International Journal of Research in Medical Sciences
Debbarma R et al. Int J Res Med Sci. 2016 Oct;4(10):4279-4285
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20163177

Research Article

Incidence of intracranial haemorrhage in low-birth weight infants and its outcome: a hospital based prospective study

Rajesh Debbarma[1], Asim De[2]*, Sanjib Debbarma[3]

[1]Department of Pediatrics, Khowai district hospital, Khowai, Tripura, India
[2]Department of Radiodiagnosis, [3]Department of Paediatrics, Agartala Government Medical College, Agartala, Tripura, India

Received: 15 August 2016
Accepted: 31 August 2016

***Correspondence:**
Dr. Asim De,
E-mail: drasimde@rediffmail.com

ABSTRACT

Background: Intracranial haemorrhage (ICH) is one of the most important neurological complications in low birth weight (LBW) infants, especially in very low birth weight (VLBW) infants during the neonatal period. The objectives of the present study was to determine the incidence of intracranial hemorrhage among the low birth weight infants (<2.5kg), to determine the outcome of intracranial hemorrhage among the low birth weight infants (<2.5 kg) and to establish the relationship between the birth weight and degree of intracranial hemorrhage.
Methods: It is a prospective observational study. The study was conducted from November 2011- April 2013 in the neonatal unit, Department of pediatrics medicine in collaboration with Department of radio diagnosis in Agartala, Government Medical College and GBP Hospital, Agartala, India.
Results: Out of 400 infants, 32 (8%) of infants were ≤1 kg and 177 (44.25%) were 2-2.5 kg. Infants who had normal delivery 213 (53.25%) and 37 (9.25%) had difficult in vaginal delivery. Incidence of ICH among low birth weight newborns was 29%.Incidence of intra-ventricular hemorrhage (IVH) among low birth weight newborns detected in the study was 19.5% (79 out of 400). Among different types of intracranial hemorrhage IVH comprises the larger part (68.1%). Regarding various grading (severity) of IVH, found the study were, grade I IVH 35.4%, grade II IVH-41.7%,grade III IVH- 16.4% and grade IV IVH -6.3%. There was a direct association between birth weight and ICH and significant (p=03) association was found especially in babies below 1 kg. Overall mortality rate among newborn following various types of ICH was found to be 22.4%. Regarding long outcome of attending follow up clinic for 10 months showed delayed developmental milestone 13%, 8.6% develop seizure disorder and 13% develop hydrocephalus and 21.7% develop early sign cerebral palsy.
Conclusions: Low gestational age, specially <34 weeks, very low birth weight, male gender, difficult vaginal delivery, birth asphyxia, and hypothermia are risk factors for intracranial hemorrhage, specially intra-ventricular hemorrhage. For better evaluation of risk factors for ICH and its outcome, multicentric study should be performed with large number of simple and longer time period of follow up with the help of newer modalities of investigation.

Keywords: ICH, IVH, LBW, Outcome of ICH

INTRODUCTION

Intracranial hemorrhage (ICH) is one of the most important neurological complications in low birth weight (LBW) infants, especially in very low birth weight (VLBW) infants during the neonatal period. Intracranial hemorrhage (ICH) occurs in various parts of brain includes subependymal- intraventricular hemorrhage (SHE-IVH), anterior fossa haemorrhage (intra-parenchymal and subdural hemorrhage), posterior fossa

hemorrhage [cerebellar, subdural hemorrhage (SDH)] and subarachnoid hemorrhage (SAH). The peculiarities of the CNS microvasculature in low birth weight, particularly in very low birth weight infants favour the onset of intraventricular hemorrhage.

Vascular factor that contribute to GMH/IVH include the fragile nature of the involutions vessels of the germinal matrix, there is no muscular is mucosa and little adventitia in this area of relatively large diameter, thin walled vessels; all of these factors make the vessels particularly susceptible to rupture.[1] Several factors have been implicated in ICH pathogenesis. Birth trauma, difficult and prolonged deliveries and other factors involving ICH specially SEH–IVH.

