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Abstracts

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ABS 1

PROLONGED JAUNDICE SCREENING: FULL BLOOD COUNT (FBC) OR NO FBC!

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INTRODUCTION

Prolonged jaundice is commonly defined as being jaundice beyond 14 days of age in term neonates and 21 days in premature neonates. The National Institute for Health and Care Excellence (NICE) recently updated guidelines on prolonged jaundice screening recommends a full blood count (FBC) to be included in the set of investigations. This is based on the evidence from 3 studies, 2 from Turkey and 1 from England. In these studies, FBC results did not provide any additional information towards identification of the causes for prolonged jaundice. In certain cases where FBC would have helped with the diagnoses, for example blood group incompatibility, other investigations like blood group and direct antigen test would have been more relevant. Additionally in rarer cases of G6PD deficiency, all of the haemoglobin results were greater than 125 g/l.

In light of poor evidence behind NICE recommendations for including FBC in prolonged jaundice screening, we reviewed all our cases of prolonged jaundice referred from the community to our neonatal department over a 12 month period during Jan-Dec 2015.

METHODS

All babies referred for prolonged jaundice were reviewed by a neonatal doctor with a detailed history to ensure the babies were well. Our investigations for prolonged jaundice screen included FBC, blood film, group and DAT, split bilirubin and LFT.

RESULTS

In total, 201 patients had FBC requested. Of these, 186 babies (93%) had a result for FBC. 12 (6%) samples were clotted and 3 (1%) were insufficient and never repeated. None of the FBC results contributed to any diagnoses relating to prolonged jaundice within our cohort of patients. Results are presented in **Fig. 1**. Overall, three patients were identified with anaemia (Hb < 94 g/l). Of these, one had conjugated hyperbilirubinaemia with no identifiable cause on further investigation, and the other two did not have any further investigations performed as they were not indicated clinically. Additionally, two cases identified a significant drop in haemoglobin by greater than 50 g/l (comparing FBC from prolonged jaundice screen to previous blood results where available) but neither had any further investigations at that time. One was later diagnosed with iron deficiency anaemia at nine months of age and the other was admitted at six weeks of age for a suspected infection and the haemoglobin had dropped further with possible haemolysis on the film. Of all the FBCs performed, a blood film was done on 21 (11%) samples. There were few results commenting on the presence of target cells, platelet clumps, some degree of hypochromasia, very few spherocytes, vacuolated neutrophils and atypical lymphocytes. In summary, of all the babies investigated for prolonged jaundice, FBC analysis revealed three cases of anaemia, and 2 cases of a comparative drop in haemoglobin. Fifteen babies had a clotted or insufficient full blood count but not repeated. This might be either due to practical difficulties in bringing babies back from community for a repeat FBC when the serum bilirubin results were unremarkable or parenteral consent to recheck FBC when bilirubin result was normal. Each FBC costs £ 2.81 which equates to a total cost of £ 522.66 for the 186 FBCs performed in 1 year for prolonged jaundice. While this is not a huge cost, there is additional impact on the babies when sampling bloods for tests of less diagnostic significance.

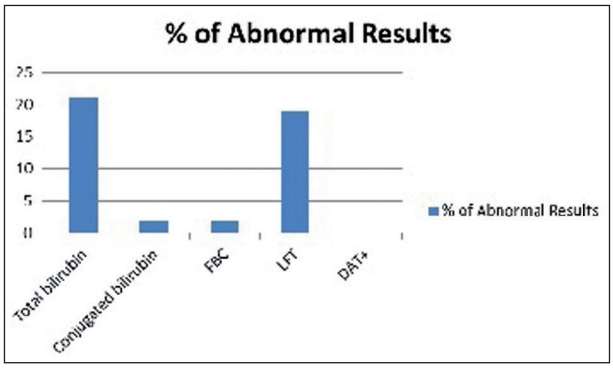

Figure 1 (ABS 1). Graph showing abnormal results detected in all babies investigated for prolonged jaundice who had a full blood count (FBC) completed.

CONCLUSIONS
In conclusion we did not find FBC as a useful test in prolonged jaundice screen. We recommend NICE committee to review evidence for this in larger studies, to avoid similar well babies with prolonged jaundice having unnecessary blood tests in other hospitals across UK.

ABS 2

EFFECT OF PROBIOTIC SUPPLEMENTATION ON BREAST MILK JAUNDICE

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INTRODUCTION
Breast milk jaundice (BMJ) is the most common cause of prolonged jaundice and is seen in 2-15% of all newborns. Many theories regarding its etiology have been formed but the exact mechanisms have not been elucidated. Being a condition, which currently does not have any specific treatment, BMJ continues to be a source of anxiety for parents and pediatricians. Recent studies have suggested that breast milk microbial content and subsequent neonatal intestinal flora may play a role in development of jaundice. Aim of this study is to evaluate the effect of probiotic supplementation on course of breast milk jaundice.
METHODS
This study was designed randomised and prospectively enrolling term and near tem babies who applied to our neonatal outpatient clinic with prolonged jaundice and eventually diagnosed as BMJ. A total of 112 babies consisting of 77 BMJ patients and 35 healthy babies was enrolled. Maternal and neonatal demographics were recorded. Thirty-seven of BMJ patients received probiotic supplementation for a week. Quantitative DNA of *L. rhamnosus*, *L. gasseri*, *L. plantorum*, *B. longum*, *B. bifidum* and *B. adolescentis spp.* was measured by real-time PCR in breast milk and fecal samples of all cases and fecal samples of BMJ patients a week later. Breast milk and fecal microbial content, effect of probiotic treatment on bilirubin levels, weight gain and fecal microbial content was compared between groups.
RESULTS
Demographics were similar between groups. Breast milk *L. rhamnosus*, *L. gasseri*, *L. plantorum*, *B. longum* and *B. bifidum* content, fecal *L. gasseri*, *L. plantorum* and *B. bifidum* content of BMJ patients were significantly lower than the control group ($p = 0.05$). Patients who received probiotic supplementation had lower mean bilirubin levels and higher rate of decline in bilirubin than patients who did not receive any treatment, but difference was not significant ($p > 0.05$). Time for dissolution of jaundice was significantly shorter in probiotic group ($p < 0.05$). Probiotic patients also had a higher weekly weight gain compared to patients who did not receive probiotic supplementation ($p < 0.05$).
CONCLUSIONS
There is accumulating evidence that breast milk and intestinal microbial content may play a role in development of breast milk jaundice. Many studies have shown that probiotic bacteria, particularly *Lactobacillus spp.*, decrease intestinal permeability. *Bifidobacterium spp.* are the predominant bacteria in the neonatal period, preparing the gut for colonisation of other probiotic species. These bacteria may reduce the intensity and duration of jaundice by increasing intestinal passage and decreasing permeability. The facts that BMJ patients has lower breast milk and fecal bacteria and probiotic supplementation has a reducing effect on bilirubin levels and duration of jaundice suggest that probiotics might be a treatment option for BMJ. Further investigation is required to determine the ideal combination, dose and duration of treatment for BMJ.

