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EPIDEMIOLOGICAL STUDY OF HYPOXIC- ISCHEMIC ENCEPHALOPATHY IN NEWBORN BABIES IN AL-KHANSAA AND AL-BATOOL TEACHING HOSPITALS IN MOSUL CITY.

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ABSTRACT

Hypoxic-ischemic encephalopathy (HIE) is an important cause of neonatal morbidity and mortality that may lead to permanent damage to brain tissue. It is result from lack of oxygen and /or ischemia to the brain before, during and after delivery. To determine the prevalence rate of Hypoxic Ischemic Encephalopathy (HIE) in Al-Khansaa and Al-Batool Teaching Hospitals in Mosul city from the April 1st 2018 until the end of December 2018, and to assess selected risk factors which may be reliable predictors for HIE, as well as the contribution of these risk factors to the severity of HIE . This is a case control study, 94 cases (43 among 16950 in Al-Khansaa teaching hospital and 51 among 18450 in Al-Batool teaching hospital) of the total number of 35400 born in these two hospitals had HIE The babies were delivered at one of these two hospitals during 9 months between April 1st , 2018, and the end of December 2018, with Apgar scores of <7 at 5 minutes and displayed any clinical criteria of HIE (altered tone, depressed level of consciousness, or seizures), with or without the signs and symptoms of other asphyxiated organs; after the exclusion of other differential diagnoses of HIE by related clinical examinations and laboratory investigations. The total number of live births delivered in Al-Khansaa and Al-Batool Teaching Hospitals during this 9 month study was 35,400. Of the total number of live births, 94 met the clinical criteria of HIE included in this study. The incidence of newborns with HIE was 2.65/1000 live births. The number of newborns with mild HIE was 17, the number of newborns with moderate HIE was 32, and the number of newborns with severe HIE was 45 (as shown in table 1). The incidence of moderate to severe HIE was 2.17 /1000 live births.

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INTRODUCTION

Asphyxia is the most common and preventable cerebral injury occurring in neonatal period (1). Asphyxia is an insult to the fetus or newborn due to lack of oxygen or lack of perfusion to various organs (2). There are many reasons a baby may not be able to take in enough oxygen before, during, or just after birth, this may affect the brain as well as other organs and in severe cases may lead to brain injury or even death. The major difficulty in collecting accurate epidemiological data on birth asphyxia is the lack of common definition of the condition although asphyxia at birth is a commonly made diagnosis (3).

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The better terminology for birth asphyxia is perinatal asphyxia, as brain insult secondary to hypoxia may occur in utero, at birth or in the post natal period. The World Health Organization (WHO) has defined perinatal asphyxia as a " failure to initiate & sustained breathing at birth "(4)

Aims of the Study: To determine the prevalence rate of Hypoxic Ischemic Encephalopathy (HIE) in Al-Khansaa and Al-Batool Teaching Hospitals in Mosul city from the April 1st 2018 until the end of December 2018, and to assess selected risk factors which may be reliable predictors for HIE, as well as the contribution of these risk factors to the severity of HIE. Patients and Methods:-This is a case control study, 94 cases (43 among 16950 in Al-Khansaa teaching hospital and 51 among 18450 in Al-Batool teaching hospital) of the total

number of 35400 born in these two hospitals had HIE The babies were delivered at one of these two hospitals during 9 months between April 1st, 2018, and the end of December 2018, with Apgar scores of <7 at 5 minutes and displayed any clinical criteria of HIE (altered tone, depressed level of consciousness, or seizures), with or without the signs and symptoms of other asphyxiated organs; after the exclusion of other differential diagnoses of HIE by related clinical examinations and laboratory investigations. Proper examinations had been performed to assess the severity of HIE as mild, moderate, or severe. Additionally, the following information was documented: detailed prenatal, natal, and postnatal history, the need for immediate resuscitation, the birth weight, and the gestational age. The following information regarding the maternal history has been documented: maternal age, complications or the use of sedation during labor, certain maternal risk factors like hypertension, antepartum haemorrhage and mode of delivery, the antenatal care, maternal diseases, and parity. Of the 35,400 live newborns that were born during the 9 month period of the study, 94 normal neonates were selected as a control group for the purposes of this study. Detailed information was documented for the control group, in the same manner that was previously mentioned for the diseased group. For each risk factor, the corresponding number and percentage of patients with HIE has been documented. Additionally, the number and percentage of patients with different degrees of severity of HIE, has been documented within each risk factor. Statistical significance has been assessed through the analysis of the chi-square test $\chi 2$ and the p-value.

