

Research Article

A study of clinical profile and outcome of intra ventricular hemorrhage in neonates admitted to neonatal intensive care unit of a tertiary care hospital, Eluru, Andhra Pradesh, India

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ABSTRACT

Background: The human hemostatic system is dynamic and is profoundly influenced by age. Although considered immature in the new-born, it is a physiological system which results in few problems for the healthy term neonate, but may contribute to morbidity in the sick and preterm infants when additional acquired abnormalities may be present. The objectives were, the study has been conducted to evaluate the clinical presentation, etiological risk factors of Intraventricular haemorrhage (IVH) and to correlate the birth weight, gestational age, sex, mode of delivery, perinatal factors with the incidence of IVH and to study the immediate outcome.

Methods: This is a prospective study which included neonates admitted in the Neonatal intensive care unit (NICU) of Department of Paediatrics, Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India during the period of March 2013 and September 2014. We enrolled 135 newborns in the study and blood investigations and transcranial USG was done in all.

Results: Incidence of IVH in new-borns admitted in NICU at Alluri Sita Rama Raju Medical College was 13.3% (18 out of 135 babies), whereas incidence of IVH in preterm babies was 26.9% (17 out of 63 babies) and incidence of IVH in term babies was 1.3% (1 out of 72 babies). 94.4% of the new-borns with IVH had prolonged prothrombin time ($p < 0.01$). Thrombocytopenia was responsible in 83.4% as an associated risk factor in the development of IVH ($p < 0.01$).

Conclusions: Intraventricular Hemorrhage constitutes an important cause of morbidity and mortality in neonate. Need for assisted ventilation irrespective of the co morbidities, presence of metabolic acidosis, have been associated with increased incidence of IVH. Deranged coagulation profile (Thrombocytopenia, prolonged prothrombin time (PT)) have been associated with increased risk for the incidence of IVH in new-borns.

Keywords: IVH, PT, Activated partial thromboplastin time (APTT)

INTRODUCTION

The haemostatic system is dynamic throughout the childhood.¹ The haemostatic system in the neonate has many unique features when compared with older children.² Although considered immature in the new-born, it is a physiological system which results in few problems for the healthy term neonate, but may

contribute to morbidity in the sick and preterm infants when additional acquired abnormalities may be present.

Hemorrhage both localized and generalized is a significant cause of morbidity and mortality in the neonatal period. Significant haemorrhagic complication accounts to about 1-2% of all NICU admissions and accounts to 40% of deaths associated with hemorrhage.

The identification of the cause of bleeding is of paramount importance for the appropriate management and for prognostication.

Intraventricular hemorrhage (IVH) is a leading cause of morbidity and mortality in the new-borns most common in the preterm neonates. The paucity of Indian studies on Intraventricular hemorrhage in new-borns prompted us to do this study looking at the incidence, etiological risk factors, clinical features and the immediate outcome among the new-borns.

The aim and objectives of the study was to evaluate the clinical presentation, etiological risk factors of IVH by history, physical examination and available relevant lab investigations, to correlate the birth weight, gestational age, sex, mode of delivery, perinatal factors with the incidence of IVH and to study the immediate outcome.

METHODS

This is a prospective study which included neonates admitted in the Neonatal intensive care unit (NICU) of Department of Paediatrics, Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India during the period of March 2013 and September 2014.

Sample size

135 neonates irrespective of their co morbidities, admitted in NICU at Department of Paediatrics, Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India were included in the study.

Out of 391 total admissions during the specified time period, 135 new-borns were screened using relevant history, available laboratory methods and Cranial Ultrasound Examination for the evidence of IVH. Incidence, Risk factors and Immediate outcome i.e., survival or death among the neonates with Intraventricular hemorrhage were analysed using Chi-Square test and the level of significance by P-value <0.05.

Inclusion criteria

All the Neonates admitted in the Neonatal Intensive Care Unit at Department of Paediatrics, Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India irrespective of the co morbidities were included in the study.

Exclusion criteria

Neonates who died within the first 48 hours of life, those with lack of Cranial Ultrasound examination within the first 10 days of life, and those without parent consent for screening Cranial Ultrasound Examination were excluded from the present study.

