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DISORDERS OF THE NEONATAL LIVER AND BILE DUCTS

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SUMMARY

Introduction: Liver and biliary tract disorders in the neonate are relatively rare and often complex.

Aims: To evaluate the incidence of neonatal liver and biliary tract disorders, main causes, clinical presentation, treatment and outcome.

Material and Methods: Clinical, imagiological, laboratory, pathological and autopsy data concerning all newborns with liver and biliary tract disorder admitted to the neonatal intensive care unit of five tertiary medical centers from the north of Portugal, between 1997 and 2006, were retrospectively analysed.

Results: 77 neonates (incidence 0.5% – 77/14505 admissions); 44M/33F; gestational age 34 weeks (25-41); preterm 50 (65%); birthweight 1980g (570-4130), < 1500 g 29 (38%). Several causes were identified and classified as infectious, metabolic, anatomic/structural, neoplastic, vascular, traumatic, immune, genetic and idiopathic. Clinical signs appeared between days 1 and 61 of life. Jaundice was the most frequent clinical sign (92%). Cholestasis occurred in 67 (87%) patients. Duration of hospital stay was 35 days (5-146); 18 patients (23%) were deceased. Autopsy study was diagnostic in 8 cases (10%).

Conclusions: Nosocomial and intrauterine infection were the most common causes of liver and biliary tract disease. Several other rare causes represented an important challenge in diagnosis and treatment, and some were fatal. Awareness of the spectrum of liver and bile duct disorders in the neonate and recognition of the key clinical features are essential to optimize outcome.

RESUMO

DOENÇA HEPÁTICA E BILIAR NO RECÉM-NASCIDO

Introdução: No recém-nascido, as doenças com atingimento hepático e do tracto biliar são relativamente raras e frequentemente complexas.

Objectivos: Avaliar a incidência de doenças com atingimento hepático e biliar no recém-nascido, principais causas, apresentação clínica, tratamento e evolução clínica.

Material e Métodos: Análise retrospectiva de dados clínicos, imagiológicos, laboratoriais, anatomopatológicos e autópsias de recém-nascidos com doenças de atingimento hepático e do tracto biliar, admitidos nas unidades de cuidados intensivos neonatais de cinco centros hospitalares do norte de Portugal, entre 1997 e 2006.

Resultados: 77 recém-nascidos (incidência 0,5% – 11/14505 admissões); 44M/33F; mediana da idade gestacional 34 semanas (25 – 41); recém-nascidos pré-termo 50 (65%); mediana do peso ao nascimento 1980 g (570 – 4130), 29 (38%) com peso ao nascimento < 1500 g. Foram identificadas várias causas e classificadas como infecciosa, metabólica, anatómica/estrutural, neoplásica, vascular, traumática, imunológica, genética e idiopática. A apresentação clínica variou entre os dias 1 e 61 de vida. A icterícia foi o sinal clínico mais frequente (92%). Sessenta e sete doentes (87%) apresentaram colestase. A mediana da

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duração do internamento foi 35 dias (5-146); 18 doentes (23%) faleceram. A autópsia permitiu o diagnóstico em oito casos (10%).
Conclusões: As causas mais frequentes de doença hepática e biliar foram a infecção nosocomial e intra-uterina. Várias outras causas menos frequentes representaram desafios no diagnóstico e tratamento, e algumas foram fatais. O conhecimento do espectro etiológico das doenças com atingimento hepático e do tracto biliar no recém-nascido, bem como das principais manifestações clínicas, são essenciais para optimizar o tratamento e a evolução clínica.

INTRODUCTION

Liver and biliary tract disorders in the neonate are relatively rare and often complex. Some disorders can cause neonatal hepatitis syndrome, and in the majority of infants, the disease is not idiopathic[1]. Traumatic injury of the liver, usually birth related, associated or not to a vascular congenital anomaly is also rare, and may be a life threatening condition[2]. Awareness of the spectrum of diseases and recognition of the key clinical features of the various disorders is essential to optimize outcome. The consequences of a delayed diagnosis and inappropriate management may be fatal.

