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Hypoxic Ischemic Encephalopathy: Obstetric Risk Factors and Immediate Outcome at Benghazi Medical Center in 2016

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Abstract

Background: Despite the development of the medical services still hypoxic ischemic encephalopathy considered as one of the leading causes of neonatal deaths and neurological sequel in newborn. Since Libya had faced medical crisis, which affected in the medical care service. This study may be the spotlight for health care personal to improve the services in Libya. **Objectives:** To determine obstetric risk factors and to estimate immediate outcome . **Methodology:** This prospective cross sectional study. It was included 56 babies with Apgar score ≤ 7 at 5 minute and or signs and symptoms of hypoxic ischemic encephalopathy. The obstetric factors and Immediate outcome were reviewed. **Results:** All mothers who had prolonged second

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stage were primi-paras; the correlation between the two was significant(p value =0.000) . The parity and female gender were significantly associated (p<0.05) with sever HIE . Multi-parity, resuscitation with drugs, Apgar score \leq 7 at 5 minute, ventilator support and sever HIE were risk factors for neonatal death (p < 0.05). Sever HIE was (34%) mortality rate was (26.8%). **Conclusion:** Primi -parity, prolonged second stage were significantly correlated to each other . most of the risk for death can be prevented by improving the medical services

Keywords: Asphyxia ,Obstetric factor, Benghazi Medical Centre

1.0 Introduction

Despite the development in the medical services has been improving over the last decades, but still the birth asphyxia considered as one of the leading causes of neonatal death and neurological sequel in newborn babies.

Birth asphyxia is defined as failure to start regular respiration within a minute of birth. Newborn infants normally start to breathe without assistance and usually cry after delivery.by one minute after birth, most infants are breathing well. If an infant fails to establish sustained respiration after birth, the infant is diagnosed with asphyxia or hypoxic ischemic encephalopathy (Steven, Donn, Sinha, Chiswick, 2002)

In the delivery room, the infant will often exhibit low Apgar score and a weak or absent cry .the severity of neonatal encephalopathy can be classified as mild , moderate, or sever according to these clinical finding,newborns presenting with moderate to sever neonatal encephalopathy often require immediate resuscitation (Report of the American college of Obstetricians and Gynecologists' task force on neonatal encephalopathy 2014) and (Wu., et al 2014).

Fetal hypoxia may be caused by various disorders in the mother including: inadequate oxygenation of maternal blood, low maternal blood pressure, inadequate relaxation of the uterus, premature separation of placenta, impedance to the circulation of blood through the umbilical cord and placental insufficiency after birth. Hypoxia may be caused by failure of oxygenation as a result of sever forms of cyanotic congenital heart disease or sever pulmonary disease , sever anemia and sever shock enough to interfere with the transport of oxygen to vital organs from overwhelming sepsis , massive blood loss and intracranial or adrenal hemorrhage .

Hypoxic ischemic encephalopathy(HIE) is an important cause of permanent damage to central nervous system tissues that may result in neonatal death , approximately 20-30% of infant with HIE die in neonatal period and about 33-50% of survivors are left with permanent neurodevelopmental abnormalities(Kliegman,. et al 2016).

Since Libya faced a medical crisis in 2015-2016, which really affected and still are affecting in the medical care, because of lack of a lot of resources, including nursing staff and because this problem can be prevented by good antenatal care and well trained staff .this study may be the spot light for health care personnel to improve the medical services in Libya .

2.0 The problem of the study

The aim of the study was to estimate obstetric risk factors and immediate outcome of hypoxic ischemic encephalopathy including mortality rate in Benghazi Medical Center in 2016.this research will answer the following questions:-

1- Are the primi-para mothers more risky to HIE than multiparas?

2- Because the primi-paras in the study have poor pushing in the documents of labor room which lead to prolonged second stage we would like to know; Is there any significant correlation between primipara and prolonged second stage ?

3- Are the most common maternal diseases related to the risk of neonatal death?