Methods

All the neonates admitted in NICU during the study period were included in the present study done at ASRAM Medical College, Eluru.

- A detailed antenatal and birth history were obtained initially from all the neonates.

The following clinical investigative procedures were performed for all the neonates

- Complete blood count.
- Leishman stained blood smear was examined in detail to look for evidence of thrombocytopenia, DIC (fragmented RBCs) and septicemia (toxic granules, shift to left, band forms of granulocytes).
- Prothrombin time (PT) and Activated partial thromboplastin time (APTT).
- Cranial Ultrasound examination/neurosonogram.

Immediate outcome

It was noted whether the child survived or expired.

Statistical analysis

Descriptive data are presented as number and percentages. Chi-square test was used to assess the association between IVH with various factors.

Microsoft word and SPSS software were used for the analysis of the results. A p value of 0.05 or less was considered for statistical significance

RESULTS

Table 1: Incidence of IVH - Sex wise distribution of study population.

Sex	IVH (+) (%)	IVH (-) (%)	Total (%)
Male	14 (19.72)	57 (80.28)	71(100)
Female	4 (6.25)	60 (93.75)	64 (100)
Total	18	117	135

Chi Square value is 5.28 and P-value is 0.02.

Table 2: Sex wise distribution among IVH patients.

Sex	IVH +
Male	14 (77.8%)
Female	4 (22.2%)

Out of 18 babies with IVH during the study period, Incidence of IVH is more in male babies (77.8%) compared to female babies (22.2%) with P value of 0.02 at 5% level of significance.

Table 3: Incidence of IVH: gestational age wise distribution in newborns.

Gestational age	IVH (+) (%)	IVH (-) (%)	Total (%)
Term	1 (1.3)	71 (98.7)	72 (100)
Preterm	17 (27)	46 (73)	63 (100)
Total	18 (13.4)	117 (86.6)	135 (100)

Chi Square value is 19.0 and P - value is 0.000

The incidence of IVH is found to be significantly high in preterm babies (27%) compared to term babies (1.3%) in the total study population.

Table 4: Gestational age wise distribution in IVH patients.

Gestational age	IVH +
Term	1 (5.6%)
Preterm	17 (94.4%)
Total	18 (100%)

17 babies (94.4%) were preterm births with Gestational age <37 weeks.

- 1 baby (5.6%) was term birth with Gestational age >37 weeks.
- Among 63 Preterm births, incidence of IVH is 27% with 17 babies with IVH:
 - ✓ 1 baby (5.8%) belong to <28 weeks Gestational age.
 - ✓ 12 babies (70.5%) belong to 29 – 31+6 week's Gestational age.
 - ✓ 4 babies (23.5%) belong to >32 weeks Gestational age.

Table 5: Incidence of IVH: birth weight wise distribution in newborns in study population.

Birth weight	IVH (+) (%)	IVH (-) (%)	Total (%)
< 1 Kg	5 (100)	0 (0)	5 (100)
1 – 1.5 Kg	8 (61.5)	5 (38.4)	13 (100)
> 1.5 Kg	5 (4.2)	112 (95.7)	117 (100)
Total	18	117	135

Chi Square value is 67; P - value is 0.00 for 2 d.f at 5% level of significance.

Table 6: Birth weight wise distribution in newborns with IVH.

Birth weight	IVH +
<1 kg	5 (27.8%)
1-1.5 kg	8 (44.4%)
>1.5 kg	5 (27.8%)
Total	18 (100%)

Out of 135 babies:

- All 5 babies (27.8%) born with birth weight <1kg developed IVH.
- 8 babies (44.4%) out of 13 babies born with birth weight from 1 – 1.5 kg developed IVH.
- 5 babies (27.8%) out of 117 babies born with birth weight >1.5 kg developed IVH.

Table 7: Incidence of IVH: antenatal risk factor wise distribution in newborns.

Antenatal risk factor	IVH + (%)	IVH – (%)	Total no of cases (%)
Yes	15 (31.25)	33 (68.75)	48 (100)
No	3 (3.4)	84 (96.5)	87 (100)
	18	117	135

Chi Square value is 20.7 and P-value is 0.000 for 1 d.f at 5% level of significance.