RESULTS

The total number of live births delivered in Al-Khansaa and Al- Batool Teaching Hospitals during this 9 month study was 35,400. Of the total number of live births, 94 met the clinical criteria of HIE included in this study. The incidence of newborns with HIE was 2.65/1000 live births. The number of newborns with mild HIE was 17, the number of newborns with moderate HIE was 32, and the number of newborns with severe HIE was 45 (as shown in table 1). The incidence of moderate to severe HIE was 2.17 /1000 live births.

Selected Risk Factors

Antenatal Care: Of the total 94 cases of HIE, 50 had a maternal history of antenatal care during the pregnancy and 44 cases had no antenatal care. There was a significant relationship between the maternal history of antenatal care in newborns with HIE, in comparison to the control group (p-value of 0.0004). Among the cases with mild HIE, 13 had maternal history of antenatal care, while 4 cases had no antenatal care. Meanwhile, among cases with moderate HIE, 16 had a maternal history of antenatal care, while the other 16 cases had no history of antenatal care. Of the cases with severe HIE, 21 had a maternal history of antenatal care, while the remaining 24 cases had no history of antenatal care. Therefore, there was no significant relationship between the maternal history of antenatal care and the degree of HIE severity (p-value of 0.101).

Table 1. The numbers and percentages of newborns with each degree of HIE

Degree of HIE	Number of patients	Percentage %
Mild	17	18.08
Moderate	32	34.04
Severe	45	47.87
Total	94	100

Table 2. The relationship between the presence or absence of maternal antenatal care during pregnancy, and the incidence of HIE

Antenatal Care	No. of HIE cases	(%)	No. of control cases	(%)
Presence	50	53.19	73	77.65
Absence	44	46.80	21	22.34
Total	94	100	94	100

$\chi^2 = 12.439$ p = 0.004

Table 3. The relationship between the presence or absence maternal antenatal care during pregnancy, and the degree of severity of HIE

Antenatal care	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. of Severe HIE	(%)
Presence of Antenatal Care	13	76.47	16	50	21	46.66
Absence of Antenatal Care	4	23.52	16	50	24	53.33

$\chi 2 = 4.6$ p = 0.101

Table 4. The relationship between the presence of maternal Diseases during pregnancy and the incidence of HIE in the newborns

Maternal diseases	No. of HIE cases	(%)	No. of control cases	(%)
No maternal diseases	7	7.44	47	50
APH	28	29.78	18	19.14
Hypertension	53	56.38	24	25.53
DM	6	6.38	5	5.31
Total	94	100	94	100

$\chi 2 = 42.817$ p = 0.0001

Maternal Diseases during Pregnancy: Of the total 94 cases of HIE, 7 had no maternal diseases during the pregnancy, 28 cases had antepartum haemorrhage (APH), 53 cases had a maternal history of hypertension, while 6 cases had a maternal history of diabetes mellitus (DM). Therefore, there was a significant relationship between the presence of maternal diseases during pregnancy and the incidence of HIE in the newborns, in comparison to the control group (p- value of 0.0001). Among cases with mild HIE, 4 cases had no maternal diseases, 6 cases had a maternal history of APH, and 7 cases had a maternal history of hypertension. Meanwhile, among cases with moderate HIE, 2 had no maternal disease, 12 had a maternal history of APH, 12 cases had a maternal history of hypertension, and 6 cases had a maternal history of DM. Of the cases with severe HIE, 1 had no maternal disease, 10 had a maternal history of APH, and 34 cases had a maternal history of hypertension. Therefore, there was a significant relationship between the presence of maternal diseases during pregnancy and the degree of severity of HIE in the newborns (p-value of 0.0001).

Table 5. The relationship between the presence of maternal diseases during pregnancy and the degree of severity of HIE in the newborns

Maternal diseases	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. of Severe HIE	(%)
No maternal diseases	4	23.52	2	6.25	1	2.22
APH	6	35.29	12	37.5	10	22.22
Hypertension	7	41.17	12	37.5	34	75.55
DM	0	0	6	18.75	0	0

$\chi 2 = 26.572$; $p = 0.001$

Table 6. The relationship between the parity of mothers and the incidence of HIE

Parity	No. of HIE cases	(%)	No. of control cases	(%)
1	49	52.12	45	47.87
2	23	24.46	31	32.97
>2	22	23.40	18	19.18
Total	94	100	94	100