3.0 What dose distinguish this study from previous study?

This study was conducted during Libyan crisis(war) in 2016; which affects in the medical resources of the main hospitals, so this study was the spotlight to see to which extent, the effect of this crisis will be in immediate outcome and neonatal death .

It is the first study on HIE was done in Benghazi during the crisis.

4.0 Methods

This prospective cross- sectional study was carried out in neonatal intensive care unit (NICU) at Benghazi Medical Center (BMC) from January.2016 to December 31.2016 .it was included 56 babies were born with low Apgar score ≤ 7 at 5 minutes and or signs and symptoms of hypoxic ischemic encephalopathy. premature babies <34 weeks and babies with congenital malformation were excluded from this study. Data were collected using formulated checklist which involved: parity , age of the mother, mode of delivery . whether the mother had any chronic medical disease , or any antenatal problem like : pregnancy induced hypertension, antepartum hemorrhage, gestational diabetes; obstetric risk factors were mentioned ; any complications during labor like: prolonged second stage ,cord around neck ,meconium stained liquor, fetal distress, cord prolapse, shoulder dystocia ,obstructed labor. Other data covered details of birth history whether the baby term or premature, Apgar score and details of delivery events were collected, if they had been needed bagging only or cardiac compression in addition to that, or also needed umbilical

catheterization and giving of emergency drugs. The third part of checklist was about the examination of the babies which involved ; neurological examination and immediate outcome which means: requirement of ventilator support, grades of hypoxic ischemic encephalopathy and finally the outcome whether the baby discharged or died. data were analyzed by using SPSS program version 20

5.0 Results

The study were included 56 babies Between January , 2016 and December , 2016. It involved the babies with Apgar score ≤ 7 at 5 minute and had signs and symptoms of hypoxic ischemic encephalopathy or only had signs and symptoms whatever their Apgar. Apgar score that has been using as one of indicators of birth asphyxia was ≤ 7 at 5 minute in largest group of babies 27/56 (48.2%), the mean of Apgar was (5.3 ± 3.4) **figure 1**. Although there were a lot of indication for cesarean section in the cases of the study, but vaginal deliveries had the highest number 29/56 (51.8%) as compared to those of cesarean section.

5.1 Maternal factors

The maternal risk has been identified in 33/56 (59%), but the fetal factors were the most predominant in 37/56 (66%) of the cases, both fetal and maternal risks were recorded in 20/56 (35.7%) of cases, four cases 4/56 had no risk (7%). There were remarkable increase in the number of primi-para mothers of the babies with birth asphyxia 25/56(44.6%)as compared to other parities ,which all together constituted 31/56(55.4%).**figure2**.

Prolonged second stage had been found the predominant maternal factor in 9/33 (27.3%) and all the mothers who had prolonged second stage were primi-paras. Prolonged rupture of membrane, which involved only the duration of that history

lasted more than 18 hours; It was represented as second maternal factor 7/33 (21.2%) **Table 1.**

5.2 Fetal risk

The majority of babies were male 36/56 (64.3%); females were 20/56(35.7%).

Fetal distress is the factor that represented the presence of fetal tachycardia or fetal bradycardia, with other evidences support intrauterine asphyxia. The fetal distress was the most frequent fetal factor 13/37 (35%),out of them 7/13(53%) were born to primi-para mothers. postdate was the second frequent fetal factor 8/37(21.6). Fetal factors were represented in **Table 2.**

5.3 Immediate outcome

HIE was estimated in the study as mild HIE in 24/56(42.9%), moderate HIE in 13/56 (23.2%) whereas 19/56(34%) had neurological features of sever HIE **Figure 3.** Two third of the babies 21/56 (37.5%) were resuscitated after delivery with oxygen by mask and bagging only, but those babies who their resuscitation included adrenaline were 11/56 (19.6%), out of them 8/11(73%) were having sever hypoxic encephalopathy and they constituted 8/19 (42%) of the cases of sever hypoxic ischemic encephalopathy . Around half of the babies were on ventilator 27/56 (48.2%). All cases of sever HIE was intubated and kept on ventilator, out of them 15/19(79%) were on ventilator until they died; only 7/13(54 %) of moderate HIE were needed ventilator support, and one case of mild HIE was kept on ventilator just for few hours because he could not initiate his first breath regularly. **Figure 4.**