ABS 3

LABORATORY FINDINGS, DIAGNOSIS AND TREATMENT OF THE NEWBORN ADMITTED DUE TO HEMATEMESIS OR BLOODY STOOL IN 11 YEARS

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INTRODUCTION
Although bloody stool and hematemesis are well-recognized symptoms in the neonatal period, they are difficult to diagnose accurately. Many physicians diagnose by symptoms and laboratory data without using a colonoscopy or gastric fiberscope. Here, we report the symptoms, laboratory findings, final diagnosis and treatment of infants who were admitted to our hospital for bloody stool and/or hematemesis.

METHODS
We selected patients who had bloody stool and/or hematemesis and admitted to our hospital between January 2006 and December 2016. Gestational age, birth weight, administration of vitamin K, the age when infants had symptoms, age when infant were admitted to our hospital, laboratory findings, final diagnosis, treatment, and hospitalization were all extracted from medical records. The amount of bleeding was classified qualitatively as massive, medium or small by admission records or nursing records. Statistical difference was analyzed by the Wilcoxon rank sum test.
RESULTS
46 infants were included. 17 infants were male. 37 infants were transfer cases. Mean gestational age was 39 weeks and 5 days, mean birth weight was 3,008 grams. Frequency of oral vitamin K administration at the onset, 5 infants were not given, 15 infants were given one dose and 24 infants were given two doses. Hb levels of massive bleeding infants were significantly lower than those with a small amount of bleeding. Abnormal APTT and PT was seen in 10 infants. APTT and PT of the infants administered with one dose of vitamin K was significantly prolonged compared to those administered with two doses of vitamin K. Final diagnosis was acute gastric mucosal lesion suspected, anal fissure, vitamin K deficiency, milk allergy, and false melena. 41 infants received fluid therapy and 24 infants received vitamin K. Two infants in massive bleeding received blood transfusions.
CONCLUSIONS
However, two infants required blood transfusions in massive bleeding cases, all infants were making steady progress. Since all the infants were not evaluated with a gastrointestinal fiberscope, most cases were diagnosed by symptoms, blood laboratory findings and treatment. In laboratory findings together with case reports, some infants required an operation to stop bleeding. Massive bleeding cases required transfer to tertiary NICU.

ABS 4

AN UNUSUAL CAUSE OF CYANOSIS: SEVERE METHEMOGLOBINEMIA IN A PRETERM INFANT WITH SEPSIS

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INTRODUCTION
Cyanosis is an important physical finding with multiple causes in newborn infants. We present a preterm infant who developed severe methemoglobinemia associated with sepsis.
CASE REPORT
The baby was born prematurely with a gestational age of $31^{3/7}$ weeks and a birth weight of 1,215 g. He was admitted to the NICU, put on CPAP, inserted an umbilical venous catheter, and started total parenteral nutrition. On day of 14 because of increased apnea attacks and toxic-appearance tests for sepsis-workup was performed. Antibiotic therapy with Vancomycin and Cefotaxime was started empirically because of an indwelling catheter. Methicillin resistant staphylococcus epidermidis was grown in blood culture of the infant. On day 17, the 4^{th} day of antibiotic therapy the infant appeared cyanotic, irritable and had tremor. The cardiovascular examination was normal with no murmurs, no signs of respiratory distress or dehydration. Blood gas analysis revealed a methemoglobin level of 32%. Treatment with methylene blue, 1 mg per kg was immediately initiated. Over the course of few hours the methemoglobin level decreased to 4%, and not increased again until discharge.
CONCLUSIONS
Although methemoglobinemia is an uncommon cause of cyanosis, it should be suspected in differential diagnosis of toxic-appearing infants presenting with cyanosis, shock, and respiratory distress.

ABS 5

THE INFLUENCE OF INTRAUTERINE TRANSFUSION ON THE OUTCOMES OF NEWBORNS WITH SEVERE HEMOLYTIC DISEASE

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INTRODUCTION
Intrauterine transfusions are used for correction severe fetal anemia. This method prolongs pregnancy and improves the survival and outcomes of fetuses and newborns. Aim of the study is

to evaluate efficacy and safety of fetal anemia correction caused by Rhesus-D antibodies and neonatal outcomes after intrauterine transfusions.

METHODS

This is a retrospective study from 2007 to 2016 of all neonates with severe fetal anemia and presence early manifestation of hydrops. 34 newborns were included: 23 newborns after intrauterine transfusions (main group) and 11 without them (control group).

RESULTS

There is a higher delivery term, Apgar score on 1 min, hemoglobin at birth (101 g/l versus 71 g/l, $p < 0.05$) and less duration on IMV (49.5 h versus 201 h, $p < 0.05$). We observed significant increase ischemic (4.3% versus 36.3%; OR = 0.08; 95% CI: 0.007; 0.87) and hemorrhagic (13% versus 45.4%; OR = 0.18; 95% CI 0.03; 1.0) cerebral injuries in control group. There is not significant difference of neonatal morbidity.

CONCLUSIONS

Intrauterine transfusion is effective procedure for treatment of fetal anemia caused by alloimmunization and improves neonatal outcomes.

ABS 6

PATCHED SKIN BILIRUBIN ASSAY TO MONITOR EXTREMELY PRETERM NEONATES UNDERGOING PHOTOTHERAPY

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INTRODUCTION

Transcutaneous bilirubin (TcB) measurement is gaining popularity, as it is an easy, pain-free and blood sparing technique [1]. The use of modern transcutaneous bilirubinometers for full term and late preterm babies is contemplated by the American Academy of Pediatrics recommendations [2]. A recent meta-analysis pooled together data from babies less than 32 weeks' gestation and showed that TcB measurements are reliable in preterm neonates, as well [3]. Nonetheless, few extremely preterm neonates are included in this analysis and there are no data about TcB during phototherapy in extremely preterm infants. This represents the most extreme situation challenging TcB reliability but also a context where this technology might be very useful. Our aim is to verify reliability and safety of TcB measurements in patched skin areas in extremely preterm neonates under phototherapy.

METHODS

Sixty neonates (< 30 weeks' gestation) receiving phototherapy were enrolled and TcB was measured using a 2nd generation transcutaneous bilirubinometer (BiliCheck®, Philips, Eindhoven, Netherlands) in patched skin areas (of at least 2.5 cm diameter). TSB, lactate, pH, hemoglobin and skin temperature were measured within 10' from the TcB assay. Clinical decisions about phototherapy were taken only on TSB.

RESULTS

TcB and TSB showed a good correlation ($r = 0.84$; $p < 0.001$), which remains significant after adjustment for hemoglobin, pH, lactate, gestational and postnatal age (st. = 0.8; $p < 0.001$; $adjR^2 = 0.75$) or, in an alternative model, for treatment duration (st. = 0.8; $p < 0.001$; $adjR^2 = 0.7$). According to Bland-Altman analysis, TcB tends to overestimate TSB at high values (mean difference TSB-TcB: -48 (42) mol/L). Looking at TcB only, no neonate would have stopped the treatment prematurely and 21 (35%) would have continued phototherapy, when the treatment could have been stopped.

