An-Najah National University

Faculty of Graduate Studies

Effectiveness and Outcome of Implementation Therapeutic Hypothermia Asphyxiated Neonates at Governmental Hospital in West Bank

By

Elham Fayyad

Supervisor

Dr. Eman Al Shawish

This Thesis is Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Critical Care Nursing, Faculty of Graduate Studies, An-Najah National University, Nablus- Palestine.

2021

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Elham Turkman

This Thesis was Defended Successfully on 25/5/2021 and approved by:

Defense Committee Members:	**Signature**
• **Dr. Eman Al Shawish / Supervisor**	Dr. Eman Al Shawish
• **Dr. Khawther Alyasa / External Examiner**	Dr. Kawther Alyasa
• **Dr. Aidah Alkissi / Internal Examiner**	Aidah Alkissi

Dedication

الهي لا يطيب الليل الا بشكرك ولا يطيب النهار الا بطاعتك ولا تطيب اللحظات الا بذكرك ولا تطيب الاخرة الا بعفوك ولا تطيب الجنة الا برؤيتك فلك الحمد. الى سيدي وحبيبي وأطيب من وطئت قدماه الثرى الى سيدي محمد صلى الله عليه وسلم.

الى من كلله الله بالهيبة والوقار وعلمني العطاء بدون انتظار الى من احمل اسمه بكل افتخار ارجو من الله ان يمد في عمرك لترى ثمارا قد حان قطافها بعد طول انتظار، الى من رفعت رأسي عاليا افتخارا به .... والدي الحبيب إلى التي راني قلبها قبل عينيها وحضنتني احشاؤها قبل يديها الى من ساندتني في صلاتها ودعائها حفظها الله واطال في عمرها بالصالحات....أمي الغالية.

والى امي الثانية لتي كانت دعواتها الصادقة سر نجاحي.. حفظها الله ورعاها.. عمتي الفاضلة وجيهه. الى الروح التي علمتني معنى الفقد. اذ ان الوجع ليس في ايام الفقد الاولى، بل حين تأتي الايام السعيدة فتجد ان من يستطيع مشاركتك بشكل اعمق قد رحل الى كبيرة المقام ذات السيرة العطرة الى روح عمتي الغالية مريم رحمها الله.

الى سندي وعضدي الى من شاركني طفولتي وأحبني بصدق واخلاص وتعاون معي لإتمام دراستي هذه ... اخي الحنون (أحمد) أدامك الله لي سنداً. إلى من هن أقرب الي من روحي والي من شاركوني حضن امي ومهدوا امامي طريق الوصول الي ما انا عليه الان .. اخواتي الكريمات (نسرين وعروبة وهناء).

الى من سكنت روحي بروحه فكان نعم السند في رحلتي العلمية والبحثية ولم يدخر جهدا في مساعدتي.. شكرا لكونك بجانبي.. زوجي الحبيب (عمار). إلى ملاكي الصغير، الى صديقتي وقرة عيني الى بلسم جراحي الى جميلة الجميلات ابنتي (سلاف).

الى من انجبت شريك حياتي حماتي الفاضلة والي اخواتي التي لم تلدهن امي (ناديه, فادية) والي اخي العزيز (فادي) الذي تحمل معي عناء هذه الدراسة دمت لنا فخراً وعزاً.

Acknowledgment

First and foremost, praises and thanks to the GOD, the Almighty, for His showers of blessings throughout my research work to complete the research successfully and for the HIS messenger, Prophet Muhammad (peace be upon him).

Secondly I would like to express my s*pecial thanks of gratitude to* my supervisor (Dr, Eman Alshawish) who gave me in doing a lot of research and I came to know about so many new things I am really thankful to her.

Se I would like to thank my parent for their love, prayers, caring and sacrifices for educating and preparing me for my future. who helped me a lot in finalizing this project within the limited time frame.

I am very much thankful to my husband and my daughters

(Sulfa) for their love, understanding, prayers and continuing support to complete this research work. Also I express my thanks to my sisters, brother, for their support and valuable prayers. My Special thanks go to my friend and all family for the keen interest shown to complete this thesis successfully.

الاقرار

أنا الموقعة أدناه، مقدّمة الرسالة التي تحمل العنوان:

Effectiveness and Outcome of Implementation Therapeutic Hypothermia Asphyxiated Neonates at Governmental Hospital in West Bank

أقر بأن ما اشتملت عليه هذه الأطروحة إنما هو نتاج جهدي الخاص، باستثناء ما تمت الاشارة إليه حيثما ورد. وأن هذه الرسالة كاملة، أو اي جزء منها لم يقدم من قبل لنيل اي درجة او لقب علمي او بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: **اسم الطالبة:**

Signature: **التوقيع:**

Date: **التاريخ:**

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List of Abbreviation

WHO	World Health Organization
HIE	hypoxic ischemic encephalopathy
TH	Therapeutic hypothermia
NICU	Neonate Intensive care unit
APGAR	Appearance, Pulse, Grimace, Activity, Respiration
GA	Gestation age
Temp	Temperature
ABG	Arterial blood gases
HR	Heart rate
MV	Mechanical Ventilator
CT	Computerized Tomography
TFU	Trans Fontanel Ultrasound
aEEG	Amplitude integrated electroencephalography
ECHO	Echo cardiography
MRI	Magnetic resonance
CRP	C-reactive protein
SBP	Systolic blood pressure
DBS	Diastolic blood pressure
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
PT	Prothrombin time
PTT	Partial thromboplastin time
V/S	Vital Sign
WT	Weight

Effectiveness and Outcome of Implementation Therapeutic Hypothermia Asphyxiated Neonates at Governmental Hospital in West Bank

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Abstract

Background: Birth asphyxia is the medical condition resulting from deficient supply of oxygen to the infant for extended period of time during the birth process, as a result for many etiology infant usually become cyanosis, bradycardia, Apgar score is low in the first 5 min.

Extreme degrees of asphyxia are associated with high morbidity and mortality rates worldwide. There is an urgent need to improve outcomes in affected infants .Therapeutic hypothermia (TH) as whole body or selective head cooling has become a standard therapy for moderate-severe HIE in many developed countries to reduce neurological damage within the first 6 hrs of life, by systemic cooling to 34.5 ± 0.5°C for head cooling, for surface cooling (33.5 ± 0.5°C) and continuing for 72 hrs.

Aims of the Study: To assess the effectiveness and outcome of implementation therapeutic hypothermia and the relationship between therapeutic hypothermia and mortality rate, seizure and to assess relationship between therapeutic hypothermia and staying day in MV & relationship between therapeutic hypothermia and neurodevelopment defect, primitive reflexes.

Method: The study adopted the Quazi experimental design. The study included prospective study.

Experimental group baby who received therapeutic hypothermia and historical study as control group who not received therapeutic hypothermia .Survey will be carried out at Neonatal Intensive Care Unit in Governmental Hospital in Jenin. The period is one year from February 2020 to September 2020.