Table 8: Antenatal risk factor wise distribution in newborns with IVH.

Antenatal risk factors	IVH (%)
Yes	15 (83.3%)
No	3 (16.7%)
Total	18 (100%)

Out of 18 babies with IVH during the study period, Incidence of IVH in new-borns with Antenatal risk factors was 83.3% and Incidence in new-borns without Antenatal risk factors was 16.7%.

Table 9: Incidence of IVH: use of antenatal steroids in newborns.

Antenatal steroids	IVH (+) (%)	IVH (-) (%)	Total (%)
Yes	4 (57.2)	3 (42.8)	7 (100)
No	14 (11)	114 (89)	128 (100)
Total	18	117	135

Chi Square value is 12.3 and P-value is 0.000 for 1 d.f at 5% level of significance.

Table 10: Use of antenatal steroids in newborns with IVH.

Antenatal steroids	IVH +
Yes	4 (22.2%)
No	14 (77.8%)
Total	18 (100%)

Out of 18 babies with IVH during the study period:

- Incidence of IVH in infants born to mothers with history of intake of antenatal steroids is 22.2%.
- Incidence of IVH in infants born to mothers without intake of antenatal steroids is 77.8%.

Table 11: Mode of delivery and incidence of IVH in newborns.

MOD	IVH (+) (%)	IVH (-) (%)	Total (%)
Nvd	9 (11)	73 (89)	82 (100)
EM.LSCS	9 (30)	21 (70)	30 (100)
EL.LSCS	0 (0)	23 (100)	23 (100)
Total	18	117	135

Chi Square value is 11.1 and P-value is 0.004 for 2 d.f at 5% level of significance.

Out of 18 babies with IVH during the study period, Incidence of IVH in new-borns born out of NVD was 50% and incidence in new-borns born out of Em.LSCS was 50%.

Table 12: Birth asphyxia and incidence of IVH in newborns.

Birth asphyxia	IVH (+) (%)	IVH (-) (%)	Total (%)
Y	2 (8)	23 (92)	25 (100)
N	16 (14.6)	94 (85.4)	110 (100)
Total	18	117	135

Chi Square value is 0.755 and P-value is 0.385 for 1 d.f at 5% level of significance.

Table 13: Incidence of IVH in babies with asphyxia.

Birth asphyxia	IVH +
Yes	2 (11.1%)
No	16 (88.9%)
Total	18 (100%)

Out of 18 babies with IVH during the study period:

- Incidence of IVH in new-borns born with history of birth asphyxia is 11.2%.
- Incidence of IVH in new-borns born without history of birth asphyxia is 88.8%.

Table 14: Incidence of IVH: general condition of study population.

Sensorium	IVH
Normal	11.1%
Lethargic	16.6%
Comatose	72.3%

Table 15: Assisted ventilation as a risk factor for IVH in newborns.

Assisted ventilation	IVH (+) (%)	IVH (-) (%)	Total (%)
YES	14 (63.6)	8 (36.6)	22 (100)
NO	4 (3.6)	109 (96.4)	113 (100)
TOTAL	18	117	135

Chi Square value is 57.6 and P-value is 0.0000 for 1 d.f at 5% level of significance.

Out of 18 babies with IVH:

- 11.1% babies had good general condition.
- 16.6% babies were lethargic.
- 72.3% babies were comatose.

Table 16: Incidence of IVH in ventilated babies.

Assisted ventilation	IVH
Yes	14 (77.7%)
No	4 (22.3%)
Total	18 (100%)

Observations

- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination.
- Out of 135 babies:
 - ✓ 14 babies (63.6%) who were ventilated during the period of NICU stay developed IVH.
 - ✓ 4 babies (3.6%) without history of invasive ventilation developed IVH.
- Out of 18 babies with IVH during the study period:
 - ✓ Incidence of IVH in new-borns who were ventilated during NICU stay is 77.7%.
 - ✓ Incidence of IVH in new-borns without history of invasive ventilation during NICU stay is 22.3%.

Table 17: Metabolic acidosis as a risk factor for IVH in newborns.