CONCLUSIONS

TcB reliability is fair in extremely preterm babies under phototherapy. Correlation between TSB and TcB (measured in patched skin areas) is comparable to that obtained in more mature neonates and it is not influenced by clinical variables and factors affecting skin bilirubin passage. TcB tends to overestimate TSB: monitoring TcB during phototherapy does not lead to undertreat babies and could spare about 65% of blood samples.

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DECLARATION OF INTEREST

D. De Luca received travel grants from Philips in the past. This company had no role at all in this study. The other author does not have any financial relationships relevant to this article to disclose.

ABS 7

A PRETERM MODEL OF HYPERBILIRUBINEMIA-INDUCED CEREBELLAR DYSFUNCTION

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INTRODUCTION

Free bilirubin (Bf), a metabolite of heme, is a known developmental neurotoxicant. In the US, the amount of total bilirubin (the sum of free Bf, albumin bound bilirubin and bilirubin conjugated to glucuronic acid) exceeds concentrations of concern (a condition known as hyperbilirubinemia) in almost all preterm neonates < 35 weeks gestation. It is possible for hyperbilirubinemia to reach a level of severity where the concentration of Bf exceeds the plasma's capacity to bind it. Then, Bf crosses the blood brain barrier and binds to its targets including the phospholipids of neurons. Once Bf crosses the blood brain barrier, bilirubin neurotoxicity can occur. In premature infants, bilirubin neurotoxicity may occur without obvious clinical symptoms. This condition can progress to chronic symptoms including motor incoordination and balance disorders. Despite the high prevalence of hyperbilirubinemia, the mechanisms underlying the effects of Bf on neuronal function are poorly understood.

METHODS

Heterozygous (HET) and homozygous (KO) Gunn rats (-UGT1A1) (GR) were treated on postnatal day (P) 5 (day of birth = P0) with either 200 mg/kg of sulfadimethoxine (SDMX) or an equivolume of saline. P5 rat pups have equivalent cerebellar development to a 25 week preterm infant. SDMX acutely increases serum Bf by displacing it from albumin. Both constant (6 rpm) and accelerating rotarod tests (from 4 to 45 rpm in 100 seconds) were performed on P28-30 (**Fig. 1**).

RESULTS

Both HET and KO GR showed no acute effects following SDMX injection. All treatment groups performed equally well on the constant rotarod. The SDMX injected KO pups (KO + SDMX) performed significantly less well than either HET group or the KO + saline group.

CONCLUSIONS

We conclude that an acute increase in Bf in preterm infant equivalent Gunn rats results in cerebellar dysfunction in adults. The mechanism underlying this effect remains unknown.

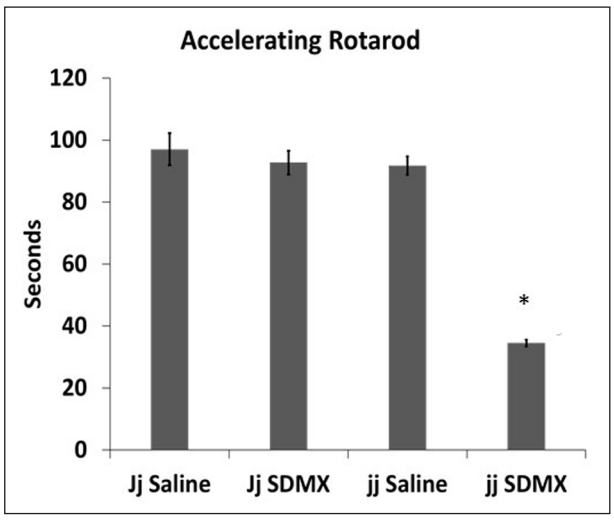

Figure 1 (ABS 7). Accelerating Rotarod. No significant differences between male and female pups.
*p < 0.0001 jj SDMX vs both jj saline and Jj SDMX.

ABS 8

PHYSIOLOGIC FREE BILIRUBIN REDISTRIBUTES L1 CELL ADHESION MOLECULE (L1) IN LIPID RAFTS

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INTRODUCTION

Hyperbilirubinemia is a common reason for developmental disability. Free bilirubin (Bf) is thought to be the neurotoxicant. Peak Bf in preterm infants requiring treatment are: very low birthweight infants: 8 nM (1.4-30.6 nM); low birthweight infants: 10.3 nM (4.1-29.6 nM). Bf binds phospholipids in cell membranes, which exist in either liquid-ordered domains (lipid rafts), or liquid-disordered domains (non-lipid rafts). The functions of L1 cell adhesion molecule (L1), a protein critical to cerebellum development, depend on trafficking through lipid rafts. Our hypothesis is that a physiologic concentration of Bf (5 nM) inhibits L1-mediated functions by disrupting L1 trafficking through lipid rafts. Our objective is to determine if a physiologic concentration of Bf redistributes the lipid raft distribution of L1 in cerebellar granule neurons (CGN).

METHODS

CGN were plated on poly-L-lysine and grown for 40 hours. Three hours prior to harvest, the cells

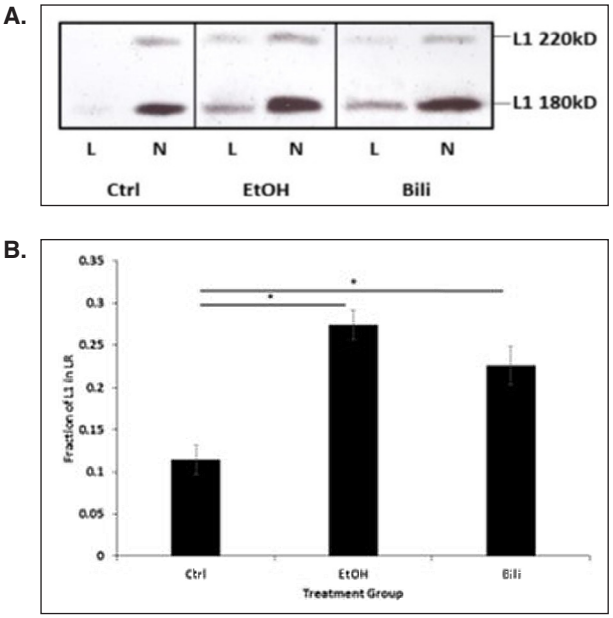

Figure 1 (ABS 8). A. Representative immunoblot for L1 in lipid raft (L) or non-lipid raft (N) pools of cells treated with no additives (Ctrl), 25 mM ethanol (EtOH) as a positive control, or 7.6 nM free bilirubin (Bili). **B.** The fraction of total L1 in the lipid raft pool. Mean ± SD are shown. Bili significantly increases the amount of L1 in the lipid raft compartment. *p < 0.05, two tailed paired t-test.

were serum starved. Culture media containing 5 uM bilirubin in 100 uM human serum albumin (measured Bf = 7.6 nM) was added and cells incubated for 1 h. Ethanol (EtOH) at 25 mM was added to some control cultures as a positive control. Cells were harvested and lipid rafts isolated by sucrose density gradients. The fraction of L1 in the L pool was calculated, mean ± SD were calculated across experiments and significance was determined by 2-tailed paired t-test.