$\chi 2 = 1.755$ $p = 0.415$

Table 7. The relationship between the parity of mothers and the degree of HIE

Parity	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. of Severe IE	(%)
1	6	35.29	15	46.87	28	62.22
2	4	23.52	10	31.25	9	20
>2	7	41.17	7	21.87	8	17.77

$\chi 2 = 5.883$ $p = 0.208$

Table 8. The relationship between the gestational age of newborn infants and the incidence of HIE

Gestational age (weeks)	No. of HIE cases	(%)	No. of control cases	(%)
28 -34	9	9.57	15	15.95
35 -37	14	14.89	35	37.23
38 - 41	35	37.23	28	29.78
≥42	36	38.29	16	17.02
Total	94	100	94	100

$\chi 2 = 18.97$ $p = 0.002$

Parity of mother

Forty nine cases with HIE had Para 1 mother, 23 cases had Para 2 and 22 cases had >2, therefore there was no significant relationship between the parity of mother in newborns with HIE in comparison to control group (p-value of 0.415). In cases of mild HIE, 6 cases had Para 1 mother, 4 case had Para 2 mother while 7 cases had > 2. In cases with moderate HIE, 15 cases had Para 1 mother, 10 cases had Para 2 and 7 cases had > 2. In cases with severe HIE, 28 cases had Para 1 mother, 9 cases had Para 2 while 8 cases had >2 and therefore there was no significant relationship between the parity of mother and the increment in HIE severity (p-value of 0.208).

Gestational age

Nine cases with HIE had a gestational age range between 28 -34 weeks, 14 cases had a gestational age range between 35 – 37 weeks, 35 cases had a gestational age range between 38 - 41 weeks and 36 cases had a gestational age of ≥42 weeks. and therefore there was a significant relationship between the gestational age of newborns with HIE in comparison to control group (p-value of 0.002). In cases with mild HIE ,6 cases had a gestational age range between 28-34 weeks , 6 cases had a gestational age range between 35 – 37 weeks and 5 cases had a gestational age of 38 -41 weeks . In cases with moderate HIE , 3 case had a gestational age range between 28 -34 weeks, 5 cases had a gestational age range between 35 – 37 weeks , 12 cases had a gestational age range between 38-41 weeks and 12 cases had a gestational age of ≥42 weeks. While in cases with severe HIE, 3 case had a gestational age between 35 – 37 weeks and 18 cases had a gestational age range between 38 – 41 weeks and 24 cases had a gestational age of ≥42 weeks and therefore there was a significant relationship between the gestational age and the increment in HIE severity (p-value of 0.0001). Thirty one cases with HIE have been born by normal vaginal delivery (NVD), 53 cases by caesarean section (C/S), from which 32 cases delivered by emergency C/S and the other 21 cases by elective C/S and 10 cases by instrumental delivery so therefore there was no significant relationship

between the mode of delivery in newborn with HIE in comparison to control group (p-value of 0.272). In cases with mild HIE, 6 cases delivered by NVD, 9 cases by C/S, from which 4 cases delivered by emergency C/S and the other 5 cases by elective C/S and 2 cases by instrumental delivery. In cases with moderate HIE, 15 cases delivered by NVD, 15 by C/S , from which 8 cases delivered by emergency C/S and the other 7 cases delivered by elective C/S and 2 cases by instrumental delivery While in cases with severe HIE, 10 cases delivered by NVD, 29 by C/S, from which 20 cases delivered by emergency C/S and the other 9 cases delivered by elective C/S and 6 cases by instrumental delivery and therefore there was no significant relationship between the mode of delivery and the increment in HIE severity (p-value of 0.266).

Birth Weight: Six cases with HIE had a birth weight range of 1 -2 kg , 12 cases had a birth weight of 2.1- 2.5 kg and 18 cases had a body weight of 2.6 -3 kg ,14 cases had a birth weight of 3.1- 3.5, 23 cases had a birth weight of 3.6 -4 and 21 cases had a birth weight of >4 kg therefore there was no significant relationship between the birth weight of newborns with HIE in comparison to control group (p-value of 0. 0.124).