This study was conducted in order to evaluate the incidence of neonatal liver and biliary tract disorders in the neonatal intensive care unit (NICU), as well as the main causes, clinical presentation, treatment and outcome of the affected newborns.

MATERIAL AND METHODS

Of all newborns admitted to the NICU of five tertiary medical centers from the north of Portugal, between 1997 and 2006, those that had the diagnosis of any liver or biliary tract disorder, including traumatic injuries, were identified. These patients were those that presented with liver function tests abnormalities, or hepatobiliary morphological findings on abdominal ultrasound. Cholestasis was defined as a conjugated hyperbilirubinaemia > 2.0 mg/dl or > 20% of total serum bilirubin[3]. All clinical, image, laboratory, pathological and autopsy data were analyzed.

Causes of disorders were grouped as: (1) infectious; (2) metabolic; (3) anatomic/structural; (4) genetic; (5)

Table 1– *Demographics of the patient population*

Patients, n (%)	**77 (100)**
Male/Female, n (%)	44/33 (57/43)
Birthweight (g), median (min-max)	1980 (570-4130)
< 1500 g, n (%)	29 (38)
Gestational age (weeks), median (min-max)	34 (25-41)
Preterm, n (%)	50 (65)

Table 2 – *Clinical conditions (n = 77)*

Diagnostic category	**Number of cases (%)**
Infection	48 (62)
bacterial	40 (52)
fungal	1 (1)
enteroviral	1 (1)
congenital cytomegalovirus	2 (3)
congenital syphilis	3 (4)
congenital toxoplasmosis	1 (1)
Metabolic	7 (9)
perinatal haemochromatosis	3 (4)
cystic fibrosis	2 (3)
α1-antitrypsin deficiency	1 (1)
biliary lithiasis	1 (1)
Anatomic/structural	
biliary atresia	7 (9)
Genetic	
tetrasomy 9p	1 (1)
Neoplastic	3 (4)
haemophagocytic lymphohistiocytosis	1 (1)
liver haemangioendothelioma	2 (3)
Vascular	3 (4)
portal vein thrombosis	2 (3)
arterial calcification	1 (1)
Immune	2 (3)
factor D and E incompatibility	1 (1)
factor D incompatibility	1 (1)
Traumatic	3 (4)
liver laceration	2 (3)
liver contusion	1 (1)
Idiopathic	3 (4)
cholestasis	1 (1)
neonatal hepatitis	2 (3)

neoplastic; (6) vascular; (7) toxic; (8) immune; (9) traumatic; and (10) idiopathic[1]. Cases of total parenteral nutrition associated cholestasis were not included.

RESULTS

A total of 77 newborns with the diagnosis of liver or biliary tract disorder were treated at our institutions during the considered period. The incidence of these disorders in the total of NICU admissions was 0.5% (77/14505), which is about 1:188. The demographics of the patient population are reported in Table 1. Nosocomial and intrauterine infections were the most common causes, but several other rare causes were diagnosed, and some were fatal, Table 2. No toxic conditions were diagnosed in this study. Clinical signs were heterogeneous (Tables 3-6) and were present in the overall population by day nine of life (1-61). Jaundice was the most common clinical sign, occurring in 71 (92%) patients. Cholestasis was diagnosed in 67 (87%) patients. Eighteen (23%) patients were deceased. Autopsy was authorized in 12 (67% of deceased newborns) cases and was diagnostic in eight cases (10%). The overall median NICU stay was 35 days (5-146).

