupture of membrane	43	21.0
	Other complications	16	7.8
Onset of labor	Spontaneous	623	89.3
	Induced	75	10.7
Duration of labor	Less than 24 h	657	94.1
	Greater than or equal to 24 h	41	5.9
Delay in initiation of breastfeeding (>1 h)	Yes	73	10.5
	No	625	89.5
Complication during labor	Yes	214	30.7
	No	484	69.3
If yes, type of complications	Obstructed labor	22	10.3
	Prolonged labor	47	22.0
	Antepartum hemorrhage	49	22.9
	Maternal DM	85	12.2
	Maternal sepsis	47	21.9
	Eclampsia	46	21.5
Mode of delivery	Spontaneous vaginal delivery	508	72.8
	Cesarean section	161	23.1
	Assisted	29	4.2

women had four and above visits, respectively. Two hundred-five (29.4%) mothers had one or more complications throughout their pregnancies. Of the total neonates included in the study, 95.4% were born in the health facility with the remaining newborns born at home (Table 2).

Reason for admission to NICU

Hypoglycemia accounted for 21.2% of the 698 neonates admitted to the NICU at HFCSUH. Sepsis was the most typical reason (59.2%) for newborn hospitalization in the area. Of the total neonates, 264 (37.8%) of them were low birth weights (Table 3).

Treatment provided and cause of death for neonates

Among neonates who received antibiotics, 346 (71.3%) of them took ampicillin and gentamycin whereas 86 (12.3%) and 150 (21.5%) neonates were treated by CPAP and resuscitation, respectively (Table 4).

Determinants of neonatal hypoglycemia

In crude analysis, preterm birth, low birth weight, asphyxia, hypothermia, neonatal sepsis, delay in initiation of breastfeeding for more than 1 h, maternal DM, maternal eclampsia,

maternal sepsis, and having any type of pregnancy complication were associated with neonatal hypoglycemia. However, only preterm birth, hypothermia, neonatal sepsis, delay in initiation of breastfeeding more than 1 h, and neonates born from diabetic mothers were significantly associated with neonatal hypoglycemia in multivariable logistic regression.

Table 3. Reason for admission among neonates admitted to NICU at HFCSUH, Eastern Ethiopia, 2021 ($n = 698$).

Variables	Categories	Frequency	Percentage (%)
Preterm birth	Yes	220	31.5
	No	478	68.5
Sepsis	Yes	413	59.2
	No	285	40.8
Congenital malformation	Yes	32	4.6
	No	666	95.4
Respiratory distress syndrome	Yes	34	4.9
	No	664	95.1
Asphyxia	Yes	198	28.4
	No	500	71.6
Hypothermia	Yes	251	36.0
	No	447	64.0
Jaundice	Yes	53	7.6
	No	645	92.4
Meconium aspiration syndrome	Yes	73	10.5
	No	625	89.5
Hyaline membrane disease	Yes	28	4.0
	No	670	96.0

Neonatal hypoglycemia was three times (AOR = 3.06; 95% CI: 1.02, 9.17) more likely to occur among preterm birth than term newborns. The chance of developing neonatal hypoglycemia among hypothermic neonates was almost three times (AOR = 2.65; 95% CI: 1.22, 5.75) more likely compared to normothermic neonates.

The probability of developing neonatal hypoglycemia among neonates with sepsis was three times (AOR = 2.61; 95% CI: 1.03, 6.59) more likely as compared to neonates without sepsis. In comparison to neonates who started breastfeeding before 1 h, those who delayed the onset of breastfeeding (after 1 h) had a fourfold (AOR = 3.89; 95% CI: 1.17, 12.89) higher risk of developing neonatal hypoglycemia. Compared to neonates born to non-diabetic mothers, neonates born to diabetic mothers had a twofold (AOR = 2.34; 95% CI: 1.03, 5.33) higher risk of developing hypoglycemia (Table 5).

Discussion

This study was conducted to assess the magnitude and determinant of neonatal hypoglycemia among neonates admitted to the NICU at HFCSUH, Eastern Ethiopia. One out of five neonates admitted to NICU at HFCSUH had hypoglycemia, preterm birth, hypothermia, sepsis, delay in the initiation of breastfeeding for more than 1 h, and neonates born from diabetic mothers were more likely to develop hypoglycemia.