The total number of babies were died due to birth asphyxia were 15/56 which represent the mortality rate of (26.8%) ; all of them were with sever hypoxic ischemic encephalopathy 15/19(79%) .The number of babies were discharged to home were 41/56(73.2%) including babies with moderate HIE and 4/19 (21%) of cases with sever HIE. **Figure 5.**

5.4 Statistical Analysis

5.4.1 Correlation between Primi-para and prolonged second stage

The association between primi-para mothers and prolonged second stage was significant p. value =0.000 . Fisher exact test =13, but the prolonged second stage was non-significant risk factor for fetal death (p value= 0.2) **Table 3.**

5.4.2 Maternal, fetal risk factors and HIE grades

Primi-paras were associated significantly with mild to moderate, while multi-paras were significantly risk factor for sever HIE(P value=0 .009). Regarding fetal factors, only female gender showed significant associated risk factor for HIE P value =0.02. Male were associated with mild to moderate grade of HIE. as shown in **Table 4.**

5.4.3 Risk factors for neonatal death

The comparison for the risk of neonatal death cross certain factors showed that there was significant association of parity, Apgar score ≤ 7 at 5 minute, resuscitation with medication, ventilator support, sever grade of HIE with neonatal death (p < 0.05), while the gender and mode of delivery were not (p > 0.05) . as shown in **Table 5**