Among the involved cardio-circulatory factors, any situation leading to an alteration in the cerebral blood flow and/or central nervous system (CNS) blood pressure may develop into IVH, such as mechanical ventilation, barotraumas, apnea crisis, congestive heart failure, sepsis, etc. Large second to second fluctuation in cerebral blood flow velocities in anterior cerebral arteries, measured by Doppler ultrasonography significantly associated with development of SHE/IVH.[2]

Intracranial hemorrhage and post-hemorrhagic ventricular dilation are common problems in small preterm infants. To determine optimal timing for ultrasound diagnosis of these abnormalities, 64 preterm infants (<1.500gm) were studied by sequential cranial ultrosonography from birth until one year of age or until death. The optimal timing for ultrasound diagnosis of intracranial hemorrhage is day 4 to 7 with follow up at day 14.

The most efficient time for ultrasound examination to diagnose ventricular dilation was day 14 with follow up at 3months.Intrcranial hemorrhage was diagnosed by ultrasound in 35 of the 64 patients (55%). In 18 of the 64 infants (28%) significant ventricular dilation was diagnosed by ultrasound during the first three month.[3] According to Kopp W et al infants with IVH had a direct relationship between the severity of hemorrhage and major handicaps on one hand and the mortality rate on the other hand.[4] Low birth weight infant with intracranial hemorrhage has severity problems such as development of hydrocephalus, seizures, static encephalopathy, blindness, mental retardation, language delay, fine motor and learning disabilities and behavioral dysfunction is higher in those with symptomatic hemorrhage.[5]

The objectives of the present study was

- To determine the incidence of intracranial hemorrhage among the low birth weight infants (<2.5 kg).
- To determine the outcome of intracranial hemorrhage among the low birth weight infants (<2.5 kg).
- To establish the relationship between the birth weight and degree of intracranial hemorrhage.

METHODS

It is a prospective observational study. The study was conducted form November 2011- April 2013 in the neonatal unit, Department of pediatrics medicine in collaboration with Department of Radiodiagnosis in Agartala, Government Medical College and GBP Hospital, Agartala, India.

Sample size includes four hundred neonates who satisfied the selection criteria and admitted in the neonatal unit of Agartala government Medical College and GBP Hospital with in the study period were taken as cases. The neonates were either delivered normally or by instrumental delivery or by caesarean section.

$N=4pp/L^2$, where P=prevalence^3 =20 (from reference)
q= (100-p); L=Limit of error
Here, limit of error=20%
So, n = 4x20x80 = 400
$[20x20]^2$= 100

Detailed history was taken regarding antenatal, natal past obstetrical history. Clinical examination was performed within 48 hours of delivery and investigations done as per protocol. Surviving cases were followed up at regular intervals following discharge in the OPD where history, detailed neurological examination and development reassessment was done and follow up investigation was performed as per requirement.

Inclusion criteria

- Neonates weighing below 2.5kg irrespective of gestational period and mode of delivery.
- Neonates having birth asphyxia, birth injury of minor congenital abnormalities.

Exclusion criteria

- Neonates having major congenital malformation which require urgent surgical intervention will be excluded.
- Parents not willing to give consent for the study will also be excluded.

Statistical analysis

Data was calculated by using chi square formula. P value <0.005 was considered significant.

RESULTS

This present study includes 400cases selected from the neonatal unit of Agartala Govt. Medical Collage and hospital for this study. Cases were selected as per inclusion criteria (weight <2.5 kg). The total cases were distributed according to sex (Male, Female), birth weight, gestational age, body temperature, mode of delivery and associated risk factors. Out of 400 infants, 32 (8%) of infants were ≤1 kg and 177 (44.25%) were 2-2.5 kg

(Table 1). Majority of infants had normal delivery 213 (53.25%) and 37 (9.25%) had difficult in vaginal delivery. 70 (17.5%) infants had induction (ARM+Oxytocin) during normal delivery and 80 (20%) were delivered by LSCS and most were done by spinal anaesthesia.

Table 1: Characteristics according to ICH occurrence during the neonatal period.

Characteristics	Number of infants	Percentage
Birth weight		
≤1kg	32	8
1-1.5 kg	58	14.5
1.5-2 kg	133	33.25
2-2.5kg	177	44.25
Parity		
Primi	262	65.5
Multi	138	34.5
Attendance to antenatal clinic		
Regular	293	73.25
Irregular	84	21
Never	23	5.75
ICH	116	29

In the present study, 65.5% mother was prim para and 34.5% were multipara who attended antenatal clinic during pregnancy. 293 mothers (21%) attended irregularly and 23 mothers (5.75%) never attended to antenatal clinic. A total of 400 infants, 116 (29%) infants developed ICH and 284 (71%) were normal on investigation.