Results: There are no significant differences at 0.05 level between Experimental group and Control group in Age of mothers, and gestational age significant differences at 0.05 level between the Control group and the Experimental group in Continued need for PPV or Intubation at 10 mints (the P-value is less than 0.05), the percentage of infants needed PPV in the experimental group was 10(30.3%) which is significantly higher than that in the control group 0(0%), while the percentage of infants needed intubation in the experimental group was 23(69.7%) which is significantly lower than that in the control group 27(100%). First day IN control group mild HIE 2(7.4%) moderate 13(48.1%),sever 12(44.5%) , in experimental group 0(0%),30(90.9%),3(9.1%) respectively but in third day of treatment in control group mild, moderate, sever 0(0.0%),3(27.3%),24(72.7%)in experimental group 24(72.7%),9(27.3).0(0.0) respectively. The percentage of mortality for infants HIE in the control group 4(14.8%) was significantly higher than that in the experimental group 1(3%), while the percentage late neonatal death 0(0%) in the experimental group was significantly lower

than that in the control group 7(25.9%) with P value 0.002.Regarding Seizures at the second and third day, the percentages of Non Seizures are 27(81.8%) and 28(84.8%) which significantly higher than that in the control group 8(29.6%) and 7(25.9%), while the percentage of Present Seizures in the experimental group are 6(18.2%) and 5(15.2%) which significantly lower than that in the control group 17(63%). Regarding MV after 6 hr from admission, the percentage in the experimental group 17 (53.1%) was significantly higher than that in the control group 7(25.9%). In the second day, the percentage in the experimental group 7(21.9%) was significantly higher than that in the control group 3(11.1%). Regarding Suck at the second day, the percentage of Weak Suck in the experimental group 25(75.8%) was significantly higher than that in the control group 7(25.9%), while the percentage of Absent Suck in the experimental group 7(21.2%) was significantly lower than that in the control group 18(66.7%) so feeding process in experimental group started feeding too early than control group who started at and above day 7 of finished cooling , but other started at day 3 of finished cooling in 9.1% , 4 day 15.2% ,5 day 45.5%, 6 day 18.2%, 7+ day 12.1%.Also the follow up assessment results showed in vision test there is no any vision loss on all babies who underwent cooling therapy compared with one vision loss on control group, the same matter in hearing test one hearing loss on control group with no losing in experimental group.

Conclusions: Hypothermia is most benefit when establish in the first ≤6 hours in term infant and late prematurity GA ≥36 weeks who in HIE to limit damage in the brain. Infants offered hypothermia should meet inclusion criteria. Eligibility criteria include a pH of ≤7.0 or a base deficit of ≥16 mmol/L in a sample of umbilical cord blood or blood obtained during the first hour after birth, history of an acute perinatal event, a 10-minute Apgar score of <5, or assisted ventilation initiated at birth and continued for at least 10 minutes. In addition, a neurologic examination demonstrating moderate to severe HIE is essential.

Recommendation: Excluded for the following baby in TH: Baby (<36 weeks), Baby WT <1800, HIE baby admitted after 6hr, Lethal congenital and chromosomal anomalies. The current hypothermia protocol is starting treatment within golden hours in the first 6 hrs of life, by systemic cooling to 34.5 ± 0.5°C for head cooling, for (surface cooling) or whole-body cooling(33.5 ± 0.5°C) and continuing for 72 hrs, also more researches needed included HIE babies who pass the first six gold hour and do TH in also first 12 hours by using wide sample size and observed the developmental defect later on like, school age.

Key word: Hypoxic ischemic encephalopathy, therapeutic hypothermia, Apgar score, acidosis, cooling therapy.

Chapter one
Introduction

1.1 Overview

Perinatal asphyxia or birth asphyxia is the medical condition resulting from deficient supply of oxygen to the infant for extended period of time during the birth process (Dickson et al,2014).The causes of perinatal asphyxia can be various as a result for many etiology as hypoventilation during anesthesia lead to inadequate oxygenation of maternal blood, cardiacdiseases, respiratory failure, hypotension, umbilical cord around the neck of infant, premature separation of placenta, so the brain and other organs do not get enough oxygen and nutrients which lead to physical and mental harm manifested as developmental delay or intellectual disability, spasticity (Dickson et al,2014). An infant usually becomes cyanosis, bradycardia, poor muscle tone, weak reflexes and respiratory effort, Apgar score is low in the first 5 min.

Extreme degrees of asphyxia are associated with high morbidity and mortality rates worldwide.

According to World Health Organization (WHO) estimated that 4 millions of neonatal deaths yearly (Aslam, ET al.2014), is a major challenge for the baby, the family, and society. There is an urgent need to improve outcomes in affected infants.

The incidence of hypoxic ischemic encephalopathy (HIE) is significantly higher lead to heavy social and economic costs. In developed countries, perinatal asphyxia estimated is two newborn per 1000 births, but in developing countries as a result of limited access to maternal and neonatal care the rate is up to 10 times of birth asphyxia (Odd et al,2017).

Therapeutic hypothermia (TH) as whole body or selective head cooling has become a standard therapy for moderate-severe HIE in many developed countries to reduce neurological damage.

The efficacy of TH in term infants with moderate to severe encephalopathy recent documented by meta-analyses (Tagin, et al. 2012; Jacobs, et al.2013), 50% from neonatal intensive Care units (NICU) in United States were reported to provide therapeutic hypothermia (Harris, et al. 2014). Also several countries in Europe have already implemented TH (Denis Azzopardi, et al.2012; Groenendaal et al, 2013). In Jenin NICU (TH) protocol has been newly implemented.

This study aims to assess the effectiveness and outcome of using (TH) protocol in this unit (Appendix 1), to identify the problems encountered in its implementation, and to assess the outcome of these newborns.

1.2 Problem Statement

Birth asphyxia has a significant burden for the patient's family, and to the society in general.

HIE is estimated to occur in between 2 newborn per 1,000 live births, and up to 85 % risk of death and the risk of cerebral palsy and mental retardation increase among survivors (Kurinczuk, et al.2010).

The advantage of therapeutic hypothermia has significantly reduced rates of death, disability (Zhou, et al 2010).

1.3 Significance of the Study

This study will support the use of therapeutic hypothermia in treatment newborns who have HIE and harvest the benefit that return to the baby, family, hospital and society by reducing the complication of birth asphyxia.

So the study is important for several reasons. Firstly, the lack of Palestinian studies that supports the implementation of cooling therapy. Secondly, this research will be the first study that deal with this type of treatment in Jenin Governmental Hospital. Thirdly, to increase the awareness of health team in the neonatal intensive care unit to the advantage of this treatment.

Finally, it decreases the cost of HIE treatment because the cooling therapy will offer benefit when decreases the severity of HIE complication.

1.4 Aims of the Study

- To assess the effectiveness and the outcomes of implementation therapeutic hypothermia.
- To assess the relationship between therapeutic hypothermia and mortality rate.
- To assess the relationship between therapeutic hypothermia and seizure.
- To assess the relationship between therapeutic hypothermia and staying day in MV.
- To assess the relationship between therapeutic hypothermia and neurodevelopment defect (hearing, vision).
- To assess the relationship between therapeutic hypothermia and improvement in primitive reflexes (sucking, Moro).

1.5 Research Hypotheses

- The benefits from implementation therapeutic hypothermia in HIES newborns in Jenin Hospital.
- The relationship between therapeutic hypothermia and reducing mortality rate.
- The relationship between therapeutic hypothermia and reducing seizure.

- The relationship between therapeutic hypothermia and reducing staying day on MV.
- The relationship between therapeutic hypothermia and reduce neurodevelopment defect (hearing, vision).
- The relationship between therapeutic hypothermia and improvement in primitive reflexes (sucking, Moro).

Chapter Two
Background

Therapeutic Hypothermia (TH) or cooling therapy has become a standard care by improving survival, reducing mortality and improving neurological recovery in moderate or severe HIE in newborn (Shankaran, et al.2005).

Current hypothermia protocol is starting treatment within golden hours in the first 6 hrs of life, by systemic cooling maintained the head cooling 34.5 ± 0.5°C and for whole-body cooling or (surface cooling) 33.5 ± 0.5°C and continuing to 72 hrs (Jacobs ,et al.2013).

Whole cooling demands applying a cooling blanket or mattress around the baby or circulating cool fluid. Head cooling is circulating cool fluid inside the cap that is wrapped around the baby head continuously monitored for baby's core temperature during the procedure (Wachtel, et al. 2011).

The core temperature taken by rectal route is considerd the gold standered (Blaž Cugmas,et al.2020). The axillary temperature is not recommended during TH (Landry et al. 2013).

First phase in asphyxia: blood flows reduce and oxygen supply decrease lead to primary energy failure characterized by decreasing Adenosine triphosphate (ATP) production lead to impaired on sodium, potassium pump and systemic acidosis from increased lactate , energy failure leads to loss of integrity of the cell membrane (Fleiss B et al,2012), calcium entry

into the cell and in severe stage it leads to cell necrosis, this stage occurs within first six hours on birth life.