RESULTS

Bf at 5 nM significantly increases the fraction of L1 in lipid rafts (**Fig. 1**).

CONCLUSIONS

Bf within the range found in preterm infants could potentially disrupt lipid raft protein trafficking leading to long term cerebellar dysfunction.

ABS 9

RETICULOCYTE HEMOGLOBIN CONTENT AS AN EARLY INDEX OF IRON DEFICIENCY IN NEONATAL PERIOD

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INTRODUCTION

Hemoglobin content of reticulocytes (CHr) is considered as an early marker of iron deficiency (ID) during infancy period and it seems to be superior of ferritin for evaluation of ID. Moreover, CHr is provided by many analyzers along with a whole blood count without additional blood loss or costs. However CHr has not been adequately studied during neonatal period. Our aim is to evaluate CHr, compared with ferritin, and blood count indices, as a marker of perinatal iron deficiency.

METHODS

Retrospective analysis of hematological parameters from the records of neonates who were hospitalized in a single-center during a six months period. In the study, were included the neonates with data on CHr at birth and CHr and ferritin at discharge. Complete blood count and reticulocyte parameters were measured with Cell-DYN Sapphire™ (Abbot) blood analyzer.

RESULTS

97 neonates were included in the study (BW 1,876 ± 637 g, GA 32.7 ± 3.3 weeks). There was not any correlation between CHr ferritin and CRP, but a positive correlation proved between CHr vs GA, MCH, MCV, Ht and Hb values both at birth ($p < 0.0001$) and at discharge ($p < 0.0001$). Multivariate analysis showed that MCV was an independent variable for the CHr. Neonates less than 32 w had significantly lower CHr values both at birth (32.1 ± 2.9 vs 34.3 ± 2.4, $p < 0.0015$) and discharge (30.7 ± 2.7 vs 32.7 ± 2.4, $p < 0.0003$).

CONCLUSIONS

A gradual reduction of CHr occurs during neonatal period with a correlation to GA. CHr seems to be an early marker of functional ID, not affected by infection. Further studies are needed to evaluate CHr could be used for the individualized monitoring of iron supplementation and follow up of premature neonates.

ABS 10

PREDICTION OF MAJOR BLEEDING IN EXTREMELY LOW BIRTH WEIGHT INFANTS (< 1,000 G) BY SEQUENTIAL COAGULATION MONITORING

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INTRODUCTION

Major bleedings such as intraventricular hemorrhage (IVH) and pulmonary hemorrhage (PH) are frequent in extremely low birth weight (ELBW, < 1,000 g birth weight) infants. A method of serial coagulation monitoring by measuring international normalized ratio (INR) with small volume samples (10 µL) provides an option for coagulation monitoring in ELBW infants. Thus, coagulation monitoring might facilitate prevention of major bleedings in ELBW infants and therefore improve outcome.

METHODS

This was a prospective longitudinal study performed at a single tertiary center (Department of Pediatrics, Medical University of Vienna, Austria) in ELBW infants, who received serial coagulation monitoring during their first 30 days of life. The primary objective was to explore whether monitoring of INR could predict major bleeding events (IVH, PH) in ELBW infants. The secondary objective was to explore whether sequential INR monitoring is feasible in this patient population.

RESULTS

127 ELBW infants were analyzed and divided in a bleeding and a no-bleeding group. 31% (39/127) of the infants developed any bleeding (IVH 21%, PH 5%, both 5%). Infants in the bleeding group were 4 days younger (bleeding group: median 25^{+2}, range 23^{+2}-29^{+0}; no-bleeding group: 25^{+6}, range 23^{+1}-33^{+4}; p = 0.05) and therefore more immature. Mortality in infants with bleeding events was 26% and significantly higher than in controls with 5% (p = 0.005). Median INR before a bleeding event was 1.5. Median INR in the first week of life in infants without any bleeding was 1.4 (p = n.s.).

CONCLUSIONS

Coagulation monitoring with this method is feasible in ELBW infants. However, there was no statistical difference between infants who developed any hemorrhage and infants who did not. Further studies with more frequent INR monitoring during the first day and during the first week of life might be more precise to detect major hemorrhage in ELBW infants.

ABS 11

IV FLUID SUPPLEMENTATION IN SEVERE NEONATAL HYPERBILIRUBINEMIA: YES OR NO

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INTRODUCTION

Severe hyperbilirubinemia is one of the most common causes of neonatal readmissions to hospitals, and phototherapy is the standard treatment for such infants. Dehydration is known to be associated with high serum bilirubin levels. It was suggested that serum bilirubin decreases much faster when full-term neonates with severe hyperbilirubinemia are given fluids in addition to phototherapy. However, other studies have revealed no relationship between extra fluid administration and bilirubin decrement. Aim of work: This study was designed to assess the effect of intravenous fluid supplementation during phototherapy on decreasing serum bilirubin levels in neonates with hemolytic or non-hemolytic hyperbilirubinemia.

METHODS

This is a retrospective case control study conducted on 100 newborns admitted to Latifa Hospital in the period of Jan. 2014 to 2015 with severe hyperbilirubinemia who needed intensive or double phototherapy. Infants were assigned into 2 groups: Group I (Case group with extra IV fluid supplementation), Group II (Control group with no IV fluid supplementation) (**Tab. 1**). These 2 groups were further subdivided to subgroups Ia, IIa: Hemolytic hyperbilirubinemia and subgroups Ib, IIb: Hemolytic hyperbilirubinemia.

RESULTS

There was a significant decrease in TSB level in Group Ia and b after 12-24 hours when compared to those upon admission (p < 0.01). On the other hand there was in significant change in TSB level upon admission compared to its level 12-24 hours in group IIa and b (p > 0.05). Length of stay didn't show any significant difference between the 2 groups.

CONCLUSIONS

In conclusion, extra fluid treatment in the first 24 hours in neonates with severe hyperbilirubinemia can significantly accelerate the reduction in the serum bilirubin levels in newborns with or without hemolytic disorder. On the other hand, length of stay was not influenced by IV fluid supplementation,

Table 1 (ABS 11). TSB in the 2 groups: Group I (case group with extra IV fluid supplementation), Group II (control group with no IV fluid supplementation).

	IV fluid group (n = 67)	Control group (n = 33)	p-value
TSB upon admission (mg/dl)	19.65 ± 2.64	18.32 ± 2.14	0.5
TSB 12-24 hours (mg/dl)	13.88 ± 1.90	13.92 ± 1.64	0.92
TSB upon discharge (mg/dl)	12.51 ± 1.44	12.52 ± 1.14	0.99
TSB difference (admission – 24 hours)	5.77 ± 2.67	4.409 ± 2.023	0.006[a]
TSB difference (admission – discharge)	7.13 ± 2.77	5.803 ± 2.29	0.013

TSB: total serum bilirubin; [a]significant.

this might be explained by limitation of IV fluid to first 24 hours of admission. Further study is needed to assess the effect of IV fluid supplementation in severely jaundice newborns on wider scale.