Out of 116 patients of ICH, intra-ventricular hemorrhage (IVH) comprises highest cases 79 (68.1%), whereas intraparenchymal hemorrhage comprises in 26 (22.4%) and subarachnoid hemorrhage (SAH) 11 (9.4%). No subdural hemorrhage (SDH) was seen in this study. Therefore the incidence of intra-ventricular hemorrhage (IVH) observed in total cases of the study was 19.5% (79 out of 400) whereas the incidence of intra-parenchymal hemorrhage observed among total cases was 6.5% (26out of 400) (Table 2).

Table 2: Incidence of ICH.

Incidence of ICH	Number of cases	Percentage
IVH	79	68.1
I	28	35.4
II	28	35.4
III	13	16.4
IV	5	6.3
Parenchymal	26	22.4
SAH	11	9.4
SDH	-	-

During the routine ultrasonogram of brain, out of 79 IVH, 75.9% was detected within 3 days of birth, 87.3% was detected between 10-14 days on all the IVH were revealed between 14-21 days (Table 3).

Table 3: Days of investigating IVH.

Days of investing	Positive finding detected	Percentage
<3	60	75.9
10-14	69	87.3
14-21	79	100

Out of 400 infants, 300 (75%) had normal temperature, 70 (17.5%) were in cold stress and 30 (7.5%) had hypothermia. Therefore infants with cold stress and hypothermia have the higher incidence of ICH (Table 4).

Table 4: Relation of body temperature with incidence of ICH.

Body temperature (c)	No. of cases	No. of cases	Percentage
Normal	300	70	23.3
Cold Stress (36-36.5)	70	30	42.8
Mild moderate hypothermia	30	16	53.3

Table 5: Incidence of ICH with infants having birth asphyxia (n=53).

No. of cases	Babies having ICH					Percentage
	IVH	Parenchyma	SAH	SDH	Total	
53	18	13	-	35	35	66
347	61	13		81	23.3	23.3

53 (13.2%) infants suffered from birth asphyxia whereas 35 (66%) infants developed ICH, out of them 18 had IVH (51.4%) and 13 had parenchymal hemorrhage (37.1%) and 4 (11.4%) developed SAH whereas babies without birth asphyxia had 23.3% incidence of ICH. Therefore, babies suffered from birth asphyxia showed a higher incidence of ICH (Table 5). Among 400 total cases, 283 delivered by normal vaginal (uncomplicated normal delivery). Out of 283 infants, 85 (30%) suffered from ICH.

Out of 37 infants faced difficulties in vaginal delivery 22 (59.4%) of cases developed ICH whereas 80 (20%) infants delivered by caesarean section showed 9 (11.2%) ICH. Therefore, the study shows that babies passing difficult normal vaginal delivery have double incidence of ICH than uncomplicated normal delivery. Whereas following caesarean section delivery baby developing ICH, incidence is much less than that of the uncomplicated vaginal delivery (Table 6).

Table 6: Relation of mode of delivery in ICH.

Mode of delivery	No .of cases	Type of hemorrhage	No. of ICH	Percentage
Uncomplicated Normal Delivery (ND)	283	IVH=60, Parenchyma=20 SAH=5	85	30
Difficult Normal Delivery (Prolonged labour instrumental vagi)	37	IVH=19, Parenchyma=5 SAH=4	22	59.4
LSCS	80	IVH=6, Parenchyma=1 SAH=2	9	11.2
Total	400	IVH=79, Parenchyma=26 SAH=11	116	29

IVH= Intraventricular hemorrhage; SAH= Subarachnoid hemorrhage

A total of 116 infants ICH 26 babies (22.4%) expired, during admission at nursery. Subsequently, during follow up, 21 babies (18.1%) did not attend the follow up clinic.

Among 69 babies (59.4%) were regular follow up, 13% developed obstructive hydrocephalus. 21.7% developed cerebral palsy, 13% developed developmental delay and 6 infants 56.5% showed neurodevelopment sequence and 43.4% showed normal outcome (Table 7).

Table 7: Outcome of ICH.