So the resuscitation and reperfusion can limit this damage by impairment of cerebral oxidative metabolism that can at least partially recover, before irreversible failure of mitochondrial function (Drury, ET al.2014). Neuroprotective interventions is effective in this phase to inhibit The activity of harmful cell processes (Drury, et al.2014; Wassink et al.2015). So TH is most benefit when establish in the first ≤6 hours in term infant and late prematurity gestational age (GA) ≥36 weeks who in HIE in acute perinatal period and baby who meet treatment criteria A, B, C according to current evidence (Committee on Fetus and Newborn, et al.2014).

(Criteria A) when Cord pH ≤7.0 or base deficit ≥−16, OR (Criteria B) pH 7.01 to 7.15 or base deficit −10 to −15.9 on blood gas within 1 h AND history of acute perinatal event (ex, uterine rupture) AND Apgar score ≤5 at first 10 minutes or at least 10 minutes of positive-pressure Ventilation. (Criteria C) presence of seizures OR at least one sign in three or more of the six categories, criteria for defining moderate and severe encephalopathy:

Moderate encephalopathy:

1. Level of consciousness (Lethargy),

2. Decreased activity

3. Posture (Distal flexion, full extension)
4. Primitive reflexes (Suck, weak), (Moro, incomplete)
5. Tone (Hypotonia)
6. Autonomic system: constricted Pupils, bradycardia, Periodic breathing.

Severe encephalopathy:

1. Level of consciousness (Stupor/coma).
2. No activity.
3. Posture Internally rotated, legs extended with feet in forced plantar flexion)
4. Primitive reflexes (Suck And Moro are absent)
5. Tone (Flaccid)
6. Autonomic system: Pupils is Skew deviation/dilated/ Nonreactive to light, Variable HR, Apnea. (Committee on Fetus and Newborn, et al.2014).

Hypothermia offered for infant who meet criteria A and C or B and C, therapeutic hypothermia Should be monitor closely for any complications that need to stop coolind and start rewarming in a case of hypotension despite inotropic support; coagulopathy despite treatment, persistent pulmonary hypertension with hypoxemia despite adequate treatment,

Subcutaneous fat necrosis, with or without hypercalcemia but these complication is rare <10% of cases and stop cooling uncommonly (Strohm, ET al.2011).

In Jenin Governmental Hospital TH protocol has been started to be used in 2019. This protocol is a Manual for Palestinian Nurseries, NICUs and Obstetric Wards for Residents, Pediatricians, Neonatologists and Neonatal Nurses: Towards Better Survival and Better Neurodevelopment in 2019 Series. Baby >36 week gestational age, meet the criteria A and B and age ≤ 6hr are Eligible for treatment for cooling therapy (Cloherty, ET al.2011). Criteria A one or more of:

- Apgar score of ≤5 at 10min after birth.
- Continued need for resuscitation included intubation or mask ventilation at 10min after birth.
- PH ≤ 7.0 within 60min of birth.
- Base deficit ≥−16within 60min of birth.

Criteria B, seizures OR moderate to severe encephalopathy consisting of:

- Alter level of consciousness reduce or absent for stimulation and
- Abnormal tone (hypotonic, flaccid).
- Abnormal Primitive reflexes (weak or absent suck , Moro response)

Continues rectal temp monitoring if not available take axillary temp q15min, target temp 33-34 ±5 c Excluded criteria form protocol:

- Normal initials an EEG tracing.
- Inability to initiate cooling by 6hr of age.
- Presence of sever congenital anomalies.
- Presence of lethal chromosomal anomaly.
- Major intracranial hemorrhage.

After 27hr on therapeutic hypothermia finished, rewarming phase started and the main goal of rewarming is to prevent the reperfusion injury that occurs when blood flow restore to injury part if return too quickly can worsen the damage and (AMC PSO, 2016) recommended that temp should increase by 0.2-0.5 degree Celsius per hour to reach 36.5 needs to 6-12 hour to reach it (Wintermark ET, al .2011).

Chapter Three
Literature Review

3.1 Overview

This chapter will present the studies, that discuss the effectiveness and outcomes of implementation therapeutic hypothermia in NICU to deal with HIE newborn.

Literature reviews using nine recent studies that showed the therapeutic hypothermia and how this improve the survival rate and decrease the severity of HIE by reducing the rate of disability.

Study for Sarafidiset al, 2014. “Therapeutic hypothermia in asphyxiated neonates with Hypoxic-ischemic encephalopathy”. It is a retrospective study for implemented whole body cooling to twelve asphyxiated neonates with GA between 36 week -40 week, by maintaining temperature 33.5 ± 0.5 C rectally for 72 hours started at the age of 5 hours after birth. During the study period for hypoxic-Ischemic encephalopathy for 12 baby 3 was moderate HIE and 9 newborn with sever HIE .After Implementation therapeutic hypothermia, 7 babies survived to hospital discharge. The neurodevelopment follow up found 1 case is normal, while 3 had mild and 1 case is moderate and 2 severe impairment. Other study was non-randomized cohort study did in the USA and UK, by Paolo Montaldo et al, 2018. “Therapeutic Hypothermia initiated within 6 hours of birth is associated with reduced brain injury on MR biomarkers in mild hypoxic-

ischemic encephalopathy" _is aimed to examine the effect of whole-body cooling on MR biomarkers and neurodevelopment outcomes on baby who mild Hypoxic-ischemic encephalopathy the examination did within 6 hours after birth they found 47 babies with mild HIE.

These studies used Whole-body cooling for 72 hours. 32 babies in therapeutic group, Non cooling group contained 15 babies, 5 of these were cooled for <12 hours. By using MRI and MR Spectroscopy (MRS) within 2 weeks after birth, Cooled babies had low scores in white matter injury versus than control group .Four babies in control group developed seizures after 6 hours of age, while no any seizures documented in therapeutic group.

Adverse neurodevelopment outcomes assessment at 2 years later on were seen in 2 babies in control group compared with no cases within cooling baby, so the therapeutic hypothermia may have a neuroprotective effect in mild HIE newborn.

Another study by Wen Jia et al, 2018. "Benefits of starting hypothermia treatment within 6 h vs.

6–12 h in newborns with moderate neonatal hypoxic-ischemic encephalopathy'', aimed to see the effectiveness of TH treatment within 12 h after birth. It compared moderate HIE and sever HIE who were treated by hypothermia in the first 6h with others who were treated between 6-12h, so the HIE in moderate degree showed curative effects for the

newborn who treated by hypothermia in first 6h versus 6-12hr by used aEEG .But in severe HIE only the newborns who were treated by hypothermia in first 6h showed curative result.

Study by Rahul Sinha et al, 2018. “The effect of whole body cooling in asphyxiated neonates with resource limitation: Challenges and experience” was a prospective interventional study to examine the effect of whole body cooling in neurological outcome. During this period number of deliveries were 1565 and 65 neonates with perinatal asphyxia divided into two group 30 under go to whole body cooling therapy and other 30 received usual intensive care. Five babies were excluded of the group study as they had mild HIE. Inclusion criteria: Neonates >36 weeks, more than 2000 g from birth WT, anyone of risk factor (cord prolapse, intrapartum fetal distress).ABG (Umbilical cord or a postnatal in the 1^{st} h of life) ,pH is <7.0 or base deficit of > or equal -16 with any two of finding: (1) Apgar score of less than 5 at 5 min; (2) positive pressure ventilation (PPV) continued for at least 10 min. Exclusion criteria: any newborn <36 weeks and HIE diagnostic after 6 h of birth were. The research result that the neurological examination was better in whole-body cooling newborn than in the control group at age 18months.

The percentage of normal neurological outcome 70% compared of 43% in control group and the cognitive delay at 18 months of age in control group is more than whole body cooling group.

The whole-body cooling for 72 hrs can be improved the outcome in asphyxiated neonate.