In comparison to studies done in Uganda (2.2%),[18] India (9.4%),[25] Iraq (16.25%),[26] Côte d'Ivoire (15.9%),[27] and Nigeria (11.0%),[28] our study's overall magnitude of neonatal

Table 4. Treatment provided for neonates at NICU of HFCSUH, Eastern Ethiopia, 2021 ($n = 698$).

Variables	Categories	Frequency	Percentage (%)
Antibiotics	Yes	485	69.5
	No	213	30.5
Type of antibiotics ($n = 485$)	Ampicillin and gentamycin	346	71.3
	Ampicillin and ceftriaxone	54	11.1
	Vancomycin and cefotaxime	31	6.4
	Ampicillin	39	8.0
	Other combination	15	3.1
Anticonvulsant	Yes	7	1.0
	No	691	91.0
Phototherapy	Yes	51	7.3
	No	647	92.7
Glucose	Yes	392	56.2
	No	306	43.8
Oxygen	Yes	437	62.6
	No	261	37.4
Blood transfusion	Yes	27	3.9
	No	671	96.1
Kangaroo mother care	Yes	82	11.7
	No	616	88.3

Table 5. Factors associated with neonatal hypoglycemia among neonates admitted to NICU at HFCSUH, Eastern Ethiopia, 2021 ($n = 698$).

Variable	Neonatal hypoglycemia		COR (95% CI)	AOR (95% CI)
	Yes	No		
Complication during pregnancy				
Yes	50	155	1.30 (0.88, 1.91)	0.55 (0.24, 1.27)
No	98	395	1	1
Maternal eclampsia				
Yes	11	35	1.17 (0.50, 2.49)	1.54 (0.58, 4.08)
No	138	514	1	1
Maternal DM				
Yes	60	25	1.39 (1.35, 2.93)	2.34 (1.03, 5.33)*
No	388	225	1	1
Maternal sepsis				
Yes	18	29	2.48 (1.10, 4.80)	1.94 (0.72, 5.23)
No	130	521	1	1
Preterm birth				
Yes	63	157	1.85 (1.27, 2.69)	3.06 (1.02, 9.17)**
No	85	393	1	1
Low birth weight				
Yes	71	193	1.70 (1.18, 2.46)	0.84 (0.28, 2.51)
No	77	357	1	1
Asphyxia				
Yes	52	146	1.49 (1.01, 2.20)	0.98 (0.42, 2.28)
No	96	404	1	1
Hypothermia				
Yes	85	166	3.12 (2.14, 4.53)	2.65 (1.22, 5.75)**
No	63	384	1	1
Neonatal sepsis				
Yes	94	319	1.26 (0.86, 1.83)	2.61 (1.03, 6.59)*
No	54	231	1	1
Delay in the initiation of breastfeeding >1 h				
Yes	25	48	2.12 (0.98, 4.19)	3.89 (1.17, 12.89)**
No	123	502	1	1

*$p < 0.05$. **$p < 0.001$.

hypoglycemia is greater. In our investigation, a cross-sectional study was undertaken, whereas a community-based cross-sectional study was carried out in Uganda[18] which may be a reason for this disparity. The method used to measure newborns' blood glucose concentrations varied, which might have made the differences in finding. The neonates in Uganda were monitored for hypoglycemia using glucose strips and confirmed by laboratory method for the first 72 h (using strict techniques to measure blood glucose concentrations), and these neonates were also observed for clinical presentation.[25]

Our study finding is in line with the study conducted in Israel (23.2%).[29] However, our finding was lower than those studies done at the Tertiary Health Facility in North Central Nigeria (30.5%)[30] and the University of Port Harcourt Teaching Hospital in Nigeria (28.3%).[17] The variation in how blood glucose concentrations is measured may help to explain this. In contrast to the study done in Nigeria which used the cord blood glucose value, our investigation used the capillary blood glucose value.[30] Shreds of evidence from different studies indicated that the cord blood glucose value had high reliability and was an effective screening tool for determining the glycemic status of neonates.[31]

In congruent with a prior study done in a university teaching hospital in Nigeria, preterm neonates were more likely to present with hypoglycemia when compared to term neonates.[28] Due to a lack of metabolic reserves and their inability to produce new glucose using gluconeogenesis pathways, neonates are extremely susceptible to hypoglycemia because they lack well-developed compensatory mechanisms to combat it.[32] To prevent the fatal consequences of hypoglycemia on their developing brain and other organs, neonates should be given enough calories and warmth.