Metabolic acidosis	IVH (+) (%)	IVH (-) (%)	Total (%)
Y	5 (83.3)	1 (16.7)	6 (100)
N	13 (10)	116 (90)	129 (100)
Total	18	117	135

Chi Square value is 26.6 and P value is 0.000 for 1 d.f at 5% level of significance.

Observations

- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination.
- Out of 135 babies:
 - ✓ 5 babies (83.3%) out of 6 babies with metabolic acidosis during the course of illness developed IVH.
 - ✓ 13 babies (10%) out of 129 babies without metabolic acidosis developed IVH.

Table 18: Thrombocytopenia as a risk factor for IVH in newborns.

Platelet count	IVH (+) (%)	IVH (-) (%)	Total (%)
Normal	3 (3)	108 (97)	111 (100)
Decreased	15 (62.5)	9 (37.5)	24 (100)
Total	18	117	135

Chi Square value is 61.1 and P-value is 0.000 for 1 d.f at 5% level of significance.

Table 19: Incidence of thrombocytopenia in IVH newborns.

Thrombocytopenia	IVH
Yes	15 (83.4%)
No	3 (16.6%)
Total	18 (100%)

Observations

- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination.
- 3 babies (3%) out of 111 babies screened had normal platelet count with IVH.
- 15 babies (62.5%) out of 24 babies screened had decreased platelet count (Thrombocytopenia) as a risk factor to develop IVH.

Out of 18 babies with IVH during the study period:

- Incidence of IVH in new-borns with Thrombocytopenia during the course of illness is 16.6%.
- Incidence of IVH in new-borns without Thrombocytopenia is 83.4%.

Table 20: Coagulopathy (Prothrombin time) as a risk factor for IVH in newborns.

PT	IVH + (%)	IVH – (%)	Total (%)
N	1 (0.9)	114 (99.1)	115 (100)
P	17 (85)	3 (15)	20 (100)
Total	18	117	135

Chi Square value is 107.00 and P-value is 0.000 for 1 d.f at 5% level of significance.

Observations

- Out of 18 babies with IVH during the study period, Incidence of IVH in new-borns with deranged or prolonged prothrombin time as a risk factor is 94.4%.
- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination
 - ✓ 1 baby (0.9%) had normal prothrombin time.
 - ✓ 17 babies (85%) had prolonged prothrombin time (↑).
- P- Value is 0.000 at 5% Level of Significance.

Table 21: Clinical presentation of IVH in newborns.

Clinical presentation	IVH (%)
Catastrophic	3 (16.6)
Saltatory	4 (22.2)
Asymptomatic	11 (61.2)
Total	18 (100)

Observations

- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination.
- Out of 18 babies:
 - ✓ 3 babies (16.6%) had catastrophic clinical presentation of IVH.
 - ✓ 4 babies (22.2%) had Saltatory clinical presentation of IVH.
 - ✓ 11 babies (61.2%) had asymptomatic clinical presentation of IVH.

Table 22: Incidence and immediate outcome of IVH in newborns of study population.

Outcome	IVH (%)
Good	13 (72.2)
Death	5 (27.8)
Total	18 (100)

Observations

- Out of 135 babies screened for IVH, 18 babies were proven to have IVH by cranial USG examination.
- Out of 18 babies with IVH:
 - ✓ 13 babies (72.2%) had good outcome.
 - ✓ 5 babies (27.8%) died during the course of illness.

Incidence of IVH

- Incidence of IVH in new-borns admitted in NICU at Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India: 13.3% (18 out of 135 babies).
- Incidence of IVH in preterm babies: 26.9% (17 out of 63 babies).
- Incidence of IVH in term babies: 1.3% (1 out of 72 babies).

DISCUSSION

In the present study out of the 391 neonates admitted in NICU in 1½ years, 135 neonates were included in the study in regards to the inclusion criterion and 18 new-borns out of 135 had IVH irrespective of co morbidity. The overall incidence of IVH in the present study is 13.3%, majority being Preterm neonates with an incidence of 26.9% and in Term neonates it was 1.3%.