ABS 12

RIGHT SUBCLAVIAN ARTERY THROMBOSIS. A CASE REPORT

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INTRODUCTION

The highest predisposition to bleeding and thrombotic events occurs during the neonatal period due to altered levels of procoagulant, fibrinolytic and anticoagulant factors. Thromboembolism can occur at 10% of infants with central catheters, however, many of them are asymptomatic. It is important to watch closely those limbs with a peripherally inserted central catheter to avoid possible complications such as phlebitis, nosocomial infection and thrombotic events.

CASE REPORT

A preterm infant was born at 33^{+5} weeks, second triplet with a history of a triplet dichorial + monochorial/biamniotic gestation conceived after *in-vitro* fertilization, followed at high-risk pregnancy consultation. Normal serological screening tests. The pregnancy course was complicated with gestational diabetes insulinized at week 31. Prenatal ultrasounds were within normality. Cesarean delivery, not ruptured bag, no need for resuscitation. The Apgar scores were 8 and 9 points at 1 and 5 minutes, respectively, pH of the umbilical cord 7.34. Birth weight was 1,535 g. Positive evolution during admission, no respiratory support required, abdominal and cranial ultrasound and echocardiography within normality. 6 days after birth, a significant edema on the right upper limb was observed during manipulation of the patient. It extended from the shoulder to the elbow region where the peripherally inserted central catheter was located. Brachial and radial pulses were present. Doppler ultrasound examination of the limb showed right subclavian vein thrombosis so the catheter was removed. After regarding different managements, it was decided to apply low-molecular-weight-heparin under anti-Xa assays to adjust doses while sequential ultrasound controls of the vasculature of the right upper limb were performed. Ultrasound control at discharge showed the thrombosis was resolved which made possible the heparinization with drawls.

CONCLUSIONS

There is controversy about when to apply anticoagulant treatment in catheter-related-thrombosis cases in the neonatal period. An ultrasound follow-up and the catheter removal of the affected limb are always necessary. In those cases, in which the heparinization is performed, it is recommended to remove the central venous line within 3-5 days after beginning of the anticoagulation therapy.

ABS 13

RISK FACTORS FOR PORTAL VENOUS THROMBOSIS IN NEWBORNS: A RETRO-SPECTIVE STUDY

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INTRODUCTION

Portal vein thrombosis (PVT) is rare in newborns and its diagnosis during the neonatal period is frequently an incidental ultrasonography (USG) finding. The principal risk factor is UVC placement. Central lines can favor the thrombosis by several mechanisms: damage to the vessel wall, infusion of hypertonic solutions, disrupted blood flow, and thrombogenic catheter materials. In this pilot study our aim is to determine the incidence of PVT considering all UVC placement in patients who underwent an abdominal ultrasonography from January 2012 to December 2014 in our NICU in order to identify possible risk factors and define a systematic or targeted approach in our caring attitude.

METHODS

All newborns with a gestational age (GA) ≥ 32 weeks and a weight ≥ 1,500 g admitted to the NICU at the Robert Debré Hospital (Paris) from January 2012 to December 2014, were considered eligible for this retrospective study if a UVC was placed and if they underwent an abdominal radiography and at least one USG. Clinical data referred to the pregnancy (maternal diabetes or preeclampsia, antenatal steroids, thrombophilia), the birth (gestational age, birth weight, gender, Apgar score at 5 minutes, funicular venous pH and lactates) and the clinical evolution within the first week in the NICU (hypothermia, sepsis, inotropic drugs, polycythemia and thrombocytopenia) were recorded. PVT grade, the eventual anticoagulation treatment, the follow-up USG and the outcome of the PVT were also gathered.

RESULTS

31 portal thromboses, on the total of 121 patients, were found. No significant differences were detected between case and controls in term of gender, weight, gestational age (GA) or intrauterine growth. All clinical data referred to the pregnancy, the birth and the clinical evolution are shown in **Tab. 1**. In case group patients with a grade I thrombosis was 13 (42%), grade II 13 (42%) and grade III 5 (16%). Hypothermia, a lower Apgar at minute 5, a higher CRP at days five and higher lactates values in the first hour resulted significant in statistical analysis of cases versus controls. Analyzing all the patients born with a GA > 36 weeks (n = 74), hypothermia was identified as a significant risk factor ($p < 0.05$), moreover all the patients with PVT who underwent hypothermia had a grade II.

CONCLUSIONS

This study confirms that infections, hypoxemia and systemic inflammation can be identified as possible risk factors to develop thrombosis. A high incidence of PVT in neonates treated with therapeutic hypothermia suggests that abdominal USG screening may be reasonable in many of these children.

Table 1 (ABS 13). Main characteristics of cases and controls.

	Case (n = 31)	Controls (n = 90)	p-value
Female/Male	13/18	39/51	NS
Gestational age (mean)	37	37	NS
Preeclampsia	4 /31 (13%)	4/90 (4%)	NS
Gestational Diabetes	7/31 (23%)	8/90 (9%)	NS
Corticotherapy	7/31 (23%)	20/90 (22%)	NS
Weight (p)	2,539 (31st)	2,495 (35th)	NS
IUGR	7/31 (23%)	25/90 (28%)	NS
Apgar (5 min)	7	8.1	$p < 0.05$
Days	3.6	3.2	NS
UVC c/p 1	17/31 (55%)	58/90 (64%)	NS
UVC C/P 2	45%--> 21% c	40% 50%	NS
Sepsis	11/31 (35%)	20/90 (22%)	NS
Hypothermia	8/31 (26%)	9/90 (10%)	$p < 0.05$
Inotrope	39% 67%	24% 54%	NS
Thrombocytopenia	55% 41% (50,000)	33% 27%	NS
CRP day 5 (> 10)	18/31	21/90	$p < 0.005$
Lactate	9.91	6.7	$p < 0.05$

ABS 14

COMPARISONS BETWEEN TRANSCUTANEOUS BILIRUBINOMETRY, POINT-OF-CARE WHOLE BLOOD BILIRUBIN AND TOTAL PLASMA BILIRUBIN MEASUREMENT IN NEONATES

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INTRODUCTION

Jaundice is a common condition that requires medical attention in neonates. Clinically decision making for treatment is made according to the

Bhutani nomogram. Differences in analytical results between laboratory methods create uncertainty in decision making. Transcutaneous bilirubinometry (TcB) is a simple, reliable, non-invasive method for screening bilirubin levels in neonates. To follow up elevated readings a whole blood bilirubin (WBB) method was evaluated. In comparison with total plasma bilirubin (TPB) methods, whole blood methods require less blood, are used as a point-of-care testing (POCT) and can easily be combined with a full set of blood gas analyses within the same amount of blood.

