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ORIGINAL ARTICLE

Does Gender Affect Levels of Hyperbilirubinemia in Term Neonates

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ABSTRACT

Introduction: Hyperbilirubinemia is a common & in most1cases, benign problem in1first month of1life which is often1physiologic & intervention is not1usually1necessary. In the first week of life, about 60.0% of term & 80.0% of preterm infants have jaundice. Jaundice could lead to major side effects like kernicterus and permanent impairment.[1]One of the most frequent disorders requiring medical1attention in babies is neonatal jaundice. It has high levels of unconjugated1bilirubin, which can occasionally lead to kernicterus.

Objective: To determine frequency of hyperbilirubinemia among neonates who present with physiological jaundice and compare the mean levels of hyperbilirubinemia among genders.

Methodology: A total of 368 consecutive neonates were included. This cross-sectional study1was conducted at Department of Paediatric Medicine, NICH Karachi during June 2020 to December 2020. All pre-term or term neonates of either gender with physiological jaundice, and get admitted to pediatric medicine department were included in this study. While Neonates who did not survive first 48 hours of life, neonates who were not exclusively breast fed as determined by History were excluded from study. Blood samples1were taken from the patients and concentrations of serum total bilirubin, In the centrifuged venous samples, direct & indirect1bilirubin concentrations were determined. Serum total,1direct& indirect bilirubin was recorded for each patient. Data was analyzed using IBM. SPSS 22 on computer.

Results: Mean ±SD age of neonates was 10.6±4.2 days. In distribution of gender, 214 (58.2%) were male while 154 (41.8%) were female. Mean ±SD of birth weight was 3.4±1.8 kg. Mean ±SD of birth weight was 3.4±1.8 kg with min to max 1.5 – 4.5 kg. majority 203 (55.2%) of neonates had birth weight was 1.5 – 3.0 kg. pre term delivery was done in 195 (53%) neonates while 173 (46.7%) were documented in term neonates. Hyperbilirubinemia was found in 156 (42.4%) patients. Mean levels of hyperbilirubinemia in male v/s female was noted as (12.3±3.8) and (11.5±3.4) respectively and P value found to be significant i.e. (P=0.038). Proportion of hyperbilirubinemia was significantly high 92 (52.9%) in neonates with age > 9 days (p=0.00). Advanced maternal age (>30 years) was also significantly associated with hyperbilirubinemia 88 (50.9%), (p=0.002; OR=1.9). C-section was significantly associated with hyperbilirubinemia 99 (49.3%), (p=0.003).

Practical Implication: This study aims to provide an answer to the question of whether gender affects the level of hyperbilirubinemia in neonates. The rationale behind this is that because both preterm and term neonates are affected by this condition, if it is determined that one gender is more affected and experiences higher levels of bilirubinemia, neonates of that specific gender can be closely monitored and followed up in the future.

Conclusion: It is to be concluded that hyperbilirubinemia is a frequent finding among neonates who present with physiological jaundice. Therefore, to correctly diagnose and treat the disease, both parents and professionals should take precautions.

Keywords: 1 Hyperbilirubinemia, Neonates, Jaundice, Risk Factors, Etiology, Hemolysis

INTRODUCTION

Hyperbilirubinemia1appears1in approximately 60.0% of the newborns at term & almost in all preterm1neonates, with prevalence greater than 80%.[2]Jaundice with total serum bilirubin levels higher than 5 mg/dl is one symptom of this. [3] Visible jaundice first emerges between 24.0 & 72.0 hours after1birth, peaks at 4.0 to 5.01days for term babies & 7.0 days for preterm babies, & then goes away by 10 to 14 days after birth.[4] This is supposedly a physiological event, in most cases, resulting from increased1bilirubin synthesis, ineffective hepatic conjugation, and increased enterohepatic circulation bilirubin absorption.[5,6,7] Although non-physiological causes like East Asian ancestry, low birth weight, prematurity, breast milk feeding, cephalhematoma, trauma from instrumental delivery, delayed meconium, hemolysis, syphilis and a sibling with neonatal jaundice, can result in this condition.[8,9,10] This neonatal hyperbilirubinemia (NH) is known to cause neurotoxic effects leading to long-term problems like delayed mentation, cerebral palsy, hearing loss, and kernicterus.[11]