In those with mild HIE, 3 cases had a birth weight range of 1-2 kg, 2 case had a birth weight range of 2.1-2.5 kg , 4 cases had range of 2.6 -3 kg , 4 cases had a range of 3.1 -3.5 kg and 4 cases had a range of 3.6 – 4 kg. In cases with moderate HIE, 2 case had a birth weight range of 1– 2 kg, 4 cases had a birth weight range of 2.1 – 2.5 kg, 7 cases had a birth weight of 2.6 -3 kg, 5 cases had a birth weight range of 3.1-3.5 kg , 8 cases had a birth weight range of 3.6 – 4 kg and 6 cases had a birth weight of >4 kg . While in cases with severe HIE, 1 case had birth weight range 1– 2 , 6 cases had a birth weight range of 2.1 – 2.5 kg ,7 cases had a birth weight range of 2.6-3 kg and 5 cases had a birth weight range of 3.1 -3.5 kg and 11 , 15 cases had a birth weight range of 3.6).

DISCUSSION

In this prospective study which was conducted over a nine month duration, the incidence of live newborns with hypoxic ischemic encephalopathy was 2.65/1000 live births, which falls within the range that was reported by Seetha S, et al. in 2011(27) in which the incidence was 1- 6/1000 live births. Additionally, the incidence of moderate to severe HIE was 2.17/1000 live births which is more than that reported by James T, in 2008(7), which was 2/1000 live births.

Table 9. The relationship between the gestational ages and the degree of HIE

Gestational Age (Weeks)	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. of Severe HIE	(%)
28 - 34	6	35.29	3	9.37	0	0
5 - 37	6	35.29	5	15.62	3	6.66
38 - 41	5	29.41	12	37.5	18	40
≥42	0	0	12	37.5	24	53.33

$\chi 2 = 32.407$: p = 0.0001

Table 10. The relationship between the mode of delivery and the incidence of HIE

Mode of delivery	No. of HIE cases	(%)	No. of control cases	(%)
NVD	31	32.97	36	38.29
Elective C/S	21	22.34	28	29.78
Emergency C/S	32	34.04	25	26.59
Instrumental Delivery	10	10.63	5	5.31
Total	94	100	94	100

$\chi 2 = 3.899$ p = 0.272

Table 11. The relationship between the mode of delivery and the degree of HIE

Mode of Delivery	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. of Severe HIE	(%)
NVD	6	35.29	15	46.87	10	22.22
Elective C/S	5	29.41	7	21.87	9	20
Emergency C/S	4	23.52	8	25	20	44.44
Instrumental Delivery	2	11.76	2	6.25	6	13.33

$\chi 2 = 7.632$ p = 0.266

Table 12. The relationship between the birth weights of newborn infants and the incidence of HIE

Birth Weight (kg)	No. of cases with HIE	Percentage (%)	No. of control cases	Percentage (%)
1 -2	6	6.38	8	8.51
2.1 -2.5	12	12.76	22	23.40
2.6 -3	18	19.14	20	21.27
3.1 -3.5	14	14.89	18	19.14
3.6 - 4	23	24.46	15	15.95
>4	21	22.34	11	11.70
Total	94	100	94	100

$\chi 2 =$ 8.641 p = 0.124

Table 13. The relationship between the birth weight and the degree of HIE

Birth Weight (kg)	No. of Mild HIE	(%)	No. of Moderate HIE	(%)	No. 0f Severe HIE	(%)
1 – 2	3	17.64	2	6.25	1	2.22
2.1-2.5	2	11.76	4	12.50	6	13.33
2.6- 3	4	23.52	7	21.87	7	15.55
3.1-3.5	4	23.52	5	15.62	5	11.11
3.6- 4	4	23.52	8	25	11	24.44
>4	0	0	6	18.75	15	33.33

$\chi 2 = 12.947$ p = 0.226

The incidence rate found in this study is relatively high when compared to the results of the Milsom I, et al. study conducted in Göteborg University, Sweden (Table 14) from 1995 to 2001, which reported the incidence rate of HIE in the Swedish population(28) as 1.8/1000 live births.

Table 14. A comparison between the Mosul and Sweden studies

Parameter	Mosul study	Sweden study
Duration of the Study	9 month	6 years
Number of Live Birth	35400	42203
Incidence of HIE	2.65/1000	1.8/1000