The chance of developing neonatal hypoglycemia among hypothermic neonates was almost three times more likely compared to normothermic neonates. A similar

explanation was found in the study conducted in the USA.[33,34] This could be because the glucose requirement increases in neonates who have hypothermia which will increase the risk of hypoglycemia.[19,35] Because of this, maintaining a suitable ambient temperature is crucial in preventing hypothermia and subsequent hypoglycemia in neonates.[36] This is the rationale for the World Health Organization recommendation that newborns get rapid treatment such as drying, and skin-to-skin contact, and that the room temperature where they are delivered be between 25°C and 28°C (77.0°F to 82.4°F).[20]

Neonatal sepsis increases the risk of developing neonatal hypoglycemia by three times when compared to neonates without sepsis. A similar study conducted in Bangladesh supports the current finding.[37] The possible justification could be that a neonate with sepsis becomes reluctant to eat which can cause hypoglycemia. Neonatal hypoglycemia is reported to be caused by sepsis in 9.6% of neonatal hypoglycemia cases.[38] Similar to sepsis, hypoglycemia can be brought on by sepsis' increased metabolic demand and hypothermia.[39]

Compared to neonates born to non-diabetic mothers, neonates born to diabetic mothers were more likely to experience hypoglycemia. This result did not line up with the study conducted in the USA.[40] This may be related to maternal hyperglycemia which causes the newborn to get too much fuel (glucose) driving the hyperplasia of the fetal pancreatic beta cells and elevating insulin and insulin-like growth factor.[41] To lessen the effects of diabetes on the fetus and newborn, preconception control of diabetes by glucose management and monitoring throughout pregnancy is crucial.

Neonatal hypoglycemia is more likely to occur among neonates who are delayed the initiation of breastfeeding for more than 1 h after delivery compared to those who initiated breastfeeding 1 h before. This corresponds to finding from Uganda.[18] The importance of encouraging moms to breastfeed their newborns during the first hour of birth is reinforced by this finding. Additionally, it clarifies a possible mechanism through which postponed breastfeeding can raise the risk of newborn morbidity and death.[42] Neonatal hypoglycemia should be treated initially with early and continuous nursing.[43]

Conclusions

Neonatal hypoglycemia was quite common among neonates. Preterm birth, hypothermia, neonatal sepsis, maternal DM, and delay in initiation of breastfeeding were determinant factors for the development of neonatal hypoglycemia. To reduce and avoid the occurrence of neonatal hypoglycemia, we thus strongly advise health-care professionals to monitor and regulate these and other determining variables of hypoglycemia while working in the postnatal unit.

Limitations of the study

Our study had some limitations. First, the cross-sectional study design's inherent limitations prevent it from demonstrating the causal link between hypoglycemia and its determinant factors. Second, we took the data including blood glucose measurement from secondary data (from the record) which could have a bias (information bias) while extracting the data.

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Author contributions

AS designed the study, performed the statistical analysis, and drafted the manuscript. KN, AE, AT, and AN participated in the study design and statistical analysis. TG, AD, and MD drafted the manuscript. All authors contributed equally to this work and read and approved the final version of this manuscript.

Availability of data and materials

The data were limited to protect the privacy of our study participants and the university. However, upon reasonable request, it is available and accessible from the corresponding author on reasonable request.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics approval

The ethical clearance of the study was obtained and approved by the Institutional Review Board of Haramaya University, College of Health and Medical Sciences, Institutional Health Research Ethics Review Committee (IHRERC) with a reference number (IHRERC/012/2020). Permission was obtained from the Medical Record Office of HFCSUH. Ethical approval for this study was obtained from the Institutional Review Board of Haramaya University *Institutional Health Research Ethics Review Committee (IHRERC) with a reference number of (IHRERC/012/2020)*.

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Informed consent

We got authorization from the head of the Medical Record Office at HFCSUH to access patient medical information after the Institutional Review Board approved the project. All findings were kept secret and exclusively utilized for the study's purposes. Informed, voluntary, written, and signed consent was obtained

from legally authorized representatives (hospital administrators and head of medical record office) and approved by Institutional Review Board of Haramaya University (IHRERC) with a reference number (IHRERC/012/2020) before the initiation of the study.

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Supplemental material

Supplemental material for this article is available online.

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