The effects of gender on neonatal hyperbilirubinemia and outcomes have continued to be a source of discussion and research, although there is no agreed-upon data on the subject.[6] Wong et al in their study, done in Malaysia, comprising of patients with wide ethnic background, reported no significant difference in gender distribution when comparing neonates with hyperbilirubinemia and with hyperbilirubinemia (p-value 0.8).[12]Bala et al showed in their study that in neonates with neonatal hyperbilirubinemia, no significant difference in mean1total bilirubin1was found, 12.27±4.39 in males and 11.74±3.41 in females, p-value >10.05.[6]Veni et al reported the mean total Bilirubin 11.43±3.29 in female infants & 11.52±2.67 in male infants, the difference was not significant (p=0.89).[4] But on the other hand, Tioseco et al reported a higher mean total bilirubin of 10.1±3.0 mg/dl in male neonates as compared to 9.2±2.8 mg/dl in female neonates, p-value <0.001.[13]Shilongo et al, elucidated that total bilirubin level of more that 17mg/dl was considered critical and required treatment, concluding that males had a higher frequency of critical1values (13.4%) as compared to females1(11.5%) & were at greater1risk of1kernicterus .[14,15] As there seems to be a wide variation in results in literature regarding whether gender does actually affects the level of hyperbilirubinemia in neonates, this study aims to answer this question with the rationale being that as a large number of preterm and term neonates are affected by this condition, if proven that a certain gender is affected more and develop higher levels of bilirubinemia, neonates of that particular gender can be monitored and followed up closely in neonatal period for rising bilirubin levels and appropriate treatment can be started early hence preventing the dangerous sequelae of neurological damage caused by neonatal hyperbilirubinemia.

METHODOLOGY

This cross-sectional study was1conducted at Department of Paediatric Medicine, NICH Karachi during June 2020 to December 2020.The estimated sample size of this study was 368 consecutive cases; sample size was calculated by using WHO calculator with prevalence of hyperbilirubinemia was 60%[2] (p) , 95% CI and 5% margin of error (d). All pre-term or term neonates of either gender

with physiological jaundice, and get admitted to pediatric medicine department were included in this study. While neonates who were not exclusively breast fed as determined by History, Neonates with cephalhematoma, presented as skull swelling in neonatal period after instrument delivery or prolonged labor, due to accumulation of blood between skull and periosteum, diagnosed by X-ray or CT scan skull, Neonates with meconium aspiration syndrome as determined by fetal respiratory distress due to aspiration of meconium just before or after delivery due to fetal distress during delivery, Neonates from a Rh +ve sensitized mother, presenting with Rh incompatibility as evident by anemia, reticulocytosis, erythroblastosisfetalis, hydropsfetalis or still birth and neonates with sepsis as diagnosed by positive cultures from any fluid plus signs of systemic inflammatory response were excluded from the study.

Patients' blood samples were drawn, and the centrifuged venous samples were used to assess the quantities of serum1total bilirubin (STB), direct bilirubin (DB) &indirect bilirubin. A proforma was used to record patient demographics like neonatal age, gender, hospital registration number. It also included fetal parameters like pre- term or term, gestational age and birth weight, Moreover, maternal parameters like maternal age and mode of delivery (vaginal or c-section) were also recorded. Lastly, values of serum total, direct and indirect bilirubin were recorded for each patient. All data was recorded by an independent observer, not involved in the study, and all neonates clinically for jaundice before admission by pediatrician with at least 5 years of post-fellowship experience to reduce bias.

Data was analyzed using IBM. SPSS 22 on computer. Mean &SD were calculated for numerical variables like neonatal age, gestational age, birth weight, maternal age and total bilirubin values. Frequency and percentages were calculated for qualitative variables like gender, born pre-term or term and mode of delivery (vaginal or c-section). Student t-test was used to compare mean values of total bilirubin values in male v/s female neonates, taking p-value ≤ 0.05 as statistically significant. Stratification was done to control confounding variables like neonatal age, gestational age, pre-term or term birth, birth weight, maternal age and mode of delivery with final outcome and post stratification chi-square test for hyperbilirubinemia and independent sample t test was used for mean level of bilirubin, taking p-value1of ≤ 0.05 as significant.