DISCUSSION

Liver disease in the neonate is a rare but serious cause of morbidity and mortality. Better awareness of the causes

Table 3 – *Characteristics and outcome of patients with infectious aetiology (n = 48)*

Diagnostic category	GA* (wks)	Day of presentation*	Clinical signs/ Laboratory	Other features	Study/ treatment	NICU stay* (days)	† n (%)
Bacterial and fungal infection [n = 41, including 37 (90%) preterm GA (25-36 wks)]	32 (25-40)	20 (1-61)	cholestasis = 41 hepatomegaly = 11 splenomegaly = 7 ascite = 2 elevation of AST/ALT = 23	congenital heart disease = 2 (Di George = 1) jejunal atresia = 1 cerebral arteriovenous malformation = 1	blood culture: gram - = 29 gram + = 11 fungi = 1 treatment: broad-spectrum antibiotic	59 (13-146)	7 (17)
Enteroviral infection (n = 1)	39	23	acute hepatitis: cholestasis, elevation of aminotransferases, spontaneous bleeding, coagulation disorder	fever diarrhea petechial rash	identification of echovirus in stools treatment: supportive	11	0
Congenital cytomegalovirus infection (n = 2)	35 (32–39)	1	hepatitis syndrome = 2 cholestasis = 2 thrombocytopenia = 2	cranial MRI: intracranial calcifications = 2	urine PCR positive for cytomegalovirus treatment: supportive	27 (19-35)	0
Congenital syphilis (n = 3)	38 (31-38)	1	hepatomegaly = 3 jaundice = 3 cholestasis = 3 elevation of AST/ALT = 2 thrombocytopenia = 1	macular rash including palms and soles = 2	VDRL + TPHA + FTAabs + biopsy: giant cell hepatitis = 1 treatment: penicillin	38 (16-42)	0
Congenital toxoplasmosis (n = 1)	29	1	cholestasis hepatic failure	hydrops fetalis hidramnio comatous > D36	autopsy: congenital toxoplasmosis with encephalomyelitis treatment: supportive	42	1

GA: gestational age at birth; * : results in median (min-max); † : deceased

Table 4 – *Characteristics and outcome of patients with metabolic aetiology (n = 7)*

Diagnostic category	GA* (wks)	Day of presentation*	Clinical signs/ Laboratory	Other features	Study/ treatment	NICU stay* (days)	† n (%)
Neonatal haemochromatosis (n = 3)	37 (31-39)	1	cholestasis = 3 hepatomegaly = 2 chronic liver failure = 3 increased serum ferritin = 3 thrombocytopenia = 2 coagulopathy = 1	ascite = 3 pleural effusion = 3	inconclusive MRI: cranial haemosiderin deposits = 1 autopsy: haemochromatosis = 3 treatment: supportive; N-acetylcystein, ursodeoxycholic acid,	26 (26-33)	3
Cystic fibrosis (n = 2)	32 (28-36)	1	cholestasis = 2 hepatic failure = 1 increased IRT = 2 ΔF 508 mut = 1	meconium ileus = 2	familial history = 1 autopsy: cystic fibrosis = 1 treatment: supportive	16 (8-24)	1
α1 antitrypsin deficiency (n = 1)	37	10	cholestasis elevation of alkaline fosfatase and γ glutamil transferase		low serum α 1 antitrypsin allelic variant PiZZ treatment: supportive	13	0
Biliary lithiasis (n = 1)	38	4	prolongued unconjugated hyperbilirubinemia		abdominal sonographic study – biliary lithiasis that resolved spontaneously during the first year of life management: expectant	13	0

GA: gestational age at birth; * : results in median (min-max); † : deceased

and their mode of presentation would lead to earlier diagnosis of treatable conditions, with considerable improvement in prognosis, and genetic counselling for those families with hereditary disorders.

Jaundice is usually the first sign of liver dysfunction, but its importance is often underestimated because of the frequent occurrence of physiological jaundice in the neonatal period. Infection is the usual cause of liver disease in NICUs, but several other rare causes represented important challenges in the diagnosis and treatment of the affected patients.