Other study by Wen-hao Zhou et al, 2010. “Selective Head Cooling with Mild Systemic hypothermia after Neonatal Hypoxic-Ischemic Encephalopathy: A Multicenter Randomized controlled Trial in China” .To investigate the efficacy and safety of head cooling in newborn Infants with mild HIE. By observe the percentage rate of mortality and severe disability in group of head cooling and control group. The study contain 194 infants were available for analysis (94 babies in control group and 100 in cooling group). In head cooling group the hypothermia therapy was initiated in the first 6 hours of the birth and observed rectal temp and maintain temp between 34.5° to 35.0°C for 72 hours. In control group the rectal temperature was maintained at 36.0° to 37.5°C. The study result as the mortality rate in head cooling was 20% and 29% in control group and the rate of severe disability in cooling group was 14% and 28% in control group. The researcher conclusions that the head cooling for 72 Hours may significantly decrease the severe disability and death compare with control group.

Suman Ghosh et al, 2016. “Therapeutic hypothermia for neonatal hypoxic ischemic Encephalopathy is associated with short-term reduction of seizures after discharge from the Neonatal intensive care unit. “A retrospective cohort study Was used selective brain cooling for 16 baby HIE and 12 baby is control group developed clinical the seizures while

inpatient. Observed all baby in both group up to 6 months, four patients in therapeutic group had continued seizures while eight patients who is in the control group.

Simbruner et al, 2010. “Systemic hypothermia after neonatal encephalopathy”. In this study 111 infants with HIE included and divided to two group were 53 in the TH group, with maintained the rectal temperature between 33-34°C for 72 hours and 58 baby in the control group with a rectal temp between 36.5-37.5°C. All babies at 18 to 21 months evaluated for sever disability and the mortality rate .In the TH group the mortality rate and severe disability were 51% and 83% in the control group. TH also had a significant protective effect and fewer clinical seizures in the group with severe HIE.

Jacobs SE, 2011. “Whole-body hypothermia for term and near-term newborns with hypoxic-Ischemic encephalopathy: a randomized controlled trial”. Multicenter, international to examine the effectiveness of whole-body hypothermia in HIE newborn with and without complicated hypothermia equipment. The study contained two groups with GA 35 weeks' and more suffer from moderate to severe clinical encephalopathy. First group was hypothermia group, included 110 newborn, received Whole-body hypothermia by making the radiant warmer turning off and using refrigerated gel packs to maintain rectal temp 33°C - 34°C for 72 hours, other group was standard care group, normothermia group contained 111 newborn, rectal temp was 37°C. Both group evaluated for the

mortality rate or major sensorineural disability at age of 2 years. Therapeutic hypothermia reduced the risk of death or major sensorineural disability at 2 years of age: (51.4%) in the hypothermia group 55 of 107 died or disability percentage (51.4%) and in the control group 67 of 101 infants (66.3%) died or had a major sensorineural disability at 2 years. Conclusion of the study found that the whole-body hypothermia is effective because the rate of mortality decreased, and increased in the survival rate with no sensorineural disability in TH.

Mariam Hakobyan, et al.2019 “Outcome of Infants with Therapeutic Hypothermia after Perinatal asphyxia and Early-Onset Sepsis ”it a retrospective cohort study of 1,084 newborn reported by a good outcome for newborn who have early-onset sepsis and TH should not be withheld from them.

Chapter Four

Methodology

4.1 Overview

This section presents research design, hypothesis, setting of the study, period of the study, population and sampling .It presented the sampling techniques, exclusion and inclusion criteria.

This part is very important by giving understanding of the methodology used.

4.2 Design

The study adopted the Quazi experimental design. The study included prospective study, experimental group baby who received therapeutic hypothermia and historical study as control group who didn’t eceived TH .Survey conducted at Neonatal Intensive Care Unit in Governmental Hospital in Jenin. The period is one year from February 2020 to 30 September 2020. Quazi experimental studies have become an increasingly important source of evidence because it lets the researcher to do historical studies and protect patient from experimental issues and advances in statistical analysis. It also generates results faster with low cost than experimental studies, and play an important role in investigating treatment outcomes (Bärnighausen, et al.2017).

4.3 Site and Setting

This study was conducted in NICU department in Governmental Hospital in Jenin.

4.4 Study Period

Data collection will start from February 2020 to September 2020.

4.5 Sample Size Calculation

The researcher targeted all the newborns who HIE admitted to intensive care unit at Jenin

Hospital, the size of the sample was 27 babies in each group according to statistic’s calculation.

Pocock's sample size formula was used. This equation assumes that the comparison is to be made across two equally sized groups. However, comparisons in observational studies are mainly made across two unequally sized groups. In this case, the sample size should be adjusted according to the actual ratio of the two groups (control and experimental) in order to reflect the inequality (Pocock, 1983). The error (a) is set to 0.05, which is the risk of making type I errors, and (b) Power (1-type II error) is set to 0.85. Minimum standard error = 1. According to efficacy analysis, 27 newborns in each group are recommended. The sample taken 27 babies in control group and 33 newborns in experimental group to cover any drop out from the study. 5 babIES meet HIE criteria but not taken in this study

because transfer to other hospital and other one miss diagnosis, three babies died before TH implemented. The control group taken historical from 2018, 2019,2020 collected 27 babIES just. Overall, we will recruit 60 babies in the current study.

$$n = \frac{[P_1 (1-P_1) + P_2 (1-P_2)]}{(P_1-P_2)^2} (Z_{\alpha/2} + Z_{\beta})^2$$

Where:

n: required sample size

P_1: Estimated proportion of study outcome in the control sample ($P_1 = 0.37$).

P_2: Estimated proportion of study outcome in the experimental sample ($P_2 = 0.75$).

α: level of statistical significance

$Z_{\alpha/2:}$ Represents the desired level of statistical significance (typically 1.96 for $\alpha = 0.05$)

$Z_{\beta:}$ Represents the desired power (typically 1.04 for 85% power)

n for each group *2= total sample (i.e. for the 2 groups)

$$n = \frac{[0.37(1-0.37) + 0.75 (1-0.75)]}{} (1.96+ 1.04)^2$$

$(0.37\text{-}0.75)^2$

$n = \frac{0.421*(8.978)^2}{(0.1444)^2}$

$n = 26.15176$

$n \approx 27$ patients

According to the analysis of power, 27 patients were recommended for experimental group.

4.6 Data collection methods and instruments

The data gathering by check list (appendix 2) and observing data sheet that was filled by researcher (appendix3) that consists several parts, included socio-demographic characteristic about the mother and the baby, baby status during and after birth, and question about therapeutic Hypothermia criteria and baby status during implementation criteria and finding that will be seen, other investigation.

After obtaining a formal approval from IRP and the ministry of health (MOH), secondary data was collected started through using neonatal register book and the baby file to observe the result of lab test and some radiology studies (February 2020 - September 2020).

4.7 Inclusion criteria

- All baby who have HIE.(based on hypothermia protocol and check list used in Jenin NICU (appendix 1,2)
- Singleton and twins.
- Baby with gestetional age above 36week.
- Baby wt > 1800
- Primigravida or multigravida .
- HIE newborn from normal delivery, cesarean delivery, instrument delivery.

4.8 Exclusion criteria

- All baby admitted to NICU not HIE .
- Baby (<36 weeks).
- Baby WT<1800.
- HIE baby admitted after 6hr.
- Lethal congenital and chromosomal anomalies.

4.9 Statistical Analysis

After data collection, data was analyzed using frequencies and percentages, statistical package for social science (SPSS), descriptive statistics to describe the study sample via mean, median, and range.

4.10 Reliability and validity

Reliability is the consistency of the measurement, or the degree to which an instrument measures the same way each time it is used under the same subjects with the same condition. Validity refers to whether the questionnaire or survey measures what it intends to measure.

The study protocol was developed by the researcher was based on the information in the files used in the neonate intensive care unit. It was reviewed by the supervisor, and experts, who suggested changes in some items like added check list to select which baby need to TH as soon as possible and added some items in observing data sheet about the mode of delivery that increases the incidence of HIE to take on consideration on future.

