PATTERN OF LIVER DISORDERS IN NEONATAL INTENSIVE CARE UNIT

By

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ABSTRACT

Objectives: *Our objective is to detect hepatic insult and its potential risk as Co-factor that can be faced by babies admitted to NICU.*

Background: *Liver may affect by many disorders in neonatal period, the most common are neonatal sepsis (mainly due to gram-negative organisms), hypoxic induced encephalopathy (the common neurological complication in perinatal period).*

Patients and Methods: *A prospective observational study carried out in NICU of El-Hussein University Hospital included 100 neonates for diagnosis of liver affection associated with other neonatal disorders with exclusion of neonates with multiple congenital anomalies and cases with inborn errors of metabolism during the period from March 2019 to September 2019.*

Results: *Our results showed a significant male admission with significant occurrence of liver insult in neonates with very low birth weight, neonatal sepsis, HIE, maternal history of PROM, maternal comorbidities, Low APGAR score, presence of splenomegaly, hepatomegaly, liver enzymes elevation, change in bleeding profile and albumin, rise in CRP and alkaline phosphatase enzyme and positive blood culture results.*

The results showed significant relation between liver insult and bad outcomes and the use of CPAP, MV.

Conclusion: *We conclude that neonates especially with low-birth weight more prone to liver affection if with neonatal sepsis and hypoxic induced encephalopathy.*

Recommendation: *Any baby admitted to NICU especially with critical disorders (HIE, Neonatal sepsis) must be investigated for liver function tests to rule out hepatobiliary dysfunction.*

Key words: *Neonatal sepsis (NS), Hypoxic induced encephalopathy (HIE), Multi-organ dysfunction (MOD), Neonatal intensive care unit (NICU), premature rupture of membranes (PROM).*

INTRODUCTION

The liver's main function is to synthesize a group of body proteins and to act as the detoxifying center for the multiple toxic metabolic byproducts endogenous to the body and the toxins ingested daily by the organism[1]. On other hand the liver performs many essential functions, including the production of bile, regulation of plasma proteins and glucose, and biotransformation of drugs and toxins[2].

Neonatal acute liver failure (ALF) is a rare condition that carries a high mortality (70%) without liver transplantation[3].

The frequency of acquired liver injury and failure in critical illness has been significantly increasing over recent decades. Currently, liver injury and failure are observed in up to 20% of patients in intensive care units and are associated with significantly increased morbidity and mortality[4].

Liver disease in early infancy encompasses a wide spectrum of conditions, including infectious, metabolic, and hematologic disorders, congenital vascular and heart diseases, drug-related toxicity, hypoxia, and gestational alloimmune liver disease associated with neonatal hemochromatosis (GALDNH)[5,6].

Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection and bacteremia in the neonatal period. Neonatal sepsis is a major cause of mortality and neurodevelopmental impairment among neonates. It contributes to nearly 30 % of neonatal deaths in developing countries[7-9].

In neonatal asphyxia; hepatic involvement is often found in the subjects as it is highly involved in so many metabolic processes. This entity is variously termed "shock liver" or ischemic hepatitis. The condition is appropriately termed hypoxic hepatopathy in which dramatic transient elevation in serum concentrations of hepatic enzymes occurs[10, 11].

Liver disorders investigated by biochemical liver function tests and specific investigations for cause of liver disease. Liver functions include **1. Bilirubin, 2. Liver enzymes (transaminases; AST and ALT), 3. Biochemistry of bile ducts,** Alkaline phosphatase (ALP) elevated in bile epithelium damage; Ɣ-glutamyltransferase (GGT) found in biliary epithelium and elevated in many forms of liver disease if normal despite high bilirubin it is diagnostic of specific intra-hepatic

cholestasis syndromes, **4. Liver functions,** Clotting factors as prothrombin (PT) is very specific for liver dysfunction/liver failure; Albumin "low in chronic liver disease", Glucose "hypoglycemia indicates severe hepatic dysfunction"[2, 12]. Other tests are often performed and include hepatitis serology, iron and copper studies, α1-antitrypsin levels and auto-antibodies that related to the possible etiology of the abnormality[13].