Infection

Infection was the most common cause of neonatal hepatitis syndrome in this study. Conjugated hyperbilirubinaemia may occur in the context of sepsis or localized extrahepatic infection. Gram-negative bacterial septicaemia is usually complicated with conjugated hyperbilirubinaemia. Jaundice may also occur with streptococcal and staphylococcal infections[1]. Serum aminotransferases may be slightly elevated. The liver and spleen are usually not enlarged. Microorganisms and their biologic products may have direct toxic effects on cells and structures responsible for the hepatocellular and ductal phases of conjugated bilirubin excretion[4]. This may be complicated by sepsis-induced haemolysis, further adding to the bilirubin load. Post-mortem examination of neonates with severe sepsis has shown centrilobular cholestasis, focal hepatocellular

Table 5 – Characteristics and outcome of patients with anatomic/ structural, genetic and neoplastic aetiology (n = 11)

Diagnostic category	GA* (wks)	Day of presentation*	Clinical signs/ Laboratory	Other features	Study/ treatment	NICU stay* (days)	† n (%)
Biliary atresia (n = 7)	39 (31-40)	12 (1-28)	unconjugated hyperbilirubinaemia = 1 cholestasis = 6 dark urine = 6 acholic stools = 4 elevation of γ glutamil transferase and alkaline phosphatase = 7	no	cholangiography = 7 treatment: Kasai portoenterostomy = 7	7(5-33)	0
Genetic (n = 1)	31	1	cholestasis hepatic failure	congenital diaphragmatic hernia ascites pleural effusion	tetrasomy 9p (47,XX, +i(9) (pter-p10::p10-pter).ish i(9) (wcp 9+) autopsy: biliary atresia treatment: surgical correction of congenital diaphragmatic hernia; supportive	33	1
Haemophagocytic lymphohistiocytosis (n = 1)	38	6	cholestasis ascites hepatosplenomegaly elevation of ALT/AST coagulation disorder elevation of α fetoprotein	no	bone marrow: inconclusiveautopsy: haemophagocytic lymphohistiocytosistreatment: supportive,desferrioxamine,transfusions	41	1
Hemangioendothelioma of the liver (n = 2)	35 (30-40)	3	hepatomegaly = 2	*Beckwith-Wiedmann* + exomphalos = 1	MRI: liver haemangioendothelioma = 2 management: expectant	34 (9-59)	1

GA: gestational age at birth; * : results in median (min-max); † : deceased

necrosis, and giant cell transformation in some patients. In others, no hepatic lesions can be demonstrated by light microscopy[4].

In this study, septicaemia related cholestasis occurred mainly in preterm newborns with prolonged hospitalization periods. Gram negatives were the most common bacterial agents associated with cholestasis. Mortality was 17%, including four patients with congenital anomalies.

Enteroviruses cause systemic viral infection in the newborn period, and severe hepatitis with acute liver failure may be a prominent feature. Vertical infection near the time of birth is associated with more severe disease in the infant. Most infants with enteric viral sepsis present between one and five weeks old[1]. Echovirus serotypes 3, 6, 7, 9, 11, 14, 19 and 21 have all been reported in severe infections with hepatitis.[5] Serotype 11 appears to be the most virulent for newborns.

Cytomegalovirus is the most common cause of congenital infection, affecting 1%-2% of newborns, most of whom are asymptomatic. Cytomegalovirus can cause neonatal liver failure, but this is uncommon. Neonatal hepatitis, when present, is usually mild and resolves completely. A few children develop hepatic fibrosis or non-cirrhotic portal hypertension. Intrahepatic calcification has been reported. Rarely, cirrhosis with chronic cholestasis eventually requires liver transplantation[1]. Cytomegalovirus is an important cause of giant-cell hepatitis. [6] In this study, the neonatal outcome of the two affected newborns was

Table 6 – *Characteristics and outcome of patients with vascular, immune, traumatic and idiopathic aetiology (n = 11)*