4.11 Ethical considerations

As the research is involving human participation, it is necessary to follow strict ethical principles.

The participants are asked to give their consent, and they are assured that participation or information provided would not be used against them. They are also assured of their right of confidentiality.

Confidentiality will be taken into consideration regarding data obtained from clinical files. And the cases will be kept anonymous without names and just with codes for data analysis.

All participants will be informed(parent), Agreement must also be taken from the MOH and medical director for the NICU and Obstetrics and Gynecology department director, also the nursing.

Chapter Five
Results

5.1 Overview

This chapter presents the study results containing the features of the respondents and the average percentages of the responses for each of the survey's items.

5.2 Characteristics of the Study Population

In this study, we were able to recruit 60 HIE newborns (33 for the experimental group and 27 Newborn as a control group) Quzi experimental design prospectively between February 2020 to 30 September 2020). This table (5.1) showed the sample with the percentage.

Table 5.1: Frequencies and Percentages of the Experimental and the Control groups of the study.

Group	Frequency	Percentage
Control	27	45.0%
Experimental	33	55.0%

5.3 Indicators and Variables about mother and mother delivery.

Table 5.2: Frequencies and Percentages of differences between the Experimental and the Control groups in some Indicators and Variables about mother and mother delivery.

Indicator or Variable	Category	Group		P-value
		Control	Experimental	
		N(%)	N(%)	
Onset of labor	Spontaneous	15(53.8%)	18 (54.5%)	0.957
	Induction	12(46.2%)	15 (45.5%)	
Distribution of parity	Nulliparous	6(22.2%)	9 (27.3%)	0.882
	Para 1	4(14.8%)	6 (18.2%)	
	Para 2	11(40.7%)	13 (39.4%)	
	Para 3+	6(22.2%)	5 (15.2%)	
Occurrence of an acute perinatal event	Variable / late heart rate decelerations	6(22.2%)	9 (27.3%)	0.374
	Prolapsed / ruptured / tight nuchal cord	5(18.5%)	4 (12.1%)	
	Maternal hemorrhage / placental abruption	5(18.5%)	2 (6.1%)	
	Other	11(40.7%)	18 (54.5%)	
Mode of delivery	Spontaneous Vaginal Cephalic	3(11.1%)	4 (12.1%)	0.701
	Vaginal Breech	0(0%)	0 (0%)	
	Caesarean section	14(51.9%)	16 (48.5%)	
	Ventouse	9(33.3%)	13 (39.4%)	
	Forceps	1(3.7%)	0(0%)	
Color of Liquor	Clear	15(55.6%)	22 (66.7%)	0.379
	Meconium	12(44.4%)	11(33.3%)	

The results in the table above show that there are no significant differences at 0.05 Level between the Control group and the Experimental group in all the indicators and variables studies in the table (all the P-values are higher than 0.05).

5.4 Indicators and Variables about baby and TH.

Table 5.3: Frequencies and Percentages of differences between the Experimental and the Control groups in some Indicators and Variables about baby and TH.

Indicator or Variable	Category	Group		P-value
		Control	Experimental	
		N (%)	N (%)	
Infant Gender	Male	15(57.7%)	17(56.7%)	0.938
	Female	12(42.3%)	15(43.3%)	
Resuscitation for infants who underwent therapeutic hypothermia	Spontaneous breath taken	0(0%)	0(0%)	0.000
	Resuscitation required	0(0%)	12(36.4%)	
	Intubation required	10(37%)	14(42.4%)	
	Chest compression required	17(63%)	7(21.2%)	
Inducing methods used for TH	Head cooling	0(0%)	0(0%)	0.000
	Surface cooling	13 (48.1%)	33(100%)	
	Not done	14(51.9%)	0(0%)	
Is cooling preformed before 6hr?	Yes	5(18.5%)	33(100%)	0.000
	No	22(81.4%)	0(0%)	
Duration of cooling (hrs)	For 72 hours	5(18.5%)	33(100%)	0.000
	Less than 72 hrs	8(29.6%)	0(0%)	
	Not done	14(51.9%)	0(0%)	

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in: Resuscitation for infants who underwent therapeutic hypothermia, inducing methods used for TH, whether cooling preformed before 6hr, duration of cooling (hrs) (the P-values are less than 0.05).

Regarding Resuscitation for infants who underwent therapeutic hypothermia, the results show that Resuscitation required in the experimental group 12(36.4%) was significantly higher than that in the control group 0(0.0%), while Chest compression required in the

experimental group 7(21.2%) was significantly lower than that in the Control group 17(63%).

Regarding inducing methods used for TH, the results show that surface cooling in the experimental group 33(100%) is significantly higher than that in the control Group 14(51.9%).

Regarding whether cooling preformed before 6hr, the results show that the Experimental group 33(100%) is significantly higher than that in the control group 5 (18.5%).

The results show that the duration of cooling was for 72 hours in all cases of the Experimental group 33(100%) which is significantly higher than that in the control Group 5(18.5%).

On the other hand, the results in the table above show that there are no significant differences at 0.05 levels between the Control group and the Experimental group in Infant Gender (the P-value is higher than 0.05).

Table 5.4: Means, Standard Deviations and the results of Mann-Whitney Test for differences between the Experimental and the Control groups in some Indicators and Variables. (Mother age, APGAR score, PH level, GA, WT, Base Deficit.

Indicator or Variable	Group		P-value
	Control	Experimental	
	Mean ± S.D	Mean ± S.D	
Age of mother	31.83 ± 5.92	29.34 ± 7.02	0.168
Apgar Score 1 Min	3.11 ± 1.05	3.85 ± 0.8	0.005
Apgar Score 5 Min	4.11 ± 1.19	5.24 ± 0.9	0.000
Apgar Score 10 Min	5.15 ± 1.2	6.39 ± 0.86	0.000
Initial pH level	6.94 ± 1.17	7.01 ± 0.15	0.000
>36 Completed weeks gestational age	181.15 ± 743.22	37.7 ± 1.36	0.106
Weight >=1800 gm	3383.7 ± 463.8	3080 ± 569.02	0.042
Base Deficit >16.0 mmol/L in any blood sample, within 60 minutes of birth	-22.75 ± 3.16	-17.33 ± 6.19	0.000

The results in the table above show that there are significant differences at 0.05 level between Experimental group and Control group in Apgar Score at 1 Min, Apgar Score at 5 Min, Apgar Score at 10 Min, Initial pH level, Weight >=1800, and in Base Deficit >16.0 in any blood sample within 60 minutes of birth (the P-values less than 0.05).

Regarding Apgar score at 1 Min, 5 Min, and at 10 Min, the results exhibit that the mean values of Apgar score in the Experimental group (3.85, 5.24, and 6.39) respectively, are significantly higher than the mean values of Apgar score in the control group (3.11, 4.11, and 5.15).

Regarding Initial pH level, the results exhibit that the mean in the Experimental group (7.01) is significantly higher than the mean in the control group (6.94).

Regarding Weight >=1800, the results exhibit that the mean in the Experimental group (3, 80 gm) is significantly lower than the mean in the control group (3,383.7 gm).

Regarding Base Deficit >16.0 in any blood sample within 60 minutes of birth, the results exhibit that the mean in the Experimental group (-17.33) is significantly lower than the mean in the control group (-22.75).

on the other hand, the results in the table above show that there are no significant differences at 0.05 level between Experimental group and

Control group in Age of mothers, and in >36 Completed weeks gestational age (P-values are higher than 0.05).

5.5 Indicators and Variables about Drugs or fluid treatment for infants underwent for TH.

Table 5.5: Frequencies and Percentages differences between the Experimental and the Control groups in some Indicators and Variables about Drugs and fluid treatment for infants underwent TH.