Outcome of ICH	Number	Percentage
Death	26	22.4
Not attended follow up	21	18.1
Attended Regular FU	69	59.4
Hydrocephalus	9	13
CP	15	21.7
Seizure disorder	6	8.6
Delayed develop	9	13
Total abnormal	39	56.5

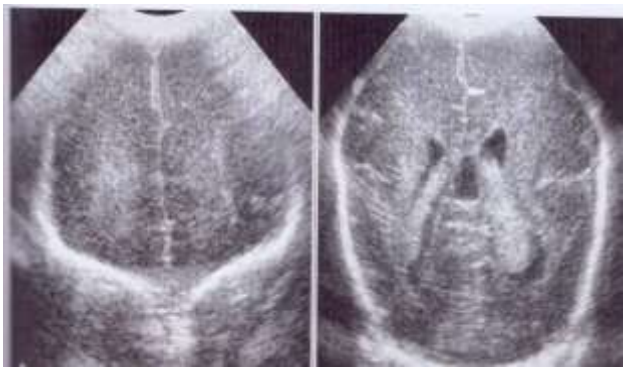

Figure 1: Coronal brain ultrasound images: normal premature newborn infant.

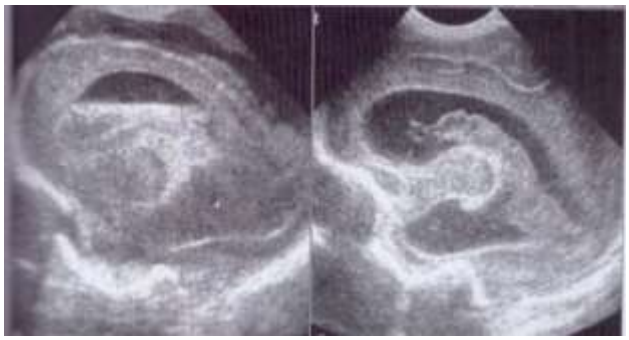

Figure 2: Intraventricular haemorrhage: sagittal sonograms.

DISCUSSION

All babies were clinically evaluated and underwent USG of brain at different ages starting from few hours after birth. The case were analyzed regarding various risk factors for intracranial hemorrhage (age, sex, birth weight, gestational age, body temperature, modes of delivery, birth asphyxia etc). Survived cases were followed up regularly at the age of 1/ months and 2 months for assessment of neuro-development outcome. Out of total cases 52% were male and 32% term babies. 13.2% babies suffered birth asphyxia and 9.25% passed difficult delivery.

Incidence of ICH

In present study, incidence of total ICH was 29% and incidence of IVH was 19.5% when compared with studies like Dincosy MY et al it was found incidence of IVH among 306 low birth infants was 24.4% whereas Mancini MC et al also found almost same incidence among very low birth weight infants.[6,7] Able HT et al

reported 47 .4% of ICH among high-risk infants.[8] In the current study incidence of IVH was 19.5%. Among them the incidence of different categories are, Grade 1-35.4%, Grade 2-41.7%, Grade 3-16.4% and Grade 4-6.4%. Mancini MC et al found the incidence of IVH was 29.8% with 70% Grade 1, 20% Grade 3 and 10% Grade 4.[7] The current incidence of IVH might have declined due to improvement of antenatal care and different intra modalities.

In present study incidence of intra parenchyma hemorrhage shows 6.5% and intra parenchyma shows 22.4% among total intracranial hemorrhage. Thorp JP et al showed that overall incidence of intraparenchymal hemorrhage among low birth weight neonates was 7.1% and Sasidharan CK et al showed that intraparenchymal hemorrhage comprises 27% among total intracranial hemorrhage.[9,10] Sulekha CS et al showed the incidence of SAH 43.3% among all types of ICH in the term newborn and Kopp W et al showed the incidence of SAH among all types of hemorrhage 37.5%.[4,11]

Timing of USG for ICH

In present Infants routinely underwent USG of brain in different periods and 75.9% detected below the age of 3days and 87.3% were detected between 10-14 days and 100% were detected between 14-21 days of age. The findings mostly correlate Perelman JM et al who showed that in very low birth weight babies 77% of IVH were diagnosed by day 3, 84% by day 10-14 days and by day 28 all cases could be diagnosed.[12]

Porridge JC et al has found that the optimal timing for ultrasound diagnosis of intracranial hemorrhage was 4-7 days with follow – up at day 14.[3]The most efficient time for ultrasound examination to diagnose ventricular dilatation was day 14 with follow-up at 3 months. Intracranial hemorrhage was diagnosed by ultrasound in 35 (55%) out of 64 patients. In 18 of the 64 infants (28%) significant ventricular dilation was diagnose by ultrasound during the first three months. The present study findings almost correlate with the findings of other observers that, USG of brain in early neonatal period <3 days can detect a higher incidence (75%) of hemorrhage and by day 10_14, majority (~90%) IVH can be revealed.