Diagnostic category	GA* (wks)	Day of presentation*	Clinical signs/ Laboratory	Other features	Study/ treatment	NICU stay* (days)	† n (%)
Portal vein thrombosis (n = 2)	39	7 (5-9)	unconjugated hyperbilirubinaemia = 2 hepatomegaly = 1 elevation of AST/ALT = 2	esophageal atresia = 1	Doppler sonography: thrombosis of the left arm of portal vein treatment: enoxiparin	27 (24-30)	0
Arterial calcification (n = 1)	36	1	unconjugated hyperbilirubinaemia acute hepatic failure	renal failure persistent pulmonary hypertension congestive heart failure ascites andpleural effusion	autopsy: calcification of the elastic layer of the medium calibre arteries with intimal hypertrophy,multiple organs including the liver. Liver presenting centrolobular hepatocitary necrosis and fibrosis treatment: supportive	33	1
Immune (n = 2)	37	2 (1-3)	cholestasis = 2	no	incompatibility: factor D = 1 factor D and E = 1	14 (12-16)	0
Traumatic (n = 3)	38 (34-39)	1 (1-13)	haemoperitoneum = 2 hepatomegaly=1 elevation of ALT/AST = 2	laceration = 2 (birth and thoracic surgery)contusion = 1 (birth)	ultrasound examination treatment: transfusional support hepatic packing = 1	8 (7-38)	1
Idiopathic (n = 3)	38 (35-40)	14(1-28)	unconjugated hyperbilirubinaemia = 2 cholestasis = 1 hepatitis syndrome = 2		inconclusive one case associated to severe combined immunodeficiency treatment: supportive	21(8-34)	0

GA: gestational age at birth; * : results in median (min-max); † : deceased

favourable with supportive therapy.

Congenital syphilis may cause intra-uterine growth restriction, anemia, and thrombocytopenia, nephritic syndrome, periostitis, nasal discharge (*snuffles*), skin rash and hepatomegaly. Jaundice may be present within 24 hours of birth, and it may be severe[7]. In this study, congenital syphilis cases were typical and the mothers, from a low socioeconomic status, had no pregnancy surveillance.

Congenital toxoplasmosis is rare and is usually associated with maternal infection in the third trimester. Neonatal hepatitis is prominent. Central nervous system involvement with chorioretinitis, hydrocephaly, and intracranial calcifications usually occurs, leading to convulsions, nystagmus and signs of increased intracranial pressure. The case in this study had a progressive worsening course culminating in death, and although the serologic study was negative, autopsy was diagnostic for toxoplasmosis with central nervous system involvement.

Metabolic

Several metabolic disorders result in hepatocellular injury in the neonatal period and give rise to a clinical pathologic syndrome that may resemble neonatal hepatitis or biliary atresia.

Neonatal haemochromatosis also called neonatal iron storage disease is an extremely rare severe liver disease in association with extrahepatic siderosis, in a distribution similar to that seen in hereditary haemochromatosis[8,9]. Its

pathogenesis remains uncertain. Most babies present shortly after birth, although a few have been diagnosed at 2-3 months of age[10-12]. Presenting findings are those of liver failure, characteristically with a discrepancy between aminotransferases elevation and hyperbilirubinaemia, and usually multi-organ failure with iron accumulation in liver, pancreas, kidneys, adrenal glands and heart[13,14]. Finding iron deposition in salivary glands on buccal biopsy or evidence of iron overload on magnetic resonance imaging supports the diagnosis. The prognosis in severe neonatal haemochromatosis is poor[13]. Treatment is supportive, aimed at reducing oxidative stress; liver transplantation may be required for survival[1,13].

In this study, the definitive diagnosis of neonatal haemochromatosis was established at post-mortem study. The salivary glands biopsies were inconclusive and the associated thrombocytopenia and/or coagulation disorder hindered the execution of a liver biopsy.