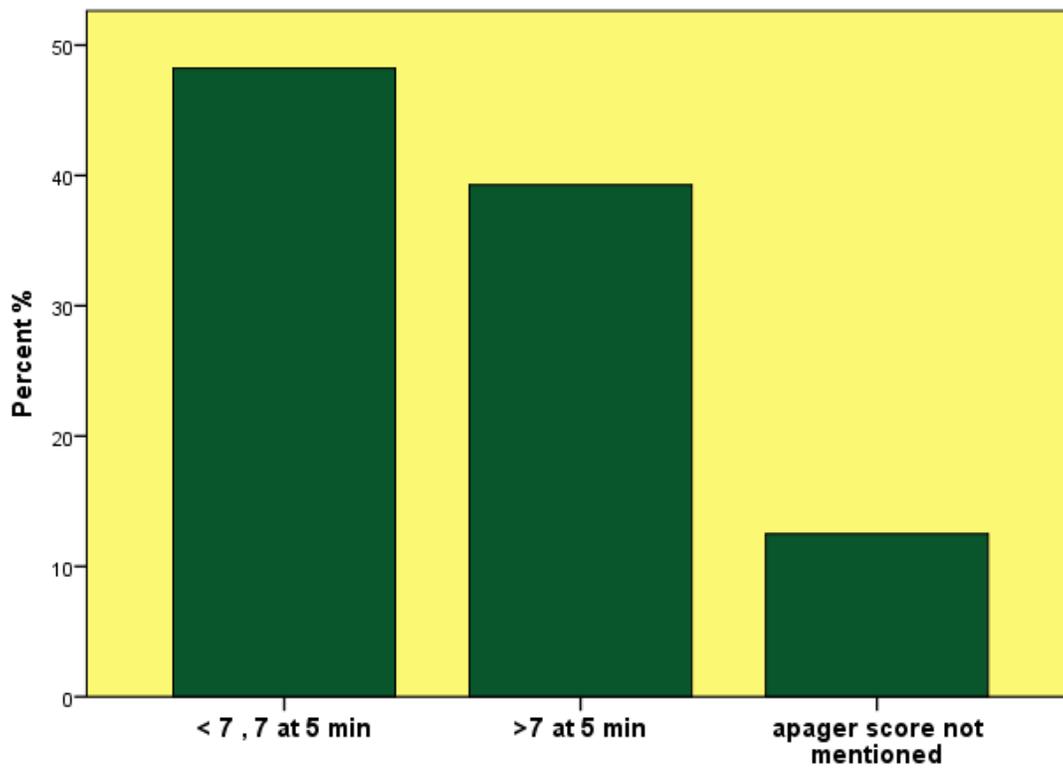


Figure (1): Apgar Score For Babies With HIE

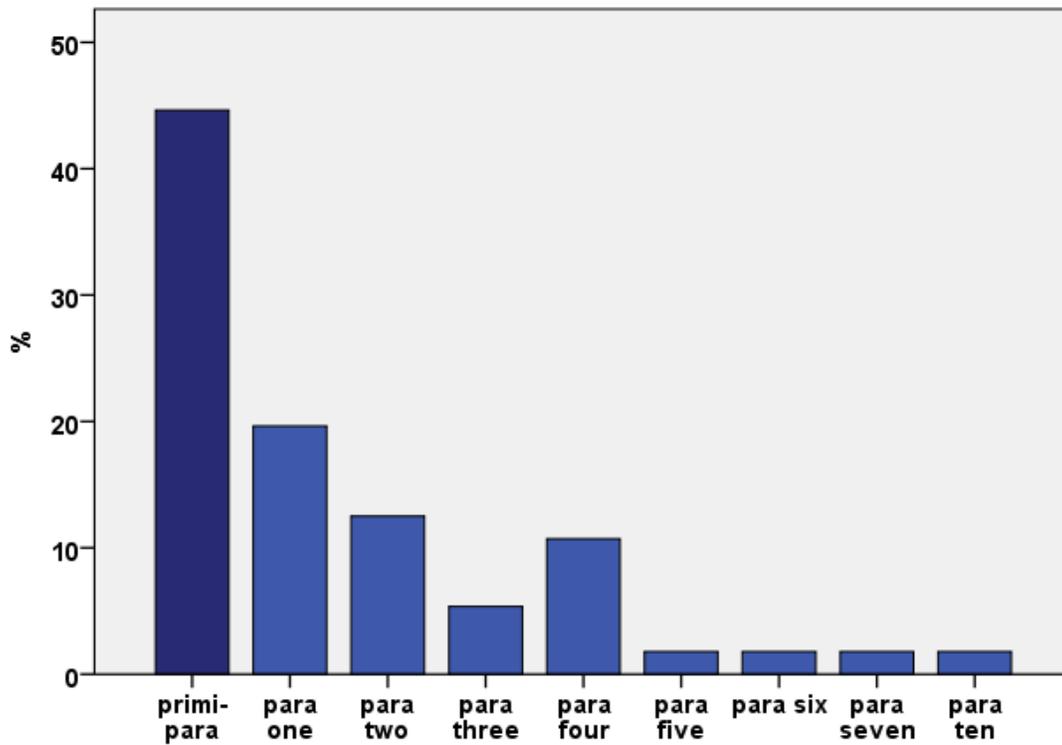


Figure (2): Distribution Of Parities In Babies With HIE

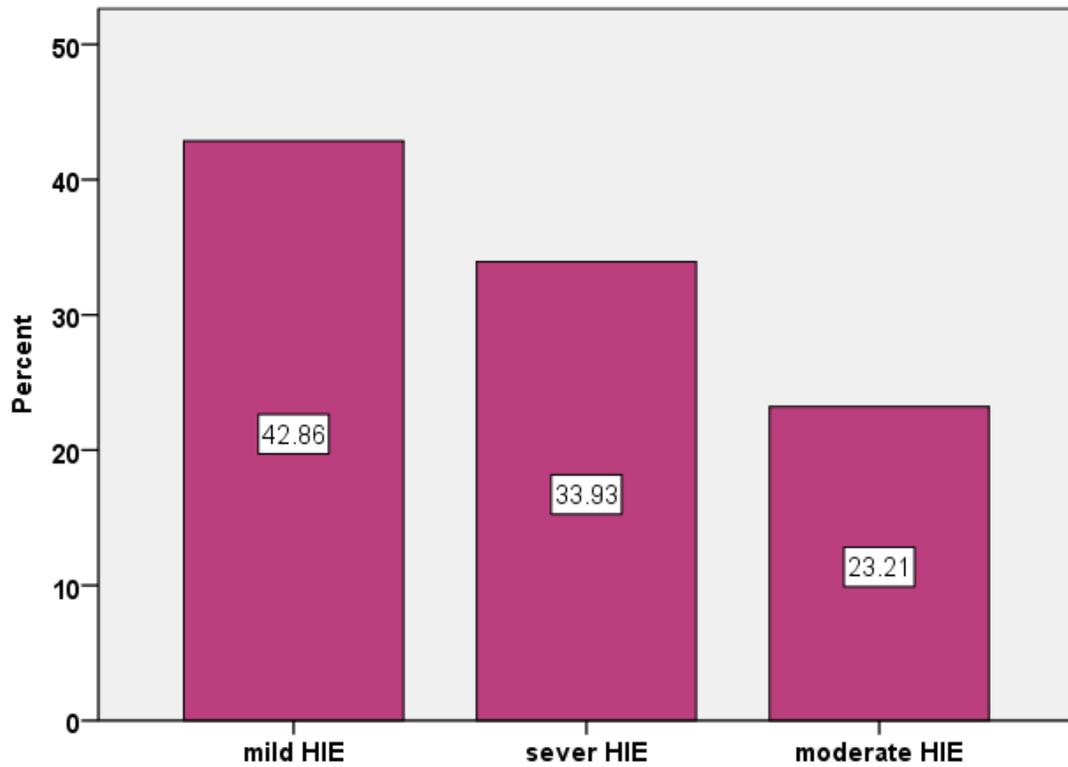


Figure (3) : Grades of Hypoxic Ischemic Encephalopathy

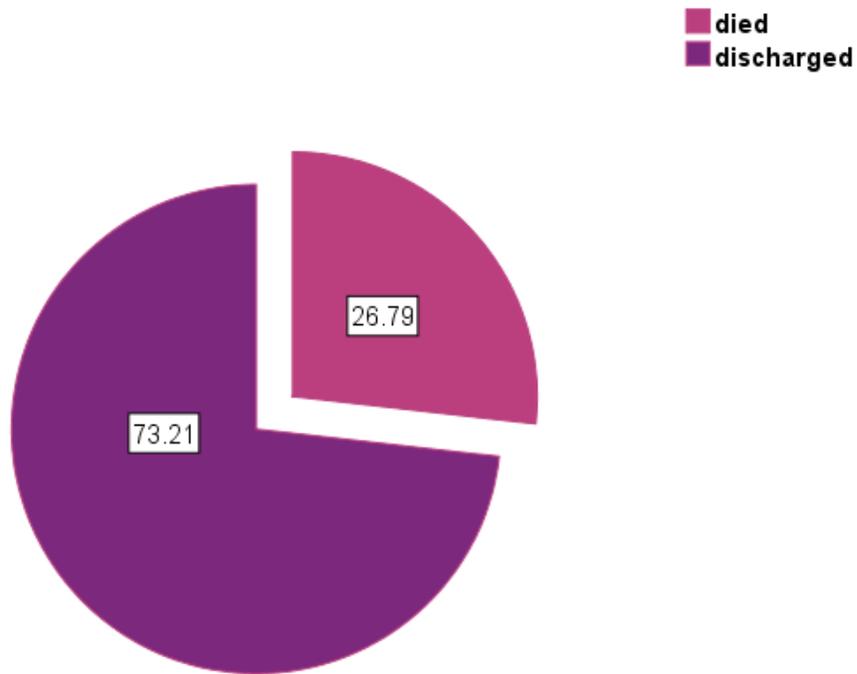