METHODS

We compared TcB, WBB and TPB in neonates born at term and near-term (> 35 gestational weeks). 93 neonates with suspected icterus and birth weights between 2,400 and 5,000 grams were studied. 62 (67%) of these babies were born via normal delivery and 31 (33%) were born via instrumental delivery. Bilirubin measurements were made between 16 and 173 hours of age. TcB was measured initially and within 30 minutes two blood samples were obtained; one was analysed immediately at the POCT blood gas instrument (ABL825 FLEX, Radiometer A/S) and one was sent to the hospital laboratory for determining TPB (BILT3, Cobas8000, Roche). Correlations between the methods were calculated and the agreement between the laboratory methods was evaluated with a Bland-Altman plot.

RESULTS

The readings from TcB had a range of 1-339 µmol/L. Corresponding invasive measurements had a range of 19-487 µmol/L for WBB and 11-442 µmol/L for TPB. An acceptable correlation (R^2 = 0.9162) was observed between WBB and TPB with a positive intercept (y = 1.0626x + 16.274) for WBB. The correlations between TcB vs WBB and TcB vs TPB were lower: R^2 = 0.7169 and R^2 = 0.7152 respectively and the intercepts were larger showing that TcB underestimates the blood/plasma concentration of bilirubin. The agreement between the two invasive methods was evaluated in a Bland-Altman plot visualizing an average positive intercept of 34 µmol/L and an average uncertainty of ± 24 umol/L per standard deviation (SD). Evaluation of the correlation between the two methods in laboratory setting with hemoglobin free plasma showed a high correlation (R^2 = 0.9986) and a much smaller positive intercept (y = 1.033x – 0.4687).

CONCLUSIONS

We found a significant difference between the three bilirubin methods. We also found the POCT whole blood bilirubin (WBB) analysis the overall most useful and reliable method for decision making regarding treatment. It offers small sample volumes, availability and has no interference from physiological hemolysis. The short time between sampling and analysis causes minimal bilirubin degradation in the sample due to light exposure.

ABS 15

RELATIONSHIP BETWEEN PLASMA LEVELS OF BILIRUBIN AND OXIDANT/ANTIOXIDANT STATUS IN THE EARLY NEONATAL PERIOD IN PRETERM INFANTS

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INTRODUCTION

Bilirubin is mostly infamous for its neurotoxicity, causing bilirubin encephalopathy or 'kernicterus' in the newborn. However, some previous studies suggest that bilirubin may be beneficial for its antioxidative capacity. Preterm infants are known to be more susceptible to damaging effects of oxidative stress than their term counterparts because of immature defense antioxidant mechanisms. Therefore, the aim of this study was to investigate a relationship between plasma levels of bilirubin and indices of oxidative stress in preterm newborn infants.

METHODS

We conducted a prospective cohort study in preterm infants born at ≤ 36 weeks gestation, who were admitted to the NICU of Perinatal Center, Tokai University Hospital. Residuals of routine daily blood tests were collected on day 0, 1 and 2 for determination of total bilirubin (TB), unbound bilirubin (UB), total hydroperoxides (TH), as a measure of oxidative stress and redox potential (RP) as a measure of antioxidant potential. Changes over postnatal days were tested by repeated measures ANOVA with Bonferroni post hoc test. Correlations with gestational age were analyzed using Spearman's rho. Correlations for all other variables were analyzed with Pearson's correlation test. P-values < 0.05 were considered significant.

RESULTS

Nineteen preterm infants were included in this study. Their median gestational age was 34.4 (IQR:

32.4-35) weeks and the median birth weight was 1,968 (IQR: 1,607-2,062) grams. Both TB and UB increased over postnatal days 0-2. TH was significantly higher on day 1 and 2 than on day 0, but not different between day 1 and 2. There was a tendency of an increase in RP and a decrease in RP/TH ratio over postnatal days 0-2, but both did not reach statistical significance. We found no correlation between TB, UB, TH, RP or RP/TH ratio. There was a negative correlation between the change in RP from day 0 to day 1 and gestational age ($r = -0.69$, $p = 0.004$, $n = 15$). All other tested variables were not correlated with gestational age.

CONCLUSIONS

Indices of antioxidant capacity in the plasma did not show a significant increase in spite of an increase in serum bilirubin in the early neonatal period. Our present results did not demonstrate evidence of bilirubin being a significant antioxidant. However, more studies should be required to draw a definitive conclusion with a larger sample size and/or different techniques to assess the level of oxidative stress.

ABS 16

RELATIONSHIP BETWEEN LEUKOCYTES AND PLATELETS AND PREMATURE RETINOPATHY

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INTRODUCTION

Are the other parameters important for occurrence and severity of premature retinopathy (ROP) except hours of oxygen exposure? Can the values of leukocytes and platelets be taken into consideration as indicators of the infections, when we follow up these premature babies for ROP?

METHODS

The purpose of this study was to establish if there is a relationship between these parameters and presence of ROP and its severity. We noted the leukocytes (L) and platelets (Plt) values during hospitalization of the premature newborns screened for ROP during one year. We analyzed these infections parameters in those who developed ROP comparative with those who did not developed ROP forms. Furthermore we analyzed the dynamics of these parameters in those who required treatment related to those premature in which ROP has regressed. The study included 105 premature newborns with gestational age < 34 weeks, and birth weight < 2,500 g. 26 cases (24.76%) developed ROP, 7 cases of them (26.92%) required treatment.

RESULTS

The results in dynamics for those who developed ROP were: a) leukocytes were statistically significant at the 8th examination ($p = 0.039$); b) platelets were statistically significant at the 6th examination ($p = 0.013$). These parameters in the treated cases were not statistically significant (the number of treated cases was small).

CONCLUSIONS

The values of leukocytes and platelets in dynamic as indices of infections in premature newborn can be taken in consideration in the development of ROP. About the indices for severity of these parameters we will analyse in future on a large number of cases.

ABS 17

CONGENITAL HEPATOCELLULAR CARCINOMA ASSOCIATED WITH NEONATAL HEMOCHROMATOSIS

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INTRODUCTION

Severe fibrotic liver disease in the newborn indicates the onset of liver injury during fetal life. Such disease has been called "congenital cirrhosis" and has been associated with the neonatal hemochromatosis phenotype. The most frequent cause of fetal liver injury leading to congenital cirrhosis and the neonatal hemochromatosis phenotype is gestational alloimmune liver disease (GALD). GALD-related alloimmunity is specifically directed at fetal hepatocytes. Maternal-fetal alloimmunity is mediated by IgG. Maternal antibodies of the IgG class are actively transported across the placenta to the fetus from about the 12th week of gestation when FcRn (the IgG chaperone) is first expressed.

CASE REPORT

A female infant with acute liver failure due to neonatal hemochromatosis (NH) underwent orthotopic liver transplantation at the age of 38 days. Soon after the reperfusion of the liver, massive abdominal and pulmonary hemorrhages due to intravascular disseminate coagulopathy happened and the baby

died. The explanted liver was studied: it was small, micro-and macronodular and deeply bile-stained. On microscopy, a micronodular cirrhosis was evident with the residual hepatocytes exhibiting either giant-cell or pseudoacinar transformation, with canalicular bile plugs. Regenerative nodules were present and one macronodule (1 cm in diameter) showed the features of a hepatocellular carcinoma HCC). Siderosis was more severe in non-neoplastic liver than in HCC.