Indicator or Variable	Category	Group		P-value
		Control	Experimental	
		N (%)	N (%)	
Q 11_1: Drugs or fluid treatment administered at birth for infants who underwent therapeutic hypothermia:	Adrenaline	20(74.1%)	7(21.2%)	0.000
	Dextrose	27(100%)	33(100%)	……
	Saline	27(100%)	33(100%)	0.020
	Sodium Bicarbonate	2(7.4%)	0(0%)	0.112
Apgar score <=5 at 10 minutes	<=5	27(100%)	30(90.9%)	0.108
	>5	0(0%)	3(9.1%)	
Continued need for PPV or Intubation at 10 mints	Intubation	27(100%)	23(69.7%)	0.002
	PPV	0(0%)	10(30.3%)	

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in Adrenaline and Saline as Drugs or fluid treatment administered at birth for infants who underwent Therapeutic hypothermia (the P-values are less than 0.05), the percentage of infants given Adrenaline in the experimental group 7(21.2%) was significantly lower than that in the control group 20 (74.1%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in continued need for PPV or Intubation at 10 mints (the P-value is less than

0.05), the percentage of infants needed PPV in the experimental group was 10(30.3%) which is significantly higher than that in the control group 0 (0%), while the percentage of infants needed intubation in the experimental group was 23(69.7%) which is significantly lower than that in the control group 27(100%).

On the other hand, the results in the table above show that there are no significant Differences at 0.05 levels between the Control group and the Experimental group in Dextrose and Saline, Sodium Bicarbonate as Drugs or fluid treatment administered For infants who underwent therapeutic hypothermia, and in Apgar score <=5 at 10 minutes (the P-values are higher than 0.05).

5.6 Indicator or Variable sedation, antibiotic, anticonvulsant, Inotropes, blood product administered for infants who underwent therapeutic hypothermia TH.

Table 5.6: Frequencies and Percentages and the results of Chi-square test of differences between the Experimental and the Control groups in some Indicators and Variables about sedation, antibiotic, anticonvulsant, Inotropes, blood product administered for infants underwent therapeutic hypothermia TH.

Indicator or Variable	Group		Chi-square	P-value
	Control	Experimental		
	N (%)	N (%)		
Total _sedation	24(88.9%)	21(63.6%)	5.051	0.025
Total _Antibiotics	26(96.3%)	33(100%)	1.243	0.265
Total _anticonvulsant	25(92.6%)	17(51.5%)	11.932	0.001
Total _Inotropes	10(37%)	1(3%)	11.470	0.001
Total _Blood products	9(33.3%)	1(3%)	9.818	0.002

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in Sedation, Blood Products, Inotropes, and Ant convulsion (the P-values are less than 0.05).

Regarding Sedation in the first day, the percentage in the experimental group 20(60.6%) was significantly lower than that in the control group 24(88.9%). In the second day, the percentage in the experimental group 8(24.2%) was significantly lower than that in the control group 17(63%). In the third day, the percentage in the Experimental group 3(9.1%) was significantly lower than that in the control group 14(51.9%). Regarding total Sedation in the three days, the percentage in the Experimental group 21(63.6%) was significantly lower than that in the control group 24(88.9%).

Regarding Anticonvulsion in second day, the percentage in the experimental group 16(48.5%) was significantly lower than that in the control group 23(85.2%). In the third day, the percentage in the experimental group 13(39.4%) was significantly lower than that in the control group 22(81.5%). Regarding total Anticonv in the three days, the percentage in the experimental group 17(51.5%) was significantly lower than that in the control group 25(92.6%).

Regarding Inotropes in the first day, the percentage in the experimental group 1(3%) was significantly lower than that in the control group

6(22.2%). In the second day, the percentage in the experimental group 1(3%) was significantly lower than that in the control group 8(29.6%). In the third day, the percentage in the Experimental group 0(0%) was significantly lower than that in the control group 8(29.6%). Regarding total Inotropes in the three days, the percentage in the Experimental group 1(3%) was significantly lower than that in the control group 10(37%).

Regarding Blood products in the first day, the percentage in the experimental group 0(0%) was significantly lower than that in the control group 3(11.1%). In the second day, the percentage in the experimental group 1(3%) was significantly lower than that in the control group 5(18.5%). In the third day, the percentage in the Experimental group 1(3%) was significantly lower than that in the control group 8(29.6%). Regarding Total Blood products in the three days, the percentage in the Experimental group 1(3%) was significantly lower than that in the control group 9(33.3%).

From the other hand, the results in the table above show that there are no significant differences at 0.05 levels between the Control group and the Experimental group in Antibiotics, and in Anticonvulsion Day1 (the P-values are higher than 0.05).

5.7 How body temperature measured.

Table 5.7: Frequencies and Percentages and the results of Chi-square test of differences between the Experimental and the Control groups in how body temperature measured.

Indicator or Variable	Category	Group		P-value
		Control	Experimental	
		N (%)	N (%)	
How body temperature measured	Rectal probe	17(65.4%)	33(100%)	0.001
	Axillary	1(3.8%)	0(0%)	
	Surface	8(30.8%)	0(0%)	

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in how body temperature measured (the P-value is less than 0.05).

The percentage of Rectal probe in the experimental group 33(100%) was significantly higher than that in the control group 17(65.4%), while the percentage of Surface in the experimental group 0(0%) was significantly lower than that in the control group 8(30.8%).

5.8 Criteria for defining moderate and severe encephalopathy:

Table 5.8: Frequencies and Percentages and the results of Chi-square test of differences between the Experimental and the Control groups in level for defining moderate and severe encephalopathy.

Indicator or Variable	Category	Group		P-value
		Control	Experimental	
		N (%)	N (%)	
level of consciousness 1st day	Hyper alert	1(3.7%)	0(0%)	0.003
	Lethargic or obtunded	13(48.1%)	29(87.9%)	
	Stupor or Coma	13(48.1%)	4(12.1%)	

level of consciousness 2nd day	Hyper alert	1(3.7%)	6(18.2%)	0.000
	Lethargic or obtunded	7(25.9%)	23(69.7%)	
	Stupor or Coma	17(63%)	3(9.1%)	
	Normal	0(0%)	1(3%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
level of consciousness 3rd day	Hyper alert	2(7.4%)	13(39.4%)	0.000
	Lethargic or obtunded	5(18.5%)	9(27.3%)	
	Stupor or Coma	17(63%)	0(0%)	
	Normal	0(0%)	11(33.3%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Activity 1st day	Decreased	15(55.6%)	29(87.9%)	0.005
	Absent	12(44.4%)	4(12.1%)	
Activity 2nd day	Normal	0(0%)	6(18.2%)	0.000
	Decreased	8(29.6%)	25(75.8%)	
	Absent	17(63%)	2(6.1%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Activity 3rd day	Normal	0(0%)	22(66.7%)	0.000
	Decreased	6(22.2%)	11(33.3%)	
	Absent	18(66.7%)	0(0%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Muscle tone 1st day	Normal	1(3.7%)	0(0%)	0.017
	Mild hypotonia	15(55.6%)	29(87.9%)	
	Flaccid	11(40.7%)	4(12.1%)	
Muscle tone 2nd day	Normal	0(0%)	9(27.3%)	0.000
	Mild hypotonia	9(33.3%)	23(69.7%)	
	Flaccid	16(59.3%)	1(3%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Muscle tone 3rd day	Normal	0(0%)	21(63.6%)	0.000
	Mild hypotonia	5(18.5%)	11(33.3%)	
	Flaccid	19(70.4%)	0(0%)	
	Undocumented	2(7.4%)	1(3%)	
	Died	1(3.7%)	0(0%)	
Posture 1st day	Mild distal flexion	2(7.4%)	1(3%)	0.036
	Strong distal flexion	14(51.9%)	28(84.8%)	
	Intermittent	10(37%)	3(9.1%)	
	Decerebration	0(0%)	1(3%)	
	Normal	1(3.7%)	0(0%)	
Posture 2nd day	Mild distal flexion	0(0%)	12(36.4%)	0.000
	Strong distal flexion	8(29.6%)	15(45.5%)	
	Intermittent	16(59.3%)	2(6.1%)	
	Decerebration	0(0%)	4(12.1%)	
	Normal	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	