Figure (5): Outcome Of Hypoxic Ischemic Encephalopathy

Benghazi Medical Center in 2016

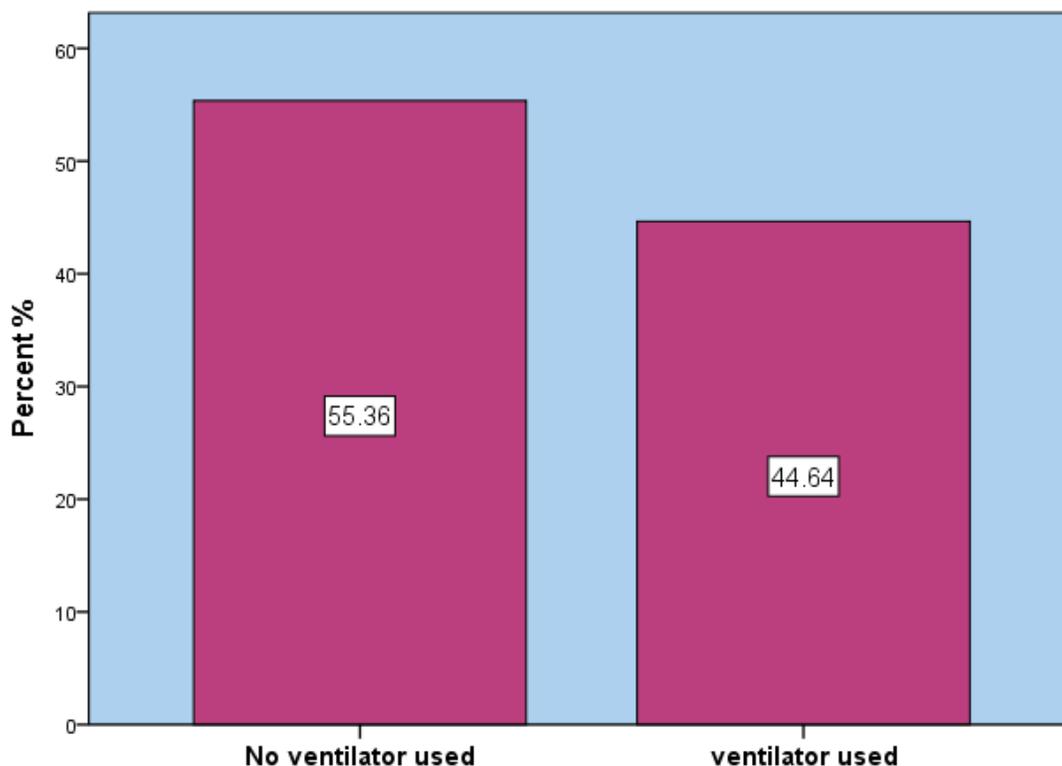


Figure (4): Ventilator Support For Babies with HIE

Table(1):Maternal factors in babies with HIE

Maternal factors	Frequency of the cases	Percent of Cases
Prolonged second stage	9	27.3%
Prolonged rupture of membrane	7	21.2%
Obstructed labor	5	15.2%
Chronic maternal illness *(D.M,HTN,Asthma,Hypothyrodism)	5	15.2%
Mother age < 19 years	4	12.1%

Benghazi Medical Center in 2016

Uterine rupture	3	9.1%
Precipitate labor	3	9.1%
Placental – Abruption	3	9.1%
Miscellaneous causes *(PET,ICSI, hypovolemic and septic shock due to cobra and snake bite)	5	15.2%

*D.M: Diabetes Mellitus, HTN: Hypertension.