In fact liver affected by many disorders in neonatal period most common are neonatal sepsis, hypoxic induced encephalopathy (HIE), neonatal hyperbillirubinemia. Recent surveys found cholestasis diseases occupying in 76% of newborn liver diseases, cancer in 2%, metabolic diseases in 9%, acute hepatic failure in 10% and cirrhosis in 3%[12].

This prospective study aimed to detect the prevalence of hepatic affection in relation to the demographic criteria, other risk factors, and associated neonatal disorders in neonates admitted to NICU.

PATIENTS AND METHODS

A prospective observational study carried out in NICU of El-Hussein University Hospital and included 100 neonates admitted from March 2019 to September 2019 with collected clinical, lab and radiological data at first 3 days of admission and 7 days later for diagnosis of liver disorders and its prognosis and outcome after 21 days with exclusion of neonates with multiple congenital anomalies, those with inborn errors of metabolism and admitted neonates with extraordinary complications e.g. (RDS complicated by sepsis after hernia repair).

After approval of local ethics committee, written consent not necessary due to this is an observational study, no conflict of interest regarding study publication; also all data of the study are confidential.

All patients in the study were subjected at first 3 days of admission to:

A. **Routine detailed history taking** including maternal, prenatal, natal, postnatal history.

B. **Complete general and systemic examination** including cardiac, chest, abdominal, neurological examination.

C. **Laboratory investigations** in the form of complete blood picture, coagulation profile, liver function tests, kidney

function tests and blood chemistry: include serum alkaline phosphatase (AP), C-reactive protein (CRP).

D. **Imaging studies:** included 1. Chest X-ray, 2. CT and/or MRI brain, 3. Echocardiography and Other lab and radiological assessment may be needed according to individual case scenario.

Diagnosis of hepatobilliary dysfunction which denotes hepatic cell injury was established with (direct bilirubin >20% of total with a minimum level of 2 mg/dL or ALT > 50 U/L) **(Khalil et al., 2012)**[14].

Persistent hepatobilliary dysfunction is abnormal lab values (direct bilirubin >20% of total with a minimum level of 2 mg/dL or ALT > 50 U/L) findings after ten days (7 days from last assessment) of follow up **(Tiker et al., 2006)**[15].

All studied patients were classified accordingly into two groups, group I (without hepatobiliary dysfunction, and group II (with hepatobiliary dysfunction).

Data were analyzed using IBM SPSS software package version 20.0 **(Belmont, Calf, 2013)**. Data were collected in tables then analyzed in regarding to Chi square (x^2) and p value less than 0.05 were considered significant.

RESULTS

Our results shows that 32 cases delivered at full-term (32/100, 32%) [5 of them (5/32, 15.6%) had liver insults while 27 (27/32, 84.4%) hadn't liver insults] and 68 delivered pre-term (68/100, 68%) [15 of them had liver insults (15/68, 22.1%) had liver insults while 53 (53/68, 77.9%) hadn't liver insults]. In cases of liver insults 15 delivered preterm (15/20, 75%) and 5 cases delivered at full-term (5/20, 25%). In case without liver insults 53 cases (53/80, 66.3%) delivered pre-term and 27 cases (27/80, 33.7%) delivered at full-term. The statistical analysis revealed a significant occurrence of liver insults with pre-term babies (P = 0.031).

64 of cases delivered with normal weight (64/100, 64%) [9 of them (9/64, 14.1%) had liver insults while 55 (55/64, 85.9%) without liver insults] and 36 (36/100, 36%) delivered with [11 of them had liver insults (11/36,

30.2%) had liver insults while 25 (25/36, 69.8%) hadn't liver insults]. In cases of liver insults 9 delivered with normal weight (9/20, 45%) and 11 cases delivered with low-birth weight (11/20, 55%). The statistical analysis revealed a significant occurrence of liver insult with low birth weight (P = 0.021 and 0.031 respectively).

Table (1): Comparison between both groups regarding diagnosis

Diagnosis	Group I n=80		Group I n = 20	
	No.	%	No.	%
EOS	7	8.8	9	45.0
X^2 P	15.644* 0.001* (S)			
LOS	6	7.5	3	15.0
X^2 P	4.11 0.033 (S)			
HIE	6	7.5	6	30.0
X^2 P	7.670* 0.013* (S)			

X^2 = Chi square test, * = significant if P <0.05, NS = Not significant
EOS= early onset neonatal sepsis, LOS=late onset neonatal sepsis, HIE= Hypoxic Induced Encephalopathy.