Posture 3rd day	Mild distal flexion	0(0%)	15(45.5%)	0.000
	Strong distal flexion	4(14.8%)	5(15.2%)	
	Intermittent	19(70.4%)	0(0%)	
	Decerebration	0(0%)	13(39.4%)	
	Normal	3(11.1%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Stretch reflexes 1st day	Overactive	2(7.4%)	6(18.2%)	0.222
	Decreased or absent	25(92.6%)	27(81.8%)	
Stretch reflexes 2nd day	Overactive	1(3.7%)	9(27.3%)	0.025
	Decreased or absent	24(88.9%)	21(63.6%)	
	Normal	0(0%)	3(9.1%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Stretch reflexes 3rd day	Overactive	1(3.7%)	7(21.2%)	0.000
	Decreased or absent	23(85.2%)	10(30.3%)	
	Normal	0(0%)	15(45.5%)	
	Undocumented	2(7.4%)	1(3%)	
	Died	1(3.7%)	0(0%)	
	Absent	19(70.4%)	18(54.5%)	
Suck 1st day	Weak	8(29.6%)	15(45.5%)	0.210
	Absent	19(70.4%)	18(54.5%)	
Suck 2nd day	Weak	7(25.9%)	25(75.8%)	0.002
	Absent	18(66.7%)	7(21.2%)	
	Normal	0(0%)	1(3%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Suck 3rd day	Weak	6(22.2%)	19(57.6%)	0.000
	Absent	18(66.7%)	1(3%)	
	Normal	0(0%)	13(39.4%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Moro 1st day	Strong	0(0%)	0(0%)	0.017
	Weak	15(55.6%)	29(87.9%)	
	Absent	11(40.7%)	4(12.1%)	
	Normal	0(0%)	0(0%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	0(0%)	0(0%)	
Moro 2nd day	Strong	0(0%)	0(0%)	0.000
	Weak	11(40.7%)	25(75.8%)	
	Absent	13(48.1%)	2(6.1%)	
	Normal	0(0%)	6(18.2%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Moro 3rd day	Strong	0(0%)	2(6.1%)	0.000
	Weak	5(18.5%)	10(30.3%)	
	Absent	17(63%)	0(0%)	
	Normal	1(3.7%)	21(63.6%)	
	Undocumented	3(11.1%)	0(0%)	
	Died	1(3.7%)	0(0%)	

Tonic Neck 1st day	Slight	4(14.8%)	4(12.1%)	0.021
	Strong	11(40.7%)	23(69.7%)	
	Absent	12(44.4%)	4(12.1%)	
	Normal	0(0%)	2(6.1%)	
Tonic Neck 2nd day	Slight	0(0%)	12(36.4%)	0.000
	Strong	10(37%)	11(33.3%)	
	Absent	15(55.6%)	1(3%)	
	Normal	0(0%)	9(27.3%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Tonic Neck 3rd day	Slight	0(0%)	12(36.4%)	0.000
	Strong	6(22.2%)	4(12.1%)	
	Absent	18(66.7%)	0(0%)	
	Normal	0(0%)	17(51.5%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Pupils 1st day	Mydriasis	2(7.4%)	1(3%)	0.001
	Miosis	6(22.2%)	12(36.4%)	
	Variable; often unequal	9(33.3%)	0(0%)	
	Fixed	2(7.4%)	0(0%)	
	Normal	8(29.6%)	20(60.6%)	
Pupils 2nd day	Miosis	4(14.8%)	8(24.2%)	0.000
	Variable; often unequal	12(44.4%)	0(0%)	
	Fixed	2(7.4%)	0(0%)	
	Dilated	1(3.7%)	0(0%)	
	Normal	5(18.5%)	25(75.8%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Pupils 3rd day	Mydriasis	0(0%)	2(6.1%)	0.000
	Miosis	3(11.1%)	2(6.1%)	
	Variable; often unequal	9(33.3%)	0(0%)	
	Fixed	2(7.4%)	0(0%)	
	Dilated	3(11.1%)	0(0%)	
	Normal	5(18.5%)	29(87.9%)	
	Undocumented	4(14.8%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Seizures 1st day	None	14(51.9%)	22(66.7%)	0.244
	Present	13(48.1%)	11(33.3%)	
Seizures 2nd day	None	8(29.6%)	27(81.8%)	0.001
	Present	17(63%)	6(18.2%)	
	Undocumented	1(3.7%)	0(0%)	
	Died	1(3.7%)	0(0%)	
Seizures 3rd day	None	7(25.9%)	28(84.8%)	0.000
	Present	17(63%)	5(15.2%)	
	Undocumented	2(7.4%)	0(0%)	
	Died	1(3.7%)	0(0%)	

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in level of consciousness in the three days (the P-values are less than 0.05).

Regarding level of consciousness at the first day, the percentage of Lethargic or obtunded in the experimental group 29(87.9%) was significantly higher than that in the control group 13 (48.1%), while the percentage of Stupor or Coma in the experimental group 4 (12.1%) was significantly lower than that in the control group 13 (48.1%).

Regarding level of consciousness at the second day, the percentage of Hyper alert in The experimental group 6(18.2%) was significantly higher than that in the control group 1(3.7%), and the percentage of Lethargic or obtunded in the experimental group 23(69.7%) was significantly higher than that in the control group 7(25.9%), while the percentage of Stupor or Coma in the experimental group 3(9.1%) was significantly lower than that in the control group 17 (63%).

Regarding level of consciousness on the third day, the percentage of hyper alert in the experimental group 13 (39.4%) was significantly higher than that in the control 2 (7.4%), and the percentage of Lethargic or obtunded in the experimental group 9(27.3%) was significantly higher than that in the control group 5 (18.5%), while the percentage of Stupor or Coma in the experimental group 0 (0%) was significantly lower than that in the control group 17(63%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in activity and in muscle tone in the three days (the P-values are less than 0.05).

Regarding activity on the first day, the percentage of decreased activity in the Experimental group 29(87.9%) was significantly higher than that in the control group 15(55.6%), while the percentage of absent activity in the experimental group 4(12.1%) was significantly lower than that in the control group 12(44.4%).

Regarding activity on the second day, the percentage of decreased activity in the Experimental group 25(75.8%) was significantly higher than that in the control group 8(29.6%), while the percentage of absent activity in the experimental group 2(6.1%) was significantly lower than that in the control group 17(63%).

Regarding activity on the third day, the percentage of Normal activity in the Experimental group 22(66.7%) was significantly higher than that in the control group 0(0%), and the percentage of decreased activity in the experimental group 11(33.3%) was significantly higher than that in the control group 6(22.2%), while the percentage of absent activity in the experimental group 0(0%) was significantly lower than that in the control group 18(66.7%).

Regarding muscle tone on the first day, the percentage of mild hypotonia in the Experimental group 29(87.9%) was significantly higher than that in the control group 15(55.6%), while the percentage of flaccid in the experimental group 4(12.1%) was significantly lower than that in the control group 11(40.7%).

Regarding Muscle tone on the second day, the percentage of normal muscle tone in the experimental group 9(27.3%) was significantly higher than that in the control group 0(0%), and the percentage of mild hypotonia in the experimental group 23(69.7%) was significantly higher than that in the control group 9(33.3%), while the percentage of flaccid in the experimental group 1(3%) was significantly lower than that in the control group 16(59.3%).

Regarding muscle tone on the third day, the percentage of normal muscle tone in the Experimental group 21(63.6%) was significantly higher than that in the control group 0(0%), and the percentage of mild hypotonia in the experimental group 11(33.3%) was significantly higher than that in the control group 5(18.5%), while the percentage of flaccid in the experimental group 0(0%) was significantly lower than that in the control group 19 (70.4%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in Posture in the three days (the P-values are less than 0.05).

Regarding posture on the first day, the percentage of Strong distal flexion in the Experimental group 28(84.8%) was significantly higher than that in the control group 14(51.9%), while the percentage of Intermittent in the experimental group 3(9.1%) was significantly lower than that in the control group 10(37%).