Birth weight and ICH

In the present study, infants below 1kg showed the incidence of ICH was 68.7% (22 out of 32) [P value=0.03]. The incidence gradually declined in the following order, 34.4% [p value=0.04], 32.3% [p value=0.07], 17.5% respectively among different groups 1-<1.5kg, 1.5kg -<kg and 2.5kg.

So there is association between increment of birth weight and decline in the incidence of ICH, especially significant in the infants below 1kg. Similarly infants with IVH have a good correlation between birth weight and incidence of IVH. Infants below 1kg incidence of IVH is 68.7% [p value=0.002]. The incidence gradually declines with increment of birth weight, as in babies between 2-2.5kg, incidence declines to 10.16%. There is significant correlation between with weight and development of IVH, especially infants below 1 kg. Therefore low birth weight is risk factor for development of IVH and such findings correlate with. Mancini MC et al, Antiknock S and da Silva RV et al in which their studies found that birth weight as an independent of risk factor for IVH.[7,13]

Gestational age and ICH

In present study infants ≤30 weeks showed an incidence of 50% (20 out of 40). In preterm infants, the incidence of IVH declines with increment of gestational age in the following order, 22.2% (24out of 108) and 20.38% (32 out of 127) and 21.04% (20 out of 95) in 30 -<34, 34-<37 and >37 weeks respectively. Therefore there is decline in the incidence of IVH with maturation of the babies and statistically significant difference is seen in babies below 34 weeks of gestation. Mancini MC et al, Din soy MY, Thorp JA et al and Glassier M et al also showed low gestational age as risk factors for IVH. Therefore lower gestational age is a risk factors for IVH specially babies <34 weeks.[6-8,14]

Hypohermia and ICH

In the current study, normothermic low birth weight babies shows an incidence of IVH 23 (3%), whereas hypothermic (mild to moderate) babies have a higher incidence of IVH (53.3%)[p value] =0.04]. Glassier M et al reported that from 3721 premature infants, showed the body temperature of 35º C or less is risk factor for IVH.[14]

According to Dincsoy MY et al 82 low birth weight newborns showed higher incidence of ICH among hypothermic infants during 1 week of life (34/82 versus 20/82, p<0.02), but the study regarded hypothermia as a manifestation of ICH during subsequent follow up neonatal period.[6] So, the current study correlates of higher incidence of ICH associated with hypothermia comparison to normothermic infants.

Sex and ICH

In present study, incidence of ICH among male infants is 31.7% and female infants 26%. Hence, there is higher incidence of IVH among the male infants.

Birth ashyxia and ICH

From the present study shows infants suffering from birth asphyxia had the incidence of ICH is 66% (35 out of 53, so the p=0.03). Whereas the babies having no history of birth asphyxia, had incidence of ICH 23.3% (81 out of 347). So there is a significant (p=0.03) association between birth asphyxia and ICH. This finding correlates

with Konstantinidis G et al, Antonivk S et al, Thorp JA et al and Dincsoy MY.[5,6,9,13]

Modes of delivery and ICH

In present study incidence of ICH following uncomplicated normal delivery is 30%, whereas infants born to mothers sufferings from difficult deliveries (prolonged labour and instrumental vaginal deliveries) have a higher incidence 59.4% (22 out of 37) of ICH [p=0.002] and infants by LSCS do not show any difference in incidence of ICH compared with uncompleted normal delivery .

Outcome

In the present study, among 116 ICH babies, 26 (22.4%) expired during stay in nursery. Overall mortality among ICH babies was 22.4% which is similar with Sulekha CS et al in which their study found 18% neonatal death following ICH.[11]

In present study among 69 babies attending follow up clinic regularly, 13% (9 out 116) infants developed post hemorrhage hydrocephalus and 21.7% (15 out of 116) developed cerebral palsy, 13% (9 out of 116) developed delayed developmental milestone and 8.6% developed seizure disorder. Marconi et al also reported hydrocephalus in 30% of VLBW babies during follow up.[7] But the lower incidence of hydrocephalus in study is probably due to improved antenatal and prenatal care.