Cystic fibrosis may present with abnormalities of liver function tests or on liver biopsy in about one third of the affected patients. Hepatic pathology is highly variable. The spectrum of hepatic pathology includes giant-cell hepatitis, extrahepatic bile duct obstruction by inspissated bile, massive hepatic steatosis usually without conjugated hyperbilirubinemia, and paucity of small (portal tract) bile ducts. Neonatal hepatitis is very uncommon[15]. Many infants who have severe liver disease also have meconium ileus. In this study one of the cystic fibrosis patients was deceased (a 28 weeks gestational age/970 g birthweight female, deceased on day eight of life because of respiratory failure) and the autopsy revealed giant-cell hepatitis and thick mucous plugs in the terminal airways. Parents were first degree cousins and both carriers of a cystic fibrosis gene mutation (Δ F508).

Alfa1-Antritrypsin deficiency is the most common inherited cause of neonatal hepatitis syndrome. Only a small proportion ever develops liver disease. Cholestasis may be severe with totally acholic stools and a non-draining hepatobiliary scan. Clinical diagnosis rests upon finding low serum concentrations of α1-antitrypsin and identifying an allelic variant. The long-term outlook for infants with jaundice and α 1-antitrypsin deficiency is often very good, although a small proportion develop chronic liver disease[1].

Biliary lithiasis in the neonate is not usually associated to any maternal, obstetrical or fetal predisposing factor. The diagnosis is purely instrumental and is not correlated with known clinical or humoral data. The most frequent evolution is spontaneous resolution of the biliary echogenic images in the absence of clinical manifestations[16,17].

Anatomic/ structural

Biliary atresia involves a progressive destruction of the extrahepatic bile ducts with scarring, obliteration and concomitant damage to small and medium-sized intrahepatic bile ducts. Currently, biliary atresia is often categorized into two general patterns: embryonal/fetal or *early* and perinatal or *late*. The majority of infants have the *late* pattern. They appear to have had a normal biliary system, which has become involved in a fibrosing inflammatory process towards the end of gestation or shortly after birth. The cause of biliary atresia is unknown[18]. Approximately 10%-20% have additional congenital abnormalities[1]. Early diagnosis is vital because surgical treatment, the Kasai portoenterostomy, is less likely to be successful the later it is performed[19,20].

In this study we did not find any associated congenital anomalies in biliary atresia patients. All performed the Kasai procedure and one infant underwent liver transplantation by the age of two years.

Genetic

Some cytogenetic abnormalities, including trisomies 13 and 18, deletion of the short arm of chromosome 18 (46,XX,del 18 p-) and 49,XXXXY have been associated with biliary atresia[21]. An association between trisomy 21 and biliary atresia is not well substantiated[1]. Giant-cell hepatitis has been found in infants with cytogenetically confirmed trisomy 18[1]. In our revision, a female newborn (gestational age 31 weeks, bithweight 1810 g) presented with a dysmorphic syndrome including a left congenital diaphragmatic hernia. The cytogenetic analysis revealed a nonmosaic case of an isochromosome of the entire short arm of chromosome 9 with no involvement of the heterochromatic region of the long arm [47,XX, +i(9)(pter-p10::p10-pter).ish i(9)(wcp 9+)]. She died on day 33 of life and the post-mortem study revealed, along with other abnormalities, a biliary atresia[22].

Haemophagocytic lymphohistiocytosis

Haemophagocytic lymphohistiocytosis is a rare disorder involving inappropriate activation of macrophages. It is divided into a primary, familial form and a secondary form usually triggered by infection in a immunocompromised host[23]. The primary form can present as neonatal liver failure with hepatosplenomegaly, markedly abnormal liver function tests and a high serum ferritin which poses a differential diagnosis with neonatal haemochromotosis[24]. Other diagnostic clues are fever, raised triglycerides, hypofibrinogenaemia and cytopenias. The diagnosis is usually confirmed by evidence of haemophagocytosis in a bone

marrow aspirate. Initial management includes chemotherapy, usually dexamethasone and etoposide, but long term survival requires a bone marrow transplant[25]. In one series, five year survival was 21%[26]. Orthotopic liver transplantation is contra-indicated due to recurrence in the graft[24]. In this study, the clinical case of haemophagocytic lymphohistiocytosis was characterized by hepatosplenomegaly, abnormal liver function tests, high serum ferritin and cytopenias. The study was inconclusive. The diagnosis of a haemophagocytic lymphohistiocytosis was obtained at the post-mortem examination.