Our results demonstrates that neonates with liver affection commonly presents with EOS (9/20, 45%), HIE (6/20, 30%), LOS (3/20, 15%), with a significant occurrence of these disorders in cases of liver affection **(Table 1)**.

Table (2): Comparison between both groups regarding abdominal examination

Abdominal examination	Group I (n = 80)		Group II (n = 20)	
	No.	%	No.	%
Splenomegaly	**3**	**3.8**	**3**	**15.0**
X^2 **P**	**4.13** **(0.031 (S))**			
Hepatomegaly	**1**	**1.25**	**13**	**65.0**
X^2 **P**	**4.13** **(0.031 (S))**			

X^2 = Chi square test, * = significant if P <0.05, NS = Not significant

We are noticed that regarding abdominal examination; neonates with liver affection showed a significant percentage of splenomegaly (3/20, 15%), as well as hepatomegaly (13/20, 65%) with (P= 0.021, 0.031 respectively) **(Table 2)**.

Also our results showed that liver function tests of neonates

revealed that there was a significant increase in the liver function tests "ALT, AST, GGT, PT, PTT, INR" with a significant decrease in the serum albumin and significant increase of alkaline phosphatase in neonates with liver affection **(Table 3)**.

Table (3): Comparison between both groups regarding liver function tests

Liver function test	Group I n = 80	Group II n = 20	T test	P value
ALT (U/dL)			109.053	0.0001*
Range	4.00-50.00	16.00-198.00		
Mean±S.D	20.40±10.71	87.15±53.81		
AST (U/dL)			114.319	0.0001*
Range	9.00-65.00	36.00-380.00		
Mean±S.D	34.05±14.30	137.05±82.51		
GGT (U/dL)			71.418	0.0001*
Range	14.00-625.00	104.00-640.00		
Mean±S.D	74.71±68.72	254.05±132.41		
PT (Sec)			27.237	0.0001*
Range	10.00-16.80	10.90-18.60		
Mean±S.D	12.63±1.40	14.66±2.06		
PTT (Sec)			39.603	0.0001*
Range	24.00-55.00	31.00-98.00		
Mean±S.D	33.87±5.85	48.86±18.06		
INR			11.844	0.001*
Range	0.10-1.80	0.90-2.00		
Mean±S.D	1.07±0.25	1.29±0.28		
Serum Albumin (gm/dL)			60.046	0.0001*
Range	1.80-5.20	1.20-4.20		
Mean±S.D	3.98±0.46	2.90±0.86		
TSB (mgm/dL)			1.94	0.05*
Range	0.80-80.00	0.30-18.50		
Mean±S.D	8.25±3.86	11.9±4.81		
DSB (mg/dL)			2.07	0.043*
Range	0.10-6.60	0.10-3.70		
Mean±S.D	0.69±0.77	1.11±0.99		
Alkaline phosphatase (IU/L)			39.017	0.001*
Range	91.00-625.00	160.00-783.00		
Mean±S.D	246.94±74.74	385.90±132.74		

t = student t-test, P was significant if ≤ 0.05, * Significant difference at level 0.05

ALT, Alanine transferase, AST, Aspartate transferase, GGT, Gamma glutamyl transferase, PT, Prothromine time, PTT, Partial thromboplastin time, INR, International Normalization Ratio, TSB, Total serum Bilirubin, DSB, Direct Serum Bilirubin

In our study, 15 babies (15/100, 15%) with hepatomegaly in abdominal U.S, 13 babies of those with hepatobiliary dysfunction with hepatomegaly in abdominal U.S (13/20, 65%), we noticed that neonates with liver affection showed significant increase in the incidence of hepatomegaly in abdominal U/S findings (P = 0.01).

Table (4): Comparison between both groups regarding abdominal U.S

Abdominal U.S	Group I n = 80		Group II n = 80	
	No.	%	No.	%
Normal	78	97.5	7	35.0
Hepatomegaly	2	2.5	13	65.0
X^2	6.58(S)			
P	0.01			

X^2 = Chi square test, P was significant if ≤ 0.05, NS = Not significant

Our results showed that neonates with liver affection had significant increase in the incidence of mortality (7/20, 35%) than those without liver affection and those of the overall mortality rate (P = 0.001) **(Table 5)**.