RESULTS

Total of 368 neonates of either gender were included. Demographics of cases are shown in in Table 1. Out of 368 neonates, 194 (52.7%) had age 3 – 9 days and 174 (47.3%) had age >9 days. Mean ±SD of age was 10.6±4.2 days (min–max=3-28 days). In distribution of gender, 214 (58.2%) were male while 154 (41.8%) were female. Mean ±SD of birth weight was 3.4±1.8 kg with min to max 1.5 –

4.5 kg. majority 203 (55.2%) of neonates had birth weight was 1.5 – 3.0 kg. pre term delivery was done in 195 (53%) neonates while 173 (46.7%) were documented in term neonates. Mean ± SD of maternal age was 36.5±9.3 years (min-max=18-42 years). majority 195 (53%) of mothers had age 18 – 30 years. Mean ±SD of gestational age was

37.9 ±8.4 weeks. A total of 221 (60.1%) women had gestational age 34 – 37 weeks. In distribution of mode of delivery 167 (45.4%) deliver vaginally while 201 (54.6%) were deliver via cesarean section. Educational status showed that 92 (25%) fathers were illiterate, 154 (41.8%) had primary education, 78 (21.2%) had secondary while 44 (12%) had matric or above education. Educational status showed that 143 (38.9%) mothers were illiterate, 114 (31%) had primary education, 71 (19.3%) had secondary while 40 (10.9%) had matric or above education.

Hyperbilirubinemia was found to be in 156 (42.4%) patients as shown in Figure 1. Mean± SD of total bilirubin values was 11.2±3.6 mg/gl. Mean levels of hyperbilirubinemia in male v/s female was noted as (12.3±3.8) and (11.5±3.4) respectively and P value found to be significant i.e. (P=0.038) as shown in Figure 2.

Stratification of hyperbilirubinemia were done with respect to neonates age, gestational age, birth type of neonates, birth weight, maternal age and modes of delivery among neonates with physiological jaundice in order to found significant difference shown in Table 2. Proportion of hyperbilirubinemia was significantly high 92 (52.9%) in neonates with age > 9 days (p=0.0001; OR=2.3, 95% CI = 1.5 - 3.5). Advanced maternal age (>30 years) was also significantly associated with hyperbilirubinemia 88 (50.9%), (p=0.002; OR=1.9, 95% CI = 1.3 – 2.9). C-section was significantly associated with hyperbilirubinemia 99 (49.3%), (p=0.003; OR=1.87, 95% CI = 1.2 - 2.9)

Table 1: Demographics of Cases (n = 368)

Demographics		Frequencies	Percentages
Neonates Age (days) Mean ±SD=10.6 ±4.2 Min-Max=3-28	3 - 9	194	52.7%
	> 9	174	47.3%
Gender	Male	214	58.2%
	Female	154	41.8%
Birth Weight (Kg) Mean ±SD=3.4 ±1.8 Min-Max=1.5 - 4.5	1.5 - 3.0	203	55.2%
	> 3.0	165	44.8%
Birth Type	Pre-Term	195	53.0%
	term	173	47.0%
Maternal Age (Years) Mean ±SD=36.5 ±9.3 Min-Max=18 - 42	18 - 30	195	53.0%
	> 30	173	47.0%
Gestational Age (Weeks) Mean ±SD=37.9 ±8.4 Min-Max=34 - 41	34 - 37	221	60.1%
	> 37	147	39.9%
Mode of Delivery	Vaginal	167	45.4%
	C-Section	201	54.6%
Father's Education	illiterate	92	25.0%
	Primary	154	41.8%
	Secondary	78	21.2%
	Matric & Above	44	12.0%
Mother's Education	illiterate	143	38.9%
	Primary	114	31.0%
	Secondary	71	19.3%
	Matric & Above	40	10.9%