CONCLUSIONS

In the pathogenesis of GALD, injury to fetal hepatocytes leads to regeneration and fibrosis. This pathophysiologic process occurs in the background of developing liver and represents chronic liver disease of the fetus. Beginning around midgestation and extending to term, immune injury to hepatocytes predisposes to abnormal fibrogenesis and aberrant regeneration that, even if rarely, may culminate in the malignant transformation and cause HCC.

ABS 18

INVESTIGATION OF THE RELATIONSHIP BETWEEN UMBILICAL CORD BLOOD RMI LEVEL AND PERINATAL EVENTS

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INTRODUCTION

Newborn hematopoiesis shows differences from adults. By the advances in technology, exact reticulocyte counts and new reticulocyte parameters can be calculated which carry significant value to clinicians. A new parameter (reticulocyte maturity index, RMI) which represents an independent parameter of erythropoiesis gives a great hope for the future. In this study, establishment of reference intervals of RMI for newborns was planned for use in the clinics according to available clinical and demographic characteristics of the baby and mother.

METHODS

A study was conducted at the Kirikkale University Medical Faculty Hospital with 123 newborn who carry criteria of inclusion. Umblical venous blood samples are taken into suitable tubes immediately after cord clamping in the delivery room and send to the hospital laboratory. Beckman Coulter® LH 780 was used for the CBC and RMI parameters and Siemens Rapidlab® 348 for blood gas parameters. For the reference ranges, 2.5 and 97.5 percentiles were used.

RESULTS

Study group was consisted of 59 female and 64 male newborns. 24 of the babies born as preterm and 99 of the babies as term. 32 of the babies born with vaginal birth while 91 of them with caesarean section. As percentiles of birth, 19 of the baby was SGA, 98 of them AGA and 6 of them LGA. There was a history of preeclampsia in 10 mothers, diabetes in 7 mothers, multiple pregnancy in 4 mothers and smoking in 14 mothers. There was no significant difference between groups for RMI, but gestational week. Term newborns have higher median RMI values than preterm ones. RMI median value and reference range was 0.51 and 0.16-0.85 for general group, 0.34 and 0.16-0.73 for preterm newborns and 0.52 vs 0.17-0.89 for term newborns, respectively. There were significant differences between groups for CBC and blood gas parameters.

CONCLUSIONS

The results of this study showed that newborns need their special reference ranges for RMI by showing similar results with the literature, which has similar study populations while showing differences from the literature, which has not similar study populations.

ABS 19

OUTCOME OF BABIES WITH SERUM BILIRUBIN LEVEL OF GREATER THAN 400 MICROMOL/L

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INTRODUCTION

Jaundice is one of the most common conditions requiring medical attention in newborns with 60% and 80% of term and preterm babies developing jaundice in the first week of life respectively. A double volume exchange transfusion is performed in babies with bilirubin levels at or above exchange thresholds specific for gestation and/or with clinical features and signs of acute bilirubin encephalopathy. Intravenous Immunoglobulin is used as an adjunct to phototherapy in cases of Rhesus/ABO hemolytic disease as per the NICE guidance.

METHODS

Babies with SBR > 400 micromol/L were identified from the biochemistry department over a 3 year period between 01/01/2013 and 31/12/2015. The management and outcomes were extracted from

the maternity K2 and neonatal Badgernet electronic patient databases. A standardised proforma was used to collate the data.

RESULT

21 babies were identifies with SBR > 400 micromol/L during this period. 14 babies (66%) were readmissions from home. 3 babies had ABO incompatibility and 2 babies had G6PD deficiency (SBRs 426 and 457). Two babies admitted from home with SBRs of 714 and 566 had exchange transfusions. One baby from postnatal ward with SBR of 649 needed exchanged transfusion despite treatment with IVIG. The rest of the babies were managed with phototherapy + intravenous fluids and/or management for possible sepsis. There were no babies with positive blood culture or a significant CRP level. All babies were discharged home.

CONCLUSIONS

In our review, only 3 babies had "extreme" hyperbilirubinaemia (SBR > 510 micromol/L) who were managed with exchange transfusion. The remainder of the babies were managed with phototherapy and intravenous fluids. The small number of cases with "extreme" hyperbilirubinaemia could be a reflection of early identification of jaundice following strict adherence to the NICE guidance, which was published in 2010.

ABS 20

AN AUDIT OF USE OF EMERGENCY 0 NEGATIVE BLOOD IN NEONATES FOR EMERGENCY BLOOD TRANSFUSIONS AND EXCHANGE TRANSFUSIONS

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INTRODUCTION

A stock of emergency 0 negative blood is always kept in the operating theatre of our hospital in case of need for an emergency blood transfusion in a newborn. This blood is also available for use in an exchange transfusion situation, if deemed suitable for an infant with haemolytic disease of the newborn (HDN). This blood contains some plasma including factor VII and IX and is therefore different from the SAGM (Saline Adenine Glucose Mannitol) blood used in the preparation of paedipacks for neonates. Therefore, theoretically emergency 0 negative blood is thought to be more suitable for the newborn infant with DIC as it contains some clotting factors. However the frequency of use and indications for use of this emergency 0 negative blood in our institution is unknown. Aims: 1) To quantify the use and examine the indications for use of emergency 0 negative blood for neonates in our hospital over the last 10 years; 2) To examine the haematological and bilirubin indices for each infant who received emergency 0 negative blood over the last 10 years; 3) To review index infants for evidence of coagulopathy (clinical or laboratory) with a view to examining whether SAGM blood instead of emergency 0 negative blood could just as safely have been used for these emergency transfusions despite the lack of clotting factors in SAGM blood; 4) To calculate the exact time between the official request for blood for exchange transfusion from the haematology laboratory and actual time of exchange transfusion commencing.

METHODS

We performed a review of the haematology laboratory database to identify index infants who received emergency 0 negative blood. We performed a review of the medical notes for these patients. The length of time taken to initiate transfusion was calculated by looking up the time the request was logged on the laboratory computer system to the time of commencement of transfusion, as stated in the medical notes. We also collected haemoglobin and bilirubin results for index infants from our online laboratory results system.

RESULTS

We identified 71 babies who received emergency 0 negative blood over the 10 year study period.