Table (5): Comparison between both groups regarding outcome

Outcome	Group I n = 80		Group II n = 20	
	No.	%	No.	%
Discharge	76	95.0	13	65.0
Died	4	5.0	7	35.0
X^2	8.64			
P	0.001 (S)			

X^2 = Chi square test, P was significant if ≤ 0.05

Our study demonstrates that neonates with liver affection had significant increase in the incidence of mortality (7/20, 35%) than those without liver affection and those of the overall mortality rate (P = 0.001), 3 babies (3/7, 42%) died before 7 days reassessment and 4 babies (4/7, 57%) died after (before day 21), with significant relation between mortality and neonatal sepsis in comparison to mortality with HIE **(Table 6)**.

Table (6): Comparison between outcome regarding HIE, neonatal sepsis

Outcome of hepatobillay dysfunction	HIE "n = 6"		N. sepsis "n = 12"	
	No.	%	No.	%
Died				
No	6	100.0	5	41.7
Yes	0	0.0	7	58.3
X^2	5.727*			
p	0.038* (S)			

X^2 = Chi square test, S = significant, HIE= hypoxic ischemic encephalopathy

Our study showed that after 2 weeks follow-up of patients there was a significant increase in number of patients still abnormal in babies with neonatal sepsis (5/9, 55%) in relation to babies with HIE (P = 0.44) **(Table 7)**.

Table (7): Comparison between prognosis of hepatobillay dysfunction in HIE, Neonatal sepsis regarding persistent hepatobillay dysfunction

Prognosis of hepatobillay dysfunction after 2 weeks reassessment	HIE "n = 6"		N. sepsis "n = 9"	
	No.	%	No.	%
No	6	100.0	4	44.4
Yes	0	0.0	5	55.6
X^2	5.0*			
p	0.044* (S)			

X^2 = Chi square test, N.S. = Not significant, * Significant difference when P <0.05
HIE, hypoxic ischemic encephalopathy

DISCUSSION

This prospective observational study carried out at El-Hussein University Hospital on 100 (one hundred) cases of neonates whom were followed up from first 3 days of admission to 10 days of admission for diagnosis of liver disorders.

Our results revealed a male predominance without difference in occurrence of liver insult regarding gender.

In disagreement with our study, **da Rocha and his colleagues, (2017)**, found that there was a predominance regarding female gender[6]. Also, **İpek and his colleagues, (2013)**, found that no predominance regarding gender which conflicting with our results **(İpek et al., 2013)**[16].

In agreement with our results **Yuri and coworkers, (2018)**, found that there was predominance regarding male gender[3].

Our study revealed a significant occurrence of liver insult in premature babies especially if of low birth weight.

Accepting with what we found hepatobilliary dysfunction commonly occurred in low birth weight, **da Rocha and his colleagues, (2017)**, found that the most babies was very low birth weight which[6].

Also, in agreement with our results **İpek and his colleagues, (2013)**, found that neonatal hepatobiliary dysfunction was common in babies with low birth weight[16].

In agreement with our results **Yuri and coworkers, (2018)**, found that liver insult commonly occurred in low birth weight neonates[3]. Also, **Clarke and coworkers, (2016)**, found that neonates with liver insult presented antenatally by intrauterine growth restriction, prematurity, hydrops fetalis, oligohydramnios, fetal hepatomegaly, and ascites which run in lines with our results[17].

Our results revealed a significant occurrence of CS between groups but this of no significance clinically in our study.

Accepting with what we found **da Rocha and his colleagues, (2017)**, found in that the most babies was delivered by CS[6]. Also, in agreement with our study **El-Kabbany and coworkers, (2017)**, found that most babies were delivered by CS method which was[11].

We noticed that The statistical analysis revealed predominance of CS delivery in admitted babies but this of no significance clinically in our study (P = 0.527)

Against our results, **Yuri and coworkers, (2018)**, found in their study that there were significant difference about mode of delivery, most babies was delivered by normal vaginal delivery[3]. In addition, **Mersha and his colleagues, (2019)**, found that there was no significance difference between mode of delivery by which the babies were delivered which disagree with our results[8].