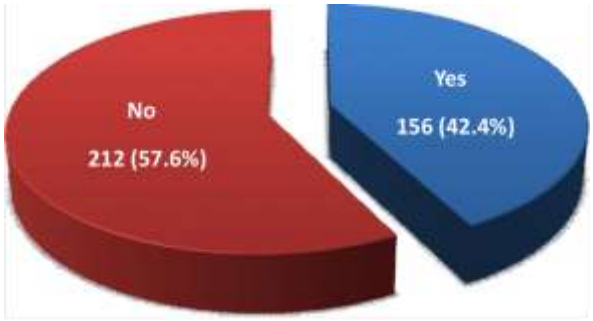

Figure 1: Frequency of Hyperbilirubinemia (n = 368)
Mean (±SD) = 11.2 (±3.6) mg/dl

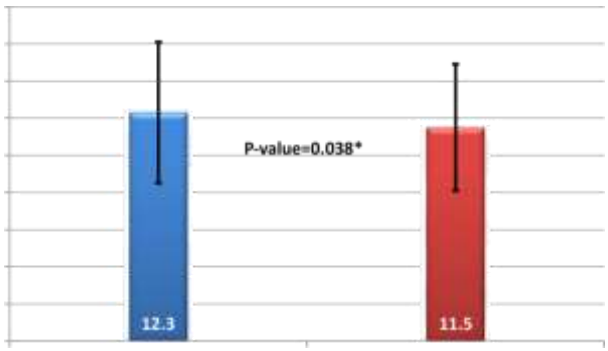

Figure 2: Comparison of Mean Hyperbilirubinemia between Gender (n=368)

Table 2: Demographics of Cases (n = 368)

		Hyperbilirubinemia		P-values	OR (95% CI)
		Yes	No		
Neonates Age (Days)	3 - 9	64 (33%)	130 (67%)	0.0001	2.3 (1.5 - 3.5)
	> 9	92 (52.9%)	82 (47.1%)		
Birth Weight (Kg)	1.5 - 3.0	81 (39.9%)	122 (60.1%)	0.284	1.3 (0.8 - 1.9)
	> 3.0	75 (45.5%)	90 (54.5%)		
Birth Type	Pre-Term	76 (39%)	119 (61%)	0.159	1.4 (0.9 - 2)
	term	80 (46.2%)	93 (53.8%)		
Maternal Age (Years)	18 - 30	68 (34.9%)	127 (65.1%)	0.002	1.9 (1.3 - 2.9)
	> 30	88 (50.9%)	85 (49.1%)		
Gestational Age (Weeks)	34 - 37	93 (42.1%)	128 (57.9%)	0.883	1.03 (0.7 - 1.6)
	> 37	63 (42.9%)	84 (57.1%)		
Mode of Delivery	Vaginal	57 (34.1%)	110 (65.9%)	0.003	1.87 (1.2 - 2.9)
	C-Section	99 (49.3%)	102 (50.7%)		

DISCUSSION

When a newborn has neonatal jaundice, their skin turns yellow within the first few days of life. The skin appears yellowish as a result of an elevated blood1pigment called1bilirubin that then accumulates there. This is frequently a typical process that affects roughly two-thirds of all healthy neonates. However, it could occasionally indicate a problem with the infant's eating, level1of1hydration, or lifespan of red blood cells.

Jaundice may also be caused by other uncommon conditions such liver illness, gland dysfunction, or problems of the metabolism. Only the doctor can establish whether the infant's jaundice is normal, and they may also request a blood1test to1help in the1diagnosis. A total blood bilirubin level greater than 5.0mg/dL is considered to be neonatal hyperbilirubinemia.About 60% of term and 80% of preterm babies experience this common issue during the first week of life.[16,17]At one1month, 10% of breastfed infants still1had jaundice.[16]The skin & mucous membranes'1yellowish tint is caused by the deposition1of unconjugated bilirubin pigment.[17]Neonatal jaundice is typically seen as a transient condition with few clinical findings, associated with1hepatic, red1cell & gastrointestinal1immaturity.[16,18]However, severe conditions include hemolytic1disease, metabolic and endocrine diseases,1anatomic abnormalities of the liver & infections can all1be linked to hyperbilirubinemia during1the newborn period.[17]Acute bilirubin-associated neuropathy that develops as a result of a severe increase in total serum bilirubin levels frequently develops into kernicterus, a persistent neurologic disease. The latter is characterised by a severe form of athetoid1cerebral palsy, issues with hearing & vision, dental1enamel1dysplasia & less1frequently, cognitive and other dysfunctions.[16,17,19,20]Although genetically determined diseases are receiving more attention, environmental&1genetic variables interact. Despite the increased focus on hereditary illnesses, environmental and genetic factors interact to create neonatal1hyperbilirubinemia.[21-23]