Vohr B et al reported neurodevelopment outcome of VLBW infants having early onset that showed that 25% of infants during follow up undeveloped cerebral palsy.[15] Sulekha CS et al regarding the outcome of various types of hemorrhage till 2½ months follow-up 51 babies (43.9%) have found normal outcome.[11]

Abel HT et al, showed in their study that 72% of grade I IVH, and 42% of order grades IVH developed normal neurodevelopment outcome.[8] Kopp et al showed in his study that infants with IVH, there was direct relationship between the severity of hemorrhage and the mortality rate whereas Maurine et al in their study found a higher incidence of complication in newborns with IVH grade III and IV.[4,7]

CONCLUSION

From the present study it was concluded that intracranial hemorrhage, especially intraventricular hemorrhage is important complication of low birth weight infant. Low gestational age, specially <34 weeks, very low birth weight, male gender, difficult vaginal delivery, birth asphyxia, and hypothermia are risk factors for intracranial hemorrhage, specially intraventricular hemorrhage. Infants in present study showed higher mortality rate, development delay, seizure disorder and development of post hemorrhage hydrocephalus. Since the study period was short in his study, hyper-responsiveness to light, scarf sign, muscle tone, palatial angle were considered as the early marker of cerebral palsy.

For better evaluation of risk factors for ICH and its outcome, multicentric study should be performed with large number of simple and longer time period of follow up with the help of newer modalities of investigation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Pearlman JM, Volpe JJ. Seizures in the preterm infants, Effect of cerebral blood flow velocity, intracranial pressure, and arterial blood pressure. J Pediatr.1983;102(2):288-93.
2. Partridge JC, Babcock DS, Steichen JJ, Han BK. Optimal timing for diagnostic cranial ultrasound in low birth- weight infants: Detection of intracranial hemorrhage and ventricular dilation. J Pediatr. 1983;102(2):281-7.
3. Kopp W, Tölly E, Kaulfersch W, Fritsch G, Schneider GH. Intracranial hemorrhage in mature and Premature infants and clinical follow-up studies. Monostich Klnderheilked. 1986;134(2):84-8.
4. Konstantindis G, Velisavljev G, Bregun-Doronjski A, Nikolić N, Latinović R, Konstantinidis N. Asphyxia and Intracranial hemorrhage in high risk neonates of various gestational ages. Med Pregl. 1997;50(1-2):33-6.
5. Dincsoy MY, Siddiq F, Kim YM. Intracranial hemorrhage in hypothermic Low birth weight neonates. Child Nan Cyst.1990;6(5):245-8; discussion 248-9.
6. Mancini MC, Barbosa NE, Banwart D, Silveira S, Guerpelli JL, Leone CR. Intraventricular hemorrhage in very low birth weight infants: associated risk factors and outcome in the rental period. Rev Hosp ClinFac Med Sao Paulo. 1999;54(5):151-4.
7. Kleinhans F, von Rohden L, Meder S. Intracranial hemorrhage in Preterm and full term and newborn: Frequency and prognosis for development. Kinderaztl Plax.1991;59(7-8):211-5.
8. Thorpe JA, Jones PG, Clark RH, Knox E, Peabody JL. Prenatal risk factors associated Withsevere Intracranial hemorrhage. Am J Obstetric Gynecology. 2001;185(4):859-62. (ISSN 0002-9378).
9. Sasidharan CK, Chennai B. Intracranial hemorrhage in neonates. Abstract NNF, 2003.
10. Sulekha CS, Mohammedkunja PA, Santos Kumar A. One year serial follow -up study on neurodevelopment outcome of intracranial hemorrhage in neonates. Abstract NNF: 2003.

11. Perelman JM,McMenamin JB, Volpe JJ. Fluctuating cerebral blood-flow velocity in respiratory-Distress syndrome. Relation to the development of intraventricular hemorrhage. N Engl J Med. 1983;309(4)204-9.
12. Antiknock S, da Silva RV.Per ventricular and hemorrhage in the premature Infants. Revistade Neuralgia. 2000;31(3):238-43.
13. Glassier M, Jorch G, Aviaries S. Risk factor for intraventricular hemorrhage In low birth cohort of 3721 premature infants. J Pertinent Med. 2000;28(2)104-10.
14. Vohr B, Allan WC, Scott DT, Katz KH, Schneider KC,Makuch RW. Early onset intracranial hemorrhage in Preterm neonate: incidence of neurodevelopment handicaps. Semen Prenatal. 1999;23(3):212-7.

Cite this article as: Debbarma R, De A, Debbarma S. Incidence of intracranial haemorrhage in low-birth weight infants and its outcome: a hospital based prospective study. Int J Res Med Sci 2016;4:4279-85.