Regarding the diseases, our study revealed neonatal sepsis, HIE, had a higher significant percentage of neonates with hepatobilliary dysfunction.

Comparable with our results, **Chalasani and his colleagues,**

(2015) and **Wendon with his colleagues, (2017)**, revealed that HLI is the most common cause of massive elevation of transaminase level in critically ill patients which was in agreement with our results[18, 19]. Also, **Yuri and coworkers, (2018)**, found that the baby in PICU had encephalopathy with evident signs of sepsis which was in agreement with our results that liver insult commonly occurred in neonates with neonatal hypoxia and sepsis[3].

Our results revealed a significant occurrence of PROM, and maternal comorbidities with no difference between neonates with liver affection or those without liver affection with irrelevant maternal history of DM, HTN and other historical elements.

In disagreement with our results **Mersha and his colleagues, (2019)**, found that there was no significance difference for occurrence of pregnancy induced hypertension, PROM in babies delivered with liver insult[8].

Our study revealed significant occurrence of liver insult in neonates with neonatal asphyxia especially with low Apgar score <3 at 5 min.

Conflicting with our results **da Rocha and his colleagues, (2017)**, found that the baby had APGAR score 6 and 8 after 1 min and 5 min.[6]. Also, **Yuri and coworkers, (2018)**, found that the APGAR score of the reported baby didn't affected by liver insult which disagree with our results[3]. In addition, **Mersha and his colleagues, (2019)**, found that there was no significance difference of occurrence of low APGAR score in neonates delivered with liver insults which disagree with our results[8]. And **Chiou with coworkers, (2017)**, found that there was no difference between babies with liver insults and those without liver insults regarding APGAR score at 1 min or 5 min which disagree with our results[20].

Regarding systemic examination there were no difference between babies with hepatobilliary dysfunction and those without liver insult regarding heart examination, chest examination, head and neck examination and examination of extremities with a significant occurrence of hypotonia in neonates with liver affection. On this way, **Yuri and coworkers, (2018)**, found that the baby had hypotonia which was in agreement with our results[3].

From the abdominal examination findings,

hepatomegaly and splenomegaly associated with significant higher percentage of neonates with hepatobilliary dysfunction.

In agreement with our results **da Rocha and his colleagues, (2017)**, found in that the baby had abdominal collateral, and hepatosplenomegaly[6]. Also, **Yuri and coworkers, (2018)**, found that the baby had marked hepatomegaly with bad general condition which was in agreement with our results[3].

Conflicting with what we found in our study **Taylor and Whitington, (2016)**, found neonates with acute liver failure didn't had hepatospelenomegally[21].

Regarding the lab finding neonates with elevated liver function tests "ALT, AST, GGT, PT, PTT and INR", had a significant percentage of hepatobilliary dysfunction.

Accepting with what we found in our study **El-Kabbany and coworkers, (2017)**, found elevated levels of AST, ALT, GGT, total and direct bilirubin in neonates delivered with hypoxia (Asphyxia) and explained this by liver insult due to damaging effect of hypoxia on liver[11].

Also, **Yuri and coworkers, (2018)**, found that the baby had elevated INR and PTT and PT due to coagulopathy which was in agreement with our results that liver insult associated with coagulation defects[3].

Against our results **Taylor and Whitington, (2016)**, found that their neonates with acute liver failure had either low or normal liver enzymes[21]. In addition, **Chiou and coworkers, (2017)**, found that there was no difference between babies with liver insults and those without liver insults regarding liver function tests (AST, ALT, GGT) which disagree with our results[21].

Alkaline phosphatase and CRP were significantly elevated in neonates with liver insult while no difference between regarding RBS, urea and serum creatinine.

In agreement with our results **Chiou and coworkers, (2017)**, found that there was a significant increase of alkaline phosphates enzyme in babies with liver insults than those without hepatobilliary dysfunction[21].

Neonates with liver affection showed significant increase in the incidence of positive blood C/S.) In agreement with our results Khalil and his colleagues, (2012), found that majority of infections were caused by positive blood culture especially for Gram

negative organisms (Klebsiella)[14].