*PET: Pre-eclampsia, ICSI: intra cytoplasmic sperm injection

Table (2): Fetal factors in babies with HIE

Fetal risk	Frequency	Percent of Cases
Fetal distress	13	35.1%
Postdate	8	21.6%
Malposition	5	13.5%
Cord causes	5	13.5%
Big size and shoulder dystocia	5	13.5%
Prematurity	4	10.8%
Twin	2	5.4%

Benghazi Medical Center in 2016

Decrease fetal movement	2	5.4%
Car delivery	2	5.4%
Delay cry	1	2.7%
Secondary apnea	1	2.7%

Table (3): comparison between primi-para mothers and prolonged second stage

Primipara	Prolonged second stage		Total
	No	Yes	
Yes	16	9	25
No	31	0	31
Total	47	9	56
Fisher's exact test= 13, p. value= 0.000			

Table(4): Comparison Between Grades Of HIE and Significant Risk factors (p value < 0.05)

Risk factors	Mild-moderate HIE	Sever HIE	P value <0.05
Primi- para	21	4	0.009
Multi-para	16	15	
Male	28	8	0.02
Female	9	11	

Table (5): Risk Factors For Neonatal Death

Factors	Died	Discharged	P value
Gender			0.09
Male	7	29	
Female	8	12	

Benghazi Medical Center in 2016

Parity			
Primi-para	3	22	0.02*
Multi-para	12	19	
Apgar score			
≤ 7 at 5 min	11	16	0.02*
>7 at 5 min	4	18	
Not mentioned	0	7	
Type of resuscitation			
Mask and bag	0	22	0.02*
Intubation	3	13	
Intubation and chest compression	4	3	
Intubation, chest compression and drug	8	3	
Mode of delivery			
Vaginal delivery	6	23	0.2
Caesarian section	9	18	
Ventilator support			
No ventilator used	0	29	0.001**
Ventilator used	15	12	
HIE grades			
Mild-Moderate	0	37	0.001**
Sever	15	4	

*Significant risk factor

** Highly significant risk factor

6.0 Discussion

In the study, most of our babies who had signs and symptoms of hypoxic ischemic encephalopathy, their score at 5 minute was ≤ 7 (48.2%) similar to the study was done in Netherlands (Sabin., et al 2015). and in Sweden by Thomberg et al., 1995 As a low 5-minute Apgar score validity has been questioned, some studies recorded different results of Apgar at 5-minute in cases, as a study in Denmark by Ester., et al (2018) ; it was ≤ 5 (7), and in our study (39.3%) their Apgar > 7 at 5 minute. There are some studies depend on PH of umbilical cord with base excess ≤ 15 or PH < 7 in others, but in our study lack of these facilities made us depend on Apgar score and sings of HIE as it has been done in other study (Itoo., et al 2003). In our study some cases had Apgar score >7 but had signs and symptoms of HIE.

In the study, most of deliveries were vaginal; which may be itself considered as another risk for perinatal asphyxia, because in our situation, there is lack of a lot of facilities during crisis, like CTG ,few number of midwives and difficult to reach hospital early, but there were non-significant association between mode of delivery and HIE this result similar to other study in Denmark (Ester., et al 2018) . Some studies showed the operative and instrumental deliveries were high among cases of HIE(Itoo.,et al(2003) , Palsdottir., et al(2007) and Milsom ., et al. (2002) ; this is might be due to another risk for perinatal asphyxia already have existed; which were the indications for this mode of delivery.

In our study preexisting obstetrical risk factors for birth asphyxia were in 93% of the patients, whereas in study was done in France (Bouiller., et al 2016) only 20%of women had had obstetrical risk; this may be due to lack of antenatal care and lack of some facilities that important for monitoring of pregnant women as outpatients during Libyan crisis.

In this study, there was significant correlation between primi-paras and prolonged second stage, but it was non-significant risk factor for HIE. However, in clinical background, we can consider it as a risk factor for HIE, because in most cases the second stage was prolonged as recorded in the documents; due to poor pushing where actually most of primi-paras were not well trained during antenatal care for pelvic muscles exercises. In other study primi-paras was a risk factor for HIE but the relationship between two variables was not mentioned (Itoo.,et al 2003)

Although the total number of primi-paras with HIE is more than the other parities, but they were associated with mild to moderate HIE as compared to multi-paras, who were significant risk for severe HIE. But, our observation during follow up in neonatal clinic that; some cases of moderate asphyxia developed neurological sequelae, due to HIE; from our point of view the explanation was that ; number of our patients usually more than the capacity of NICU and number of nurses, therefore some attacks of convulsion could be missed or unnoticed , and accordingly leading to sequelae later on.