Due to newborn infants' tendency to produce more bilirubin and their inability to excrete it, they develop neonatal hyperbilirubinemia.[24]Because they have a shorter life expectancy and a greater red cell turnover rate than adults, babies, particularly preterm newborns, produce more bilirubin than adult. Approximately 6-81mg per kg per day, or1more than twice as1much as adults, are produced1of bilirubin in newborns.[17]

Other restrictions that are visible in newborn children1include restricted1ability to conjugate bilirubin due to lower1activity of the1hepatic conjugating1enzyme1UDP glucuronosyltransferase& decreased hepatic absorption of bilirubin from plasma as a result of diminished ligandin1 (UGT-1A1).[24,25]The bile transports the conjugation reaction's byproducts into the intestines. Significant amounts of conjugated1bilirubin are hydrolyzed back to1unconjugated bilirubin in the intestines of neonates. By way of the enterohepatic1circulation, unconjugated bilirubin is reabsorbed back into the1bloodstream, contributing to the liver's already excessive bilirubin load.Therefore, enterohepatic bilirubin circulation is a significant cause of newborn jaundice.[25]

The development of physiologic neonatal jaundice is caused by the simultaneous occurrence of all the mentioned characteristics in the bilirubin metabolism of newborn newborns. The most prevalent type of infant hyperbilirubinemia is physiological jaundice, which has no negative effects.[26]High toxic levels of bilirubin may contribute to neurodevelopmental problems such as athetosis, hearing loss, and in rare circumstances, intellectual deficiencies.[27]

When it first occurs, jaundice caused by physiological immaturity typically lasts between 24 and172 hours, peaks in term1newborns between the fourth & fifth day, or dissipates in1preterm infants at the seventh day.[28]

The most common form of bilirubin1is unconjugated & its serum level is often less than 15 mg/dl.[29]According to the AAP's most recent1recommendations, neonates who are healthy may have bilirubin levels as high as 17 to 18 mg/dl.[30]

In our study, the mean age was 10.6±4.2 days. The study of Maamouri G, et al[31] reported mean age as 8.7±6 days. In this study, the mean gestational age was 37.9±8.4 weeks, mean birth weight was 3.4±1.8 kg, mean maternal age was 36.5±9.3 years. In the study of Brits H. et al,[32] the mean weight of the babies was 3.15 kg and the mean gestation was 38.5 weeks. In present study, the mean total bilirubin values were 11.2±3.6 mg/gl.

In current study, out of 368 patients, 214 (58.2%) were male while 154 (41.8%) were female. In recent study, educational status showed that 92 (25%) fathers were illiterate, 154 (41.8%) had primary education, 78 (21.2%) had secondary while 44 (12%) had matric or above education whereas 143 (38.9%) mothers were illiterate, 114 (31%) had primary education, 71 (19.3%) had secondary while 40 (10.9%) had matric or above education.

In our study, birth type of neonates was classified as 195 (53%) patients for pre-term delivery while 173 (47%) were term neonates. Maamouri G, et al[31] reported that 87% were term neonates. In present study, modes of delivery showed that 167 (45.4%) had done with vaginal delivery while 201 (54.6%) was done with cesarean section. Brits H, et al [73], reported to have 46.8% vaginal delivery and 53.2% cesarean section.

In this study, hyperbilirubinemia was found in 156 (42.4%) patients. Hyperbilirubinemia was noted in 55% cases in Brits H et al.[32] In current study, stratification of confounders / effect modifiers with respect to hyperbilirubinemia, significant difference was noted in neonatal age (P=0.0001) whereas insignificant differenced was reported in gestational age (P=0.883), birth type of neonates (P=0.159), birth weight (P=0.284), maternal age (P=0.002) and modes of delivery (P=0.003).