Our results noticed a significant relation between hepatic affection and use of CPAP, mechanical ventilation without significant difference regarding use of nasal prong oxygen. **da Rocha and his colleagues, (2017)**, found that the baby needed MV shortly after birth[6].

We noticed that neonates with liver affection due to neonatal sepsis had significant increase in the incidence of mortality. In agreement with our results **Bhatia and his colleagues, (2013)**, reported in their study that **Squires with his coworkers, (2006)** found in their study that over 50% of cases of babies with liver insult in neonatal sepsis had poor outcome "died" except if subjected to liver transplantation[22].

Our study showed that after 2 weeks follow-up of patients there was a significant increase in number of patients still abnormal in babies with neonatal sepsis, **Khalil and his colleagues, (2012)**, found that at day 10 babies with neonatal sepsis still have statistical significant abnormal lab finding which run in line with our result, Chhavi and his colleagues, found that there was a statistical significant sharp decline of elevated lab value in babies with HIE which run in line with our results[14, 23].

CONCLUSION

We conclude that there was many risk factors and diseases associated with hepatobilliary dysfunction and persistent hepatobilliray dysfunction need further follow up and may affect the outcome.

RECOMMENDATION

Any baby admitted to NICU especially HIE, Neonatal sepsis must be investigated for liver function tests to rule out hepatobiliary dysfunction.

REFERENCES

1. **Carrero VMP and Piñeiro EO, (2004):** Liver. Pediatrics 113(Suppl. 3): 1097-1106.
2. **Wanless IR, (2002):** Anatomy, Histology, Embryology and Developmental Anomalies of the Liver. In: "Feldman M, Friedman LS, Sleisenger MH, eds., Sleisenger and Fordtran's Gastrointestinal and Liver Disease", 7th ed., Philadelphia, PA: WB-Saunders; Pp 1195-1201.
3. **Yuri V, Bayan H, Michael A, (2018):** Neonatal ischemic liver failure or entero-virus hepatitis presenting as acute fulminant liver failure. J Anesth Crit Care Open

Access 10(1): 00357-00362.

4. **Horvatits T, Drolz A, Trauner M, Fuhrmann V, (2019):** Liver Injury and Failure in Critical Illness. Hepatology 70: 2204-2215.
5. **Bitar R, Thwaites R, Davison S, Rajwal S, McClean P, (2017):** Liver failure in early infancy: etiology, presentation and outcome. J Pediatr Gastroentrol Nutr 64(1): 70-75.
6. **Da Rocha CRM, Guedes RR, Kieling CO, Adami MR, Cerski CTS, Vieira SMG, (2017):** Neonatal Liver Failure and Congenital Cirrhosis due to Gestational Alloimmune Liver Disease: A Case Report and Literature Review. Case Reports Pediat 2017(ID 7432859): 7 pages.
7. **Kamalakannan SK, (2018):** Neonatal sepsis: past to present. Br J Sci Tech Res 3(3): 3309-3314.
8. **Mersha A, Worku T, Shibiru S, Bante A, Molla A, Seifu G, Huka G, Abrham E, Teshome T, (2019):** Neonatal sepsis and associated factors among newborns in hospitals of Wolaita sodo Town, southern Ethiopia. Res Report Neonatol 9: 1-8.
9. **Hosseini MB, Abdoli Oskouei S, Heidari F, Sharif AS, Salimi Z, Sharif SAA, (2020):** Clinical Guideline Adaptation for Treatment of Neonatal Sepsis Based on Frequency of Microbial Agents. Iran J Neonatol 11(1): 1-11.
10. **Choudhary M, Sharma D, Dabi D, Lamba M, Pandita A, Shastri S, (2015):** Hepatic dysfunction in asphyxiated neonates: Prospective case controlled study. Clin Med Insights Pediatr 9: 1-6.
11. **El-Kabbany ZA, Hamza RT, Toaima NN, (2017):** Early Hepatic Dysfunction in Asphyxiated Full Term Newborns. J Gastroenterol 3(2): 1008s1-1008s5.
12. **Hartley J, (2011):** The child with abnormal liver function tests, 1st Global Congress CIP, Paris 2011.
13. **Limdi JK and Hyde GM, (2003):** Evaluation of abnormal liver function tests. Postgrad Med J 79(932): 307-312.
14. **Khalil S, Shah D, Kumar Y, et al., (2012):** Prevalence and Outcome of Hepatobiliary Dysfunction in Neonatal Septicemia. JPGN 54(2): 218-222.
15. **Tiker F, Tarcan A, Kilicdag H, (2006):** Early onset conjugated hyperbilirubinemia in newborn infants. Indian J Pediatr 73:409–12.
16. **İpek MS, Aydin M, Zençiroğlu A, Gökçe S, Okumuş N, Gülaldi NCM, (2013):** Conjugated hyperbilirubinemia in the neonatal intensive care unit. Turk J Gastroenterol 2013; 24 (5): 406-414.