This result of our study regarding the parity is consistent to that was done by Odd David., et al(2017) , which considered the parity as one of risk factor for HIE (12). The study was done in Saudi Arabia by Itoo.,et al (2003) reported an inverse relationship between HIE grades and parity as compared to our study; it showed that severe or grade III is significantly related to primi-para while grade II to multi- para . In another studies (Odd David., et al(2017) , Nadia Badawi., et al. (1998) , Parker., et al(2018) ; there were other maternal factors mentioned as risk factors for HIE, rather than the parity like, antepartum hemorrhage, prolonged rupture of membrane, chorioamnionitis and pre-eclampsia .

In our study male babies were associated with mild to moderate HIE and females were risk factor for sever HIE. This result was different from other studies which reported that, the male gender was a risk factor for HIE higher than females(Itoo.,et al (2003), Odd David., et al(2017) Nadia Badawi., et al. (1998) .

Most of the babies were resuscitated with mask and bag, few numbers were needed medication this is similar to other studies (Thormberg., et al. (1995), Natash., et al.,(2013).

Not all babies who resuscitated with medication had sever HIE ;however the association between low Apgar and long term outcome has been documented(Ester., et al 2018).

One third of the babies with HIE were supported with ventilator during admission due to many causes like pneumothorax, meconium aspiration syndrome, hypoventilation as side effect of drug, persistent pulmonary hypertension and multi organ failure which have been observed in cases of sever HIE who died similar to the result of study had been done in Australia (Nadia Badawi., et al. (1998) ; whereas in study that had been done in India (Siva Saranappa.,et al 2015) only few babies has been supported with ventilator .

Sever cases of HIE was 34%; nearly half of them were resuscitated with adrenaline.

Most of sever HIE (79%) were died, and they kept on ventilator from the birth till death, this is the same results in other studies in which most of the babies died were sever HIE , while none of the babies with mild nor moderate HIE died as in other studies(Thomberg et al., (1995), Itoo.,et al (2003), Azhar, Munir. Qureshi., et al. (2010).

In addition to sever grade of HIE, there were other significant risk factors for neonatal death in our study including Parity, Apgar score ≤ 7 at 5 minute, resuscitation with medication and ventilator support ,but the gender and mode of delivery were not. In another study the parity, resuscitation and gender were associated with neonatal death including other maternal risk (Odd David., et al 2017) . while in study was done in South Africa the mode of delivery , mask and bag ventilation significantly associated with survival. The other factors like gender, chest compression were not differ between survivors and non-survivors (Natash., et al., 2013).

All babies with mild and moderate HIE were discharged , and have been kept to follow our clinic.

The mortality rate of perinatal asphyxia in the study was 26.8%, the same results was high 17% recorded in another study (Itoo.,et al 2003).While in studies were done in France and India the mortality rate was less (Bouiller., et al (2016) , Siva Saranappa.,et al (2015) as compared to our study.

7.0 Conclusion and recommendation

Primi -parity, prolonged second stage were important maternal risk factors, which significantly related to each other, lack of training of these mothers during antenatal care for labor might be the reason . Parity and female gender considered risk factors for sever HIE. Multi-paras,Apgar score ≤ 7 at 5 minute, ventilator support, resuscitation with drugs and sever grade of HIE were risk factors for neonatal death. Mortality rate was high; lack of medical resources could be the cause .all of the babies who died had sever grade of hypoxic ischemic encephalopathy. Well preparing of primi-paras mother, well skilled medical staff and close

monitoring and regular evaluation of the mother and her baby during labor can eliminate this problem.

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