The minimum assessment before therapy is started should include the infant's age & postnatal course, a mother's and child's medical history, a physical examination of the child, and the measurement of the total blood bilirubin level and the rate of increase.

CONCLUSION

It is to be concluded that hyperbilirubinemia is a frequent finding among neonates who present with physiological jaundice. Therefore, to correctly diagnose and treat the disease, both parents and professionals should take precautions. Medical researchers should look for novel therapies and preventative strategies that can heal infants more quickly and without negative effects. Before getting married, partners should have their ABO blood types and Rh factor testedbeconsanguineous1unions ought to be avoided.

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REFERENCES

1. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. British Journal of Hospital Medicine. 2017 Dec 2;78(12):699-704..
2. Rennie J, Burman-Roy S, Murphy MS. Neonatal jaundice: summary of NICE guidance. Bmj. 2010 May 19;340..
3. Brits H, Adendorff J, Huisamen D, Beukes D, Botha K, Herbst H, Joubert G. The prevalence of neonatal jaundice and risk factors in healthy term neonates at National District Hospital in Bloemfontein. African Journal of Primary Health Care and Family Medicine. 2018 May 3;10(1):1-6.
4. Veni DD. The study on the effect of gender on serum bilirubin concentration in infants with neonatal hyperbilirubinemia. Int J Pharm Bio Sci. 2013;4(2):603-8.
5. Boskabadi H, Rakhshanizadeh F, Zakerihamidi M. Evaluation of maternal risk factors in neonatal hyperbilirubinemia. Archives of Iranian medicine. 2020 Feb 1;23(2):128-40.
6. Bala J, Agrawal Y, Chugh K, Kumari M, Goyal V, Kumar P. Variation in the serum bilirubin levels in newborns according to gender and seasonal changes. Archives of Medicine and Health Sciences. 2015 Jan 1;3(1):50.
7. Brits H, Adendorff J, Huisamen D, Beukes D, Botha K, Herbst H, Joubert G. The prevalence of neonatal jaundice and risk factors in healthy term neonates at National District Hospital in Bloemfontein. African Journal of Primary Health Care and Family Medicine. 2018 May 3;10(1):1-6.
8. Khairy MA, Abuelhamd WA, Elhawary IM, Nabayel AS. Early predictors of neonatal hyperbilirubinemia in full term newborn. Pediatrics & Neonatology. 2019 Jun 1;60(3):285-90.
9. MacMahan JR, Stevenson DK, Oski FA. Unconjugated hyperbilirubinemias. Avery's diseases of the newborn. 7th edition. Philadelphia, WB Saunders, 1998;1014-1020.
10. Yang H, Lin F, Chen ZK, Zhang L, Xu JX, Wu YH, Gu JY, Ma YB, Li JD, Yang LY. UGT1A1 mutation association with increased bilirubin levels and severity of unconjugated hyperbilirubinemia in ABO incompatible newborns of China. BMC pediatrics. 2021 Dec;21(1):1-8.
11. Watchko JF. Identification of neonates at risk for hazardous hyperbilirubinemia: emerging clinical insights. PediatrClin North Am. 2009;56(3):671-87.
12. Wong F, Boo N, Othman A. Risk factors associated with unconjugated neonatal hyperbilirubinemia in Malaysian neonates. J trop pediatr. 2013;2:59(4):280-5.
13. Tioseco JA, Aly H, Milner J, Patel K, El-Mohandes AA. Does gender affect' neonatal hyperbilirubinemia in low-birthweight infants? PediatrCrit Care Med. 2005;6:171-4.
14. Yaseen ZT, Alezzi JI, Khaleel SM. Unconjugated Neonatal Hyperbilirubinemia: Evaluation and Treatment. Diyala Journal of Medicine. 2020 Dec 15;19(2):31-40.