Out of 18 new-borns with IVH, 77.8% were males and 22.2% were females with a Male: Female ratio of 3.5:1. In the present study, out of 135 babies screened for IVH, 63 babies were preterm babies with gestational age less than 37 weeks. Out of 63 preterm babies admitted in NICU, 17 babies were detected to have IVH by cranial ultrasound examination. Of 17 babies with IVH, incidence of IVH was more in preterm born between 29-31+6 weeks gestational age (70.5%) compared to those born >32 weeks gestational age (23.5%) and <28+6 weeks gestational age (5.8%).

This is similar to the study done by Volpe et al. in 2001, with incidence of IVH more in preterm babies when compared to term neonates, indicating that IVH is a leading cause of brain injury in preterm new-born babies.³

In the present study, out of 18 babies with IVH, incidence of IVH in infants with birth weight <1 kg was 27.8%, birth weight between 1 kg-1.5 kg was 44.4% and birth weight >1.5 kg was 27.8 %. The association was statistically significant ($p < 0.001$).

This is similar to the findings by a study conducted by Badiie Z at Iran indicating that preterm and very low birth weight infants have an increased risk for the incidence of IVH.⁴

The risk of IVH is inversely related to gestational age and birth weight. In addition to having several adverse effects of Preterm birth, IVH is one of the morbidities. Out of 135 babies screened, 48 babies had antenatal risk factors of which, 15 babies (31.21%) developed IVH and 3 babies (3.4%) without antenatal risk factors developed IVH.

Therefore, out of 18 babies with IVH during the study period, incidence of IVH was more in new-borns with antenatal risk factors (83.3%) compared to those without any antenatal risk factors (16.7%).

Among 135 babies screened for IVH, 4 babies (57.2%) out of 7 babies born to mothers with history of intake of antenatal steroids developed IVH and 14 babies (11%) out of 128 babies born to mothers without history of intake of antenatal steroids developed IVH.

Therefore out of 18 babies with IVH during the study period, incidence in infants born to mothers with history of intake of antenatal steroids was 22.2% and in those infants born to mothers without history of intake of antenatal steroids was 77.8%.

Out of 135 babies, 9 babies (11%) out of 82 babies born out of normal vaginal delivery developed IVH and 9 babies (30%) out of 30 babies born out of emergency LSCS developed IVH.

Among 18 babies with IVH in the study period, incidence of IVH in new-borns born out of normal vaginal delivery was 50% and incidence of IVH in those born out of emergency LSCS was 50%.

In the present study which was done at a tertiary hospital, there was equal incidence of IVH in new-borns born out of normal vaginal delivery as well as emergency LSCS. In a study conducted by Wells JT, Ment LR regarding the Prevention of IVH in preterm infants, it was examined whether delivery practices affect the incidence of IVH. Although often contradictory, these results suggest the

possibility that active labor and vaginal delivery may be a risk factor for developing early onset IVH.⁵

Among these 135 babies, 2 babies (8%) out of 25 babies with history of birth asphyxia developed IVH and 16 babies (4.6%) out of 110 babies without history of birth asphyxia developed IVH.

However, among 18 babies with IVH in the study population, incidence of IVH in babies with history of birth asphyxia was 11.2% and incidence in those without history of birth asphyxia was 88.8%.

This was however statistically not significant with p-value 0.385.

In another study done by Gazzolo, Diego, Di Iorio, et al on term asphyxiated new-borns, S100B protein blood concentrations were determined at 12 hours of birth. This study suggested that elevated S100B protein blood levels represent a useful tool for the early detection of IVH in the post-asphyxia period when clinical examination and cerebral ultrasound might still be silent.⁶

However the most frequent causes of IVH in term neonates are birth asphyxia and birth trauma.

Among 135 babies screened, 14 babies (63.6%) out of 22 babies who were ventilated during the period of NICU stay developed IVH and 4 babies (3.6%) out of 113 babies without history of invasive ventilation during NICU stay developed IVH.