Haemangioendothelioma of the liver

Liver tumours are very rare and account for only 5% of all neoplasms in the fetus and newborn[27]. The most frequent are infantile haemangioendotheliomas. They may be incidental findings during pre or postnatal ultrasound investigation. However, not infrequently cause symptoms including abdominal distension and hepatomegaly, arteriovenous shunting with congestive heart failure, haemodynamic anaemia, thrombocytopenia and coagulopathy (*Kasabach-Merrit* syndrome), rupture with intraperitoneal haemorrhage, respiratory distress, and rarely, biliary obstruction and jaundice may occur. In cases with rapid growth or in patients with multiple lesions, a life-threatening status can develop shortly after birth or sometimes even during the fetal period with hydrops fetalis and intra-uterine heart failure. Most asymptomatic lesions can be managed expectantly, using serial ultrasound to visualize the anticipated spontaneous regression, as was verified in both cases in this study.

Portal vein thrombosis

Portal vein thrombosis in the neonate occurs early in life. Major risk factors are placement of umbilical venous catheter and severe neonatal illness[28]. In this study, the two reported cases were not related to umbilical venous catheter placement and, apparently, occurred spontaneously. The study was inconclusive for coagulation disorders in both cases and the outcome was favourable after anticoagulation treatment.

Arterial calcification

Idiopathic infantile arterial calcification is a rare disease characterized by extensive depositions of hydroxyapatite in the internal elastic lamina of medium-sized and large arteries, usually a fatal disorder[29,30]. In this study, a male newborn with a progressive multiorgan failure revealed, at post-mortem study, calcification of the elastic layer of the medium size arteries with internal hypertrophy in multiple organs including the liver. The liver presented centrilobular hepatocitary necrosis and fibrosis.

Immune

The *inspissated bile syndrome* is the term traditionally used for conjugated hyperbilirubinaemia complicating severe jaundice associated with haemolysis, usually due to Rhesus factor or ABO incompatibility, or erythrocyte abnormalities. Intra-hepatic cholestasis is found on liver biopsy, and cholestasis may be due to direct hepatocelular toxicity of unconjugated bilirubin. A multifactorial cause cannot be entirely excluded as these infants are often premature and present complex medical problems. The outcome is generally good, although early reports showed cirrhosis in some infants[1].

Traumatic

Although not true liver disorders, traumatic lesions of the liver or biliary system may occur and are usually a challenge for treatment. Traumatic bleeding conditions of the liver are rare in the neonate and usually related to birth injury, vascular abnormalities or coagulation disorders. They can be life threatening especially when massive bleeding follows traumatic, usually birth related, lacerations of liver[2]. Fortunately, in this study two out of tree neonates with liver traumatic injury had a good outcome.

Idiopathic

In a significant proportion of infants presenting with conjugated hyperbilirubinaemia before tree months old, no aetiology is found. These infants are classified as having idiopathic neonatal hepatitis, a condition of unknown and not necessarily unitary aetiology. The prognosis is generally good[1].

CONCLUSIONS

Disorders of the neonatal liver and biliary ducts affected 0.5% of the neonates admitted to our NICUs during the ten-year study period. Numerous causes were identified. Nosocomial and intrauterine infection were the most common causes of liver and biliary tract disease, and bacterial infection affected mainly preterm neonates with long hospitalization period. Several other rare causes represented an important challenge in diagnosis and treatment, and some were fatal. Awareness of the spectrum of liver and bile duct disorders in the neonate and recognition of the key clinical features are essential to optimize outcome.

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