17. **Clarke NE, Gilby D, Savoia H, Oliver MR, Rogerson S, (2016):** Fulminant liver failure in a neonate. J Pediatr Child Health 52(3): 338-341.

18. **Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, et al., (2015):** Features and outcomes of 899 patients with drug-induced liver injury: the DILIN prospective study. Gastroenterology 148: 1340-1352.

19. **Wendon J, Panel M, Cordoba J, Dhawan A, Larsen FS, Manns M, et al., (2017):** European Association for the Study of the Liver (EASL) Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol 66: 1047-1081.

20. **Chiou FK, Ong C, Phua KB, Chedid F, Kader A, (2017):** Conjugated hyperbilirubinemia presenting in first fourteen days in term neonates. World J Hepatol 9(26): 1108-1114.

21. **Taylor SA and Whitington PF, (2016):** Neonatal Acute Liver Failure. Liver Transplant 22: 677-685.

22. **Bhatia V, Bavdekar A, Yachha SK, (2013):** Management of Acute Liver Failure in Infants and Children: Consensus Statement of the Pediatric Gastroenterology Chapter, Indian Academy of Pediatrics. Ind Pediatr 50: 477-482.

23. **Chhavi N, Zutshi K, Singh N K, Awasthi A., et al., (2014):** Serum Liver Enzyme Pattern in Birth Asphyxia Associated Liver Injury. Pediatr Gastroenterol Hepatol Nutr 17(3):162-169.

انماط لاضطرابات الكبدية بالعناية المركزة لحديثى الولادة

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ان الكبد في الطفل حديث الولادة يظهر سمات فسيولوجية فريدة تعد غالبا جزء من عملية النمو الطبيعي للطفل. فالوظيفة الأساسية للكبد هي تصنيع مجموعة من بروتينات الجسم الضرورية وأداء وظائف أساسية عديدة متضمنا تصنيع البيليروبين وتنظيم بروتينات البلازما والجلوكوز وعملية التحول الحيوي للأدوية والسموم.

وهناك اضطرابات دائما ما تصيب الكبد وتؤدى الى اعتلاله ويتم فحصها بواسطة اختبارات الوظائف الحيوية والكيميائية وفحوصات متخصصة لأسباب مرض الكبد مثل البليروبين وإنزيمات الكبد وانزيم الفوسفاتاز القلوي وكذلك انزيم جاما جلوتاميل ترانسفيراز وعوامل التجلط مثل البروثرومبين والالبيومين. ثم ان هناك اختبارات أخري تُنفذ تتضمن فحص الاجسام المناعية لالتهاب الكبد كذلك دراسات الحديد والنحاس ونسبة بروتين الفا وان انتي تربسين والأجسام المضادة المتصلة بالسبب المحتمل للسبب المرض.

في الحقيقة ان أمراض الكبد تتأثر باضطرابات عديدة في مرحلة حديثي الولادة، الأكثر شيوعا منها: الإنتان الوليدي