15. Shilongo SN, Mukesi M, Gonzo M, Moyo SR. Prevalence of critical bilirubin results among neonatal patients in Windhoek, Namibia. SM J Environ Toxicol. 2017;1(1):1001.
16. Devi S, Dash M, Chitra F. Detection of neonatal jaundice among the newborn using Kramer's criteria. Epidemiology (Sunnyvale). 2018 Oct 26;8(355):2161-1165.
17. Hammerman C, Kaplan M. Hyperbilirubinemia in the Term Infant: Re-evaluating What We Think We Know. Clinics in Perinatology. 2021 Aug 1;48(3):533-54.
18. Abbas SH, Nafea LT, Abbas RS. Studying the Influence of Maternal Factors on Iraqi Pediatrics patients Presented with Neonatal Hyperbilirubinemia. Indian Journal of Forensic Medicine & Toxicology. 2021 Oct;15(4):2521.
19. Ma XL, Chen Z, Zhu JJ, Shen XX, Wu MY, Shi LP, Du LZ, Fu JF, Shu Q. Management strategies of neonatal jaundice during the coronavirus disease 2019 outbreak. World Journal of Pediatrics. 2020 Jun;16(3):247-50..
20. Okolie F, South-Paul JE, Watchko JF. Combating the hidden health disparity of kernicterus in Black infants: a review. JAMA pediatrics. 2020 Dec 1;174(12):1199-205..
21. Chen K, Yuan T. The role of microbiota in neonatal hyperbilirubinemia. American Journal of Translational Research. 2020;12(11):7459.
22. Nguyen TT, Zhao W, Yang X, Zhong DN. The relationship between hyperbilirubinemia and the promoter region and first exon of UGT1A1 gene polymorphisms in Vietnamese newborns. Pediatric Research. 2020 Dec;88(6):940-4.
23. Yang H, Lin F, Chen ZK, Zhang L, Xu JX, Wu YH, Gu JY, Ma YB, Li JD, Yang LY. UGT1A1 mutation association with increased bilirubin levels and severity of unconjugated hyperbilirubinemia in ABO incompatible newborns of China. BMC pediatrics. 2021 Dec;21(1):1-8.
24. Hulzebos CV, Vitek L, Coda Zabetta CD, Dvořák A, Schenk P, van der Hagen EA, Cobbaert C, Tiribelli C. Diagnostic methods for neonatal hyperbilirubinemia: benefits, limitations, requirements, and novel developments. Pediatric research. 2021 Aug;90(2):277-83.
25. Cordero C, Schieve LA, Croen LA, Engel SM, Maria Siega-Riz A, Herring AH, Vladutiu CJ, Seashore CJ, Daniels JL. Neonatal jaundice in association with autism spectrum disorder and developmental disorder. Journal of Perinatology. 2020 Feb;40(2):219-25.
26. Almansaf AA, Albalwi AB, ALSalem RA, Asiri KJ, Baeyti NY, Alrobaie KA. An Overview on Diagnosis and Management of Neonatal Jaundice. Archives of Pharmacy Practice. 2021;1:99.
27. Goyal M, Sharma R, Dabi DR. Phototherapy induced hypocalcemia in neonates: A case–control prospective study. Indian J Child Health. 2018 April; 5(3):208-212.
28. Hulzebos CV, Vitek L, Coda Zabetta CD, Dvořák A, Schenk P, van der Hagen EA, Cobbaert C, Tiribelli C. Screening methods for neonatal hyperbilirubinemia: Benefits, limitations, requirements, and novel developments. Pediatric research. 2021 Aug;90(2):272-6..
29. Maisels MJ, Gifford K. Neonatal jaundice in full-term infants: role of breast-feeding and other causes. American Journal of Diseases of Children. 1983 Jun 1;137(6):561-2..
30. Gartner LM, Lee KS. Jaundice in the breastfed infant. Clinics in perinatology. 1999 Jun 1;26(2):431-45..
31. Maamouri G, Boskabadi H, Khatami F, Mohammadzadeh A, Saeidi R, Farhat A, Kiani MA. Hyperbilirubinemia and neonatal infection. International Journal of Pediatrics. 2014 Apr 1;2(2.1):81-.
32. Brits H, Adendorff J, Huisamen D, Beukes D, Botha K, Herbst H, Joubert G. The prevalence of neonatal jaundice and risk factors in healthy term neonates at National District Hospital in Bloemfontein. African Journal of Primary Health Care and Family Medicine. 2018 May 3;10(1):1-6.