However, among 18 babies who developed IVH in the study population, incidence in babies with history of mechanical ventilation during the period of NICU stay was 77.7% and in those without history of mechanical ventilation was 22.3%. In a study conducted by Aly H, Hammad TA, Essers J, Wung JT at an American hospital, data was collected on delivery room intubation and mechanical ventilation during the first 3 days of life in very low birth weight infants.⁷

Among 135 babies screened, 5 babies (83.3%) out of 6 babies with metabolic acidosis during the course of illness developed IVH and 13 babies (10%) out of 129 babies without metabolic acidosis developed IVH in the study population.

However, among 18 babies with IVH in the study population, incidence of IVH in new-borns with metabolic acidosis as a risk factor during the course of illness was 27.7% and incidence among those without metabolic acidosis was 72.3%.

This was proven to be statistically significant in our study with p-value 0.000.

Dykes et al found that administration of sodium bicarbonate after the first day of life was also a

significant risk factor in the development of IVH. Intrapartum fetal asphyxia with metabolic acidosis, although an infrequent occurrence in the preterm infant, may account for a few cases of periventricular leucomalacia, while the more common new-born metabolic acidosis, when of sufficient degree and duration, carries a high risk of periventricular leucomalacia.⁸

Among 135 babies, 3 babies (3%) out of 106 babies with normal platelet count developed IVH and 15 babies (62.5%) out of 24 babies with decreased platelet count (Thrombocytopenia) developed IVH.

Therefore, out of 18 babies of the total study population with IVH, incidence of IVH in those born with normal platelet count was 16.6% and incidence of IVH in babies with decreased platelet count (Thrombocytopenia) is 83.4%.

Another study done at an American institute included infants <1500gms to investigate the significance of neonatal thrombocytopenia on the incidence of IVH in infants <1500 gms confirms that thrombocytopenia and IVH are not uncommon in neonates who weigh <1500 gms, and that the incidence of IVH is higher in those thrombocytopenic infants delivered vaginally.⁹

Among 135 babies, 1 baby (0.9%) out of 115 babies with normal prothrombin time developed IVH, 17 babies (85%) out of 20 babies with prolonged prothrombin time developed IVH during the course of illness in the period of NICU stay.

However, among 18 babies with IVH, incidence of IVH in new-borns with deranged or prolonged prothrombin time as a risk factor was 94.4%.

Another study was carried out by Setzer ES et al at a tertiary level hospital to investigate platelet count, bleeding time, platelet aggregation, prothrombin time, activated partial thromboplastin time, and fibrinogen level in VLBW infants during the first postnatal day to determine the relationship between hemostatic disorders and IVH. The results showed that infants with IVH had a significantly longer mean Prothrombin time than did infants with no IVH.¹⁰

Among the 18 babies with IVH in the study population, 3 babies (16.6%) had catastrophic clinical presentation of IVH, 4 babies (22.2%) had Saltatory clinical presentation of IVH, and 11 babies (61.2%) were asymptomatic at the time of presentation of IVH.

It is rare to find a catastrophic presentation unless there is additional ICH, such as large SDH or parenchymal hemorrhage.¹¹ It is a classic presentation of major hemorrhage, i.e., a neurological deterioration that usually evolved in minutes to hours and consisted of deep stupor or coma.^{12,13}

In the present study, out of 135 babies, 18 babies were proven to have IVH by cranial ultrasound examination. Among 18 babies with IVH, 13 babies (72.2%) had good immediate outcome with improved neurological status and 5 babies (27.8%) died during the course of illness in the period of NICU stay at Department of Paediatrics, Alluri Sita Rama Raju Medical College, Eluru, Andhra Pradesh, India.

CONCLUSION

From current study, we concluded that:

- Intraventricular Hemorrhage constitutes an important cause of morbidity and mortality in neonate.
- Preterm and VLBW infants have higher incidence of IVH
- IVH in term babies is a rare diagnosis and can occur due to birth trauma, birth asphyxia or deranged coagulation profile.
- Antenatal risk factors and maternal antenatal steroid intake also influence the incidence of IVH in new-borns.
- Need for assisted ventilation irrespective of the co morbidities, presence of metabolic acidosis, have been associated with increased incidence of IVH.
- Deranged coagulation profile (Thrombocytopenia, prolonged prothrombin time) have been associated with increased risk for the incidence of IVH in new-borns.

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