واعتلال نقص الأكسجين بالدماغ.والدراسات الحديثة وجدت أن أمراض الركود الصفراوي تمثل 76% من أمراض الكبد في حديثي الولادة، السرطان 2%، أمراض التمثيل الغذائي 9%، فشل الكبد الحاد 2% وتليف الكبد 3%.ولكن الإنتان الوليدي يبقي واحد من الأسباب الرئيسية للاصابة والوفاة في كاملي وناقصي النمو من حديثي الولادة. وعلى الرغم من أن التقدم في العناية بحديث الولادة قد أدي إلي تحسُّن في معدلات النجاة وتقليل المضاعفات في الأطفال ناقصي النمو، الا انه مازال الإنتان الوليدي يساهم بصورة ملحوظة في الوفاة والأمراض بين ناقصي النمو في وحدات العناية بحديثي الولادة.فالإنتان الوليدي غالبا يتصل بخلل في وظائف أعضاء متعددة مما يؤدي إلي نسبة وفيات عالية ونتيجة حتمية سيئة. كالفشل في وظائف الجهاز الكبدي الصفراوي في صورة كدر صفراوي أو ارتفاع في انزيمات الكبد وهذا تم تسجيله في أكثر من ثلثي حديثي الولادة الخدج الذين اختبروا بعد اصابتهم بتسمم الدم البكتيريا بكتيريا سالبة الجرام. وهذا الاضطراب شائع عالمياً ويمثل 75% من حالات إعادة الدخول في المستشفيات في الأسبوع الأول من العمر.

أيضا وجد ان اعتلال نقص أكسجة المخ سبب رئيسي في العجز المزمن في الطفولة الذي ينتج من نقص الأكسجة النظامي ونقص ارواء خلايا المخ مؤديا إلي نقص الأكسجين في الدم في حديثي الولادة. وهذا يمكن أن يحدث قبل الولادة في 20% من الحالات، اوأثناء الولادة في 30%، أو بعد الولادة في 10% من الحالات. ان نقص الأكسجة في الدم يمكن أن

يؤدي إلي تلف لكل نسيج وعضو في الجسم والعديد من الأعضاء المستهدفة مثل الكبد والكُلي والجهاز العصبي المركزي والقلب والأوعية الدموية والرئتين.

وهذه دراسة نفذت لتعقب حدوث الاعتلال الكبدي وعوامل الخطورة المحتملة التي يمكن أن يواجهها الأطفال المحجوزين بوحدة العناية المركزة لحديثي الولادة. وهذه الدراسة نُفذت في مستشفي الحسين الجامعي علي مائة حالة من الأطفال حديثي الولادة الذين تم متابعتهم من يومين إلي أربعة عشر يوما لتشخيص اعتلالات الكبد وتاثيراتها.

وجاءت نتائج هذه الدراسة لتظه شيوع تواجد الذكور بالدراسة بدون اختلاف في معدل اعتلال الكبد في الجنسين.كذلك أظهرت حدوث الاعتلال الكبدي بشكل كبير في الأطفال الخدج وناقصي النمو من حديثي الولادة. وايضا أظهرت غلبة للأطفال الناتجين عن ولادة قيصرية لكن بدون اختلاف اكلينيكي في النتائج.

كذلك أظهرت شيوع ملحوظ للاعتلال الكبدى في حالات الإنتان الوليدي، نقص أكسجة المخ وشيوع بشكل أقل في أمراض القلب الوراثية وحالات ارتفاع الصفراء غير المباشرة والأعراض الأخري للاعتلال الكبدي.

أيضا نتائجنا أظهرت شيوع الاعتلال الكبدى في حالات التاريخ المرضي للأم بتمزق الأغشية المبكر والأمراض المصاحبة بدون اختلاف في النتائج بين التاريخ المرضي للأم المصابة بالبول السكرى وارتفاع ضغط الدم والعوامل

المرضية الأخري.بالإضافة لذلك أظهرت دراستنا حدوث واضح للاعتلال الكبدي في حديثي الولادة في حالات الاختناق الوليدي خاصة في مقياس Apgar أقل من 3 عند عمر 5 دقائق.

كذلك نتائجنا أوضحت حدوثا ملحوظا لتضخم الكبد والطحال في حديثي الولادة المصابين باعتلال الكبد بالفحص الاكينيكى للمريض. اما بالنسبة لفحص اجهزة الجسم المختلفة فلا توجد اختلافات بين الأطفال المصابين باعتلال الكبد وبدون اعتلال الكبد وهذا بالنسبة لفحص القلب والجهاز التنفسي والرأس والعنق والأطراف، مع حدوث واضح لنقص التوتر العضلى وحدوث ارتخاء عام في الأطفال المصابين باعتلال الكبد.