Regarding posture on the second day, the percentage of mild distal flexion in the experimental group 12(36.4%) was significantly higher than that in the control group 0(0%), and the percentage of strong distal flexion in the experimental group 15(45.5%) was significantly higher than that in the control group 8(29.6%), while the percentage of intermittent in the experimental group 2(6.1%) was significantly lower than that in the control group 16(59.3%).

Regarding posture on the third day, the percentage of mild distal flexion in the experimental group 15(45.5%) was significantly higher than that in the control group 0(0%), and the percentage of deceleration in the experimental group 13(39.4%) was significantly higher than that in the control group 0(0%), while the percentage of intermittent in the experimental group 0(0%) was significantly lower than that in the control group 19(70.4%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in stretch reflexes and suck in the second and third days (the P-values are less than 0.05).

Regarding stretch reflexes on the second day, the percentage of overactive in the Experimental group 9(27.3%) was significantly higher than that in the control group 1(3.7%), while the percentage of Decreased or absent in the experimental group 21(63.6%) was significantly lower than that in the control group 24(88.9%).

Regarding Stretch reflexes at the third day, the percentage of Overactive in the Experimental group 7(21.2%) was significantly higher than that in the control group 1(3.7%), and the percentage of Normal in the experimental group 15(45.5%) was significantly higher than that in the control group 0(0%), while the percentage of decreased or absent in the experimental group 10(30.3%) was significantly lower than that in the control group 23(85.2%).

Regarding suck on the second day, the percentage of weak suck in the experimental Group 25(75.8%) was significantly higher than that in the control group 7(25.9%),

while the percentage of absent suck in the experimental group 7(21.2%) was significantly lower than that in the control group 18(66.7%).

Regarding suck on the third day, the percentage of weak suck in the experimental group 19(57.6%) was significantly higher than that in the control group 6(22.2%), and the percentage of normal in the experimental group 13(39.4%) was significantly higher than that in the control group

0(0%), while the percentage of absent suck in the experimental group 1(3%) was significantly lower than that in the control group 18(66.7%).

From the other hand, the results in the table above show that there are **no** significant differences at 0.05 levels between the Control group and the Experimental group in stretch reflexes and suck in the first day (the P-values are higher than 0.05).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in moro in the three days (the P-values are less than 0.05).

Regarding moro on the first day, the percentage of weak moro in the experimental group 29(87.9%) was significantly higher than that in the control group 15(55.6%), While the percentage of absent moro in the experimental group 4(12.1%) was significantly lower than that in the control group 11(40.7%).

Regarding moro on the second day, the percentage of weak moro in the Experimental group 25(75.8%) was significantly higher than that in the control group 11(40.7%), and the percentage of Normal Moro in the experimental group 6(18.2%) was significantly higher than that in the control group 0(0%), while the Percentage of Absent Moro in the experimental group 2(6.1%) was significantly Lower than that in the control group 13(48.1%).

Regarding moro on the third day, the percentage of weak moro in the experimental group 10(30.3%) was significantly higher than that in the control group 5(18.5%), and the percentage of normal moro in the experimental group 21(63.6%) was significantly higher than that in the control group 1(3.7%), while the percentage of absent moro in the experimental group 0(0%) was significantly lower than that in the control group 17(63%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in tonic neck on the three days (the P-values are less than 0.05).

Regarding tonic neck on the first day, the percentage of Strong tonic neck in the Experimental group 23(69.7%) was significantly higher than that in the control group 11(40.7%), while the percentage of Absent Tonic Neck in the experimental group 4(12.1%) was significantly lower than that in the control group 12(44.4%).

Regarding tonic neck on the second day, the percentage of normal tonic neck in The experimental group 9(27.3%) was significantly higher than that in the control group 0(0%), while the percentage of absent tonic neck in the experimental group 1(3%) was significantly lower than that in the control group 15(55.6%).

Regarding tonic neck at the third day, the percentage of slight tonic neck in the Experimental group 12(36.4%) was significantly higher than that in the

control group 0(0%), and the percentage of normal tonic neck in the experimental group

17(51.5%) was significantly higher than that in the control group 0(0%), while the percentage of absent tonic neck in the experimental group 0(0%) was significantly lower than that in the control group 18(66.7%), and the percentage of strong tonic neck in the experimental group 4(12.1%) was significantly lower than that in the Control group 6(22.2%).

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in Pupils on the three days (the P-values are less than 0.05).

Regarding Pupils on the first day, the percentage of miosis pupils in the experimental group 12(36.4%) was significantly higher than that in the control group 6(22.2%), and the percentage of normal pupils in the experimental group 20(60.6%) was significantly higher than that in the control group 8(29.6%), while the percentage of Variable; often unequal pupils in the experimental group 0(0%) was significantly lower than that in the control group 9(33.3%).

Regarding pupils on the second day, the percentage of miosis pupils in the experimental group 8(24.2%) was significantly higher than that in the control group 4(14.8%), and the percentage of normal pupils in the experimental group 25(75.8%) was significantly higher than that in the control group 5(18.5%), while the percentage of variable; often unequal

pupils in the experimental group 0(0%) was significantly lower than that in the control group 12(44.4%).

Regarding pupils at the third day, the percentage of normal pupils in the experimental group 29(87.9%) was significantly higher than that in the control group 5(18.5%), while the percentage of miosis pupils in the experimental group 2(6.1%) was significantly lower than that in the control group 3(11.1%), and the percentage of variable; often unequal, fixed, and dilated pupils in the experimental group also were significantly lower than that in the control group.

The results in the table above show that there are significant differences at 0.05 level between the Control group and the Experimental group in heart rate in the three days and in seizures in the second and third days (the P-values are less than 0.05).

Regarding heart rate on the first, second and thirds day, the percentage of normal heart rate in the experimental group 33(100%) was significantly higher than that in the control group, while the percentage of tachycardia, bradycardia, and variable heart rate in the experimental group 0(0%) was significantly lower than that in the control group.

Regarding seizures on the second and third day, the percentages of non seizures are 27(81.8%) and 28(84.8%) which significantly higher than that in the control group 8(29.6%) and 7(25.9%), while the percentage of

present seizures in the experimental group are 6(18.2%) and 5(15.2%) which significantly lower than that in the control group 17(63%).

On the other hand, the results in the table above show that there are no significant differences at 0.05 level between the Control group and the Experimental group in Seizures in the first day (the P-value is less than 0.05).

5.9 Grade of Encephalopathy on Treatment.

Table 5.9: Frequencies and Percentages and the results of Chi-square test of differences between the Experimental and the Control groups in grade of HIE.

Grade of HIE	Group		P-value
	Control	Experimental	
	N(%)	N(%)	
First day *	Control	Experimental	P value
Mild HIE	2(7.4%)	0(0%)	0.112
Moderate HIE	13(48.1%)	30(90.9%)	0.000
Severe HIE	12(44.5%)	3(9.1%)	0.002
Second day **			
Mild HIE	0(0.0%)	7(21.2%)	0.524
Moderate HIE	3(27.3%)	24(72.7%)	0.000
Severe HIE	24(72.7%)	2(6.1%)	0.000
Third day ***			
Mild HIE	0(0.0%)	24(72.7%)	0.000
Moderate HIE	3(27.3%)	9(27.3%)	0.425
Severe HIE	24(72.7%)	0(0%)	0.000

5.10 differences between the Experimental and the Control groups in V/S & some lab test.

Table 5.10: Means, Standard Deviations and the results of Mann-Whitney Test for differences between the Experimental and the Control groups in V/S & some lab test.

Indicator or Variable	Group		P-value
	Control	Experimental	
	Mean ± S.D	Mean ± S.D	
Total_SBP	67.54 ± 9.96	72.07 ± 3.64	0.047*
Total_DBP	37.72 ± 7.38	41.66 ± 2.42	0.013
Total_HR	133.2 ± 16.94	137.22 ± 10.67	0.632
Total_TEMP	35.97 ± 0.95	34.43 ± 0.45	0.000
Total_hemoglobin	18.03 