The indications for transfusion are outlined in **Fig. 1**. In some cases there was more than one indication for transfusion. In the APH group, the specific diagnoses were: vasa praevia (3), placenta praevia (1), placental abruption (2), fetomaternal haemorrhage (9), undefined APH (5). In the HDN group there were 8 cases of Rh HDN and 3 cases of other HDN. In the group with acute haemodynamic instability the causes were: pneumothorax (2), pneumothorax with haemorrhage into fractured femur (1), multiple AVMs (1), HIE and PPHN (1) and instability of undetermined causes (13). The group with postnatal haemorrhage consisted of: pulmonary haemorrhage (8), umbilical stump bleeding (3), subgaleal haemorrhage (5), haemorrhage from sacrococcygeal teratoma (1). Pre-transfusion Hb values were not available in all patients. In this instance, we recorded the earliest Hb taken post-transfusion. The average Hb value was 8.8 mg/dl, with a range of 2.2-19.9.

Bilirubin values were measured for 10 patients

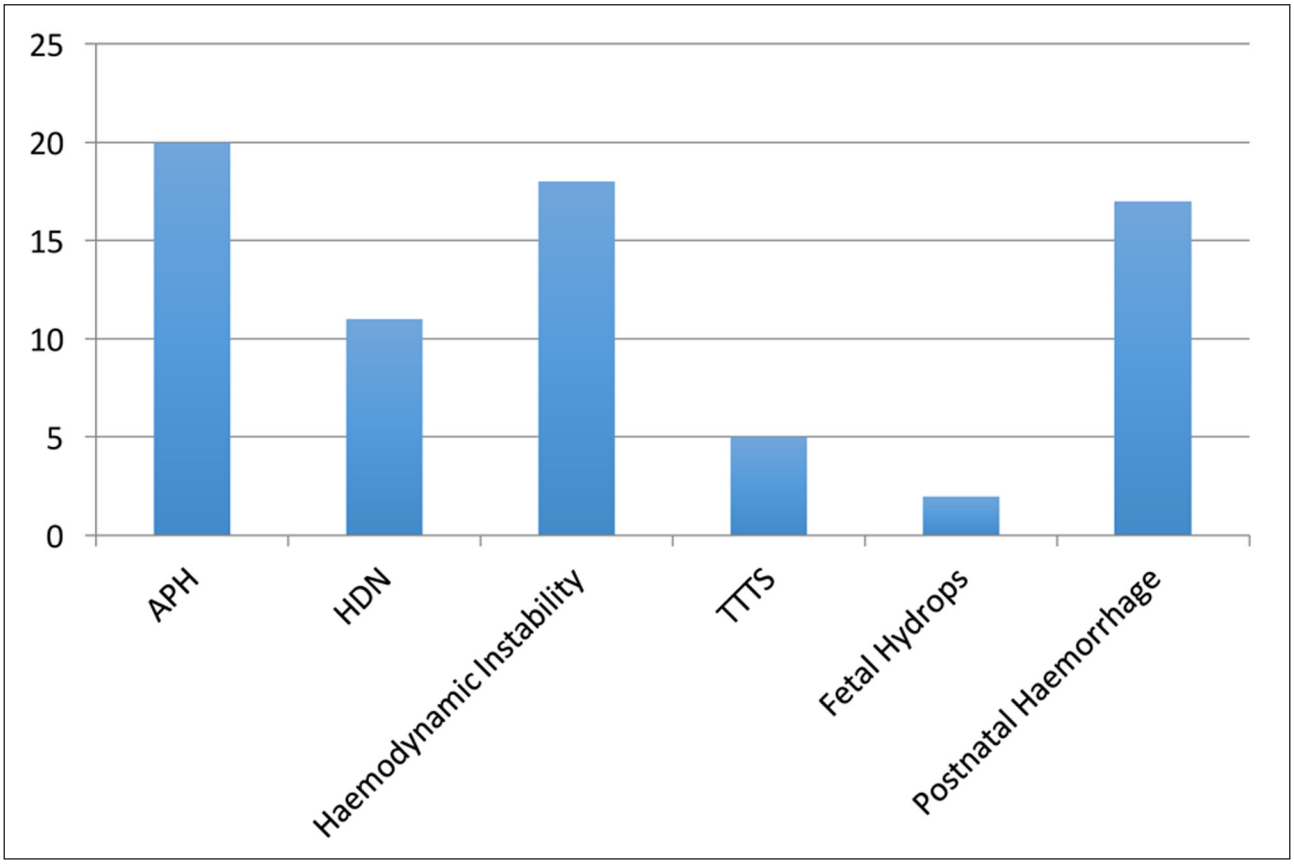

Figure 1 (ABS 20). Indications for transfusion.
HDN: haemolytic disease of the newborn.

with an average total bilirubin of 158 umol/l and a range of 2.2-19.9. Ten infants demonstrated clinical evidence alone, 16 demonstrated laboratory evidence and 16 infants demonstrated both clinical and laboratory evidence of coagulopathy. In total 42/71 (59.1%) of infants had evidence of coagulopathy. An accurate calculation of the time taken from receipt of request for transfusion was only possible in 30/71 cases. This was due to a combination of factors such as retrospective requesting of blood and poor documentation of time of commencement of transfusion. In the cases where calculation was possible the average time was 159 minutes, with a range of 2-1,239 minutes. We identified one case where emergency 0 negative blood was inappropriately given to an infant with HDN from anti-c +E antibodies resulting in a transfusion reaction.

CONCLUSIONS

This study aimed to investigate our practice with regard to emergency 0 negative blood transfusions. The majority of patients who received an emergency 0 negative blood transfusion (42/71) had evidence of coagulopathy and, therefore, would have benefited from the clotting factors which are present in emergency blood but absent in paedipacks. The study also highlighted that our documentation of time of commencement of transfusion is suboptimal and that much of our ordering and requesting of emergency blood is done retrospectively. The majority of cases of retrospective ordering arose when the blood was taken directly from the emergency fridge in theatre. In the cases in which we could calculate the duration of time from requesting to commencement of the blood transfusion, there were frequently delays, although the reason for this was not always clear. In conclusion, we recommend the continued use of emergency 0 negative blood, as opposed to SAGM blood, in infants requiring emergency transfusion. We also recommend that improvements be made in documenting the time of onset of transfusion. In cases where blood is taken directly from the emergency theatre fridge, it should be documented when this blood was removed.

ABS 21

THE COAGULATION SCREEN AS A BIO-MARKER OF NEONATAL ENCEPHALOPATHY OUTCOMES

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INTRODUCTION

Neonatal encephalopathy (NE) is associated with anaemia, thrombocytopenia and coagulation abnormalities.

METHODS

Infants with NE (n = 85) had serial coagulation testing including: prothrombin time (PT), aPTT and fibrinogen. Results were compared with MRI brain, seizures and outcome.

RESULTS

Mortality was predicted on day 1 by decreased fibrinogen (AUC = 0.95, p-value = 0.009) and by PT on day 2 with a cutoff of 21.7 seconds. An abnormal MRI was predicted by Fibrinogen on day 3 with a cut-off value of 2.02 g/L. For prediction of grade II/III NE, PT on day 2 of life was strongest with a cut-off value of 14 seconds. Only elevated APTT levels on day 1 of life were predictive of seizure occurrence (AUC = 0.65, p-value = 0.04).

CONCLUSIONS

Coagulation parameters are strong predictors of outcomes such as abnormal NE grade and death.