Despite these findings, the incidence of HIE in Mosul may actually be higher than this study has reported. This study has only captured the deliveries that have occurred in two hospitals in the centre of the city where most of the deliveries took place inside the hospitals. This is in sharp contrast to the peripheries, where most deliveries typically take place at district hospitals, or at home with the presence of a midwife, in both conditions a high incidence of HIE is expected. Additionally, most if not all pregnant women in the peripheries do not have regular antenatal care, and many of these women experience a delay in seeking hospital care, as they arrive late to the hospital, after the involvement of a midwife and with signs of fetal distress already present. In addition to this, is the unavailability of important screening tools for the early detection of fetal distress, such as the cardiotocograph (CTG) and fetal blood sampling for PH estimation. This study demonstrates that there was a significant relationship between absence maternal history of antenatal care in newborns with HIE, in comparison to the control group (Table 2). This finding is in agreement with most studies including: [AlShehri MA, et al. in Abha City 2005,Qureshi AM, et al. in Abbottabad 2010 and Butt TK, et al. in Lahore 2008] (29,30,31). In addition, there was no significant relationship between maternal history of antenatal care and the degree of severity of HIE (Table 3). This result is also consistent with AlShehri MA, et al study in Abha city, (29) which may be related to the degree of effectiveness of antenatal care. This study also illustrated a significant relationship between the history of maternal diseases during pregnancy and HIE in comparison to the control group (Table 4). Among the maternal diseases included in this study, pregnancy induced hypertension accounted for the highest proportion of cases, at (56.38%), followed by antepartum haemorrhage at (29.78%). Pregnancy induced hypertension is the main maternal disease that significantly correlated to HIE. This result was more obvious in severe cases (75.55%), as it significantly related to the degree of severity (Table 5). These results are consistent with AlShehri MA, et al. and Qureshi AM, et al. studies in Abbottabad, (29,30) in which cases with pregnancy induced hypertension and antepartum haemorrhage carried a high risk for HIE, this is explained by fetal hypoxia and placental insufficiency due to antepartum haemorrhage and maternal toxaemia respectively.

With regard to parity, there was no significant relationship between HIE and the parity of the mother (Tables 6&7) and this result is compatible with the Butt TK, et al. study in Lahore(31) which shows that the primigravidity carried a risk, but was not statistically significant for HIE. This may be due to the nature of the statistical analysis conducted in this study, which dealt with the parity of HIE in comparison to a control group, rather than comparing the relation of one parity to the other, which may be studied separately in other research. This study also shows that there was a significant relationship between HIE and the gestational age (Table 8). It shows that the number and percentage of newborns with HIE increased as the gestational age increased, and the highest percentage was found at greater than 41 weeks of gestational age. This finding is consistent with the Itoo BA, et al. study in Madina Al-Munawara 2003(32). There was a significant relationship between the gestational age and the degree of HIE severity (Table 9), as 53.33% of cases with severe HIE had a gestational age of >41 weeks, this finding was also consistent with the Itoo BA, et al. study(32). With regard to the mode of delivery, a large number of cases were delivered via emergency caesarean section, which represented 34.04% of HIE cases and 44.44% of severe cases, however, in general there was no significant relationship between the mode of delivery and the presence of HIE, in comparison to the control group (Table 10). In addition, there was no significant relationship between emergency caesarean sections and the degree of severity (Table 11). These results are identical to that of Butt TK, et al. study.(31) This statistical finding may be related to the number of cases with NVD, which is approximately that of emergency C/S, which may explain why the statistical result is not significant. This study shows that there was no significant relationship between the birth weights of newborns and the occurrence of HIE, in comparison to the control group (Table 12). In addition, there was no significant relationship between the birth weight and the severity of HIE (Table 13). However, this study has illustrated that most cases of HIE occur at a birth weight which is greater than 3.6 kg. These results are compatible with the Martinez-Biarge M, et al. study in London 2013. (33)

Conclusion

The incidence of newborns with HIE was 2.65/1000 live newborns, 17 (18.07%) cases were mild HIE, 32 cases were moderate (34.03%), and 45 cases were severe (47.87%). There was a significant relationship between the maternal history of antenatal care and the presence of HIE in newborns; However, there was no significant relationship between the absence of maternal history of antenatal care and the degree of severity of HIE. There was a significant relationship between maternal diseases and HIE in newborns, mostly with maternal hypertension. There was a significant relationship between the gestational age and HIE in newborns. There was no significant relationship between the parity, mode of delivery, and birth weight and the presence of HIE in newborns.

Recommendations

Comprehensive antenatal coverage and adequate care for pregnant mothers, particularly those with pregnancy complications such as antepartum haemorrhage and maternal toxaemia. By this one can significantly reduce the incidence, morbidity, and mortality rates associated with hypoxic ischemic encephalopathy. Close monitoring of the fetal status during labor, through a combination of continuous recording of the fetal heart rate by C.T.G. as well as fetal blood sampling for PH estimation when necessary to confirm any suspicion of HIE, especially in high risk groups. Optimal management of newborns at birth in a well-equipped NICU, in order to reduce the perinatal mortality rate and improve the quality of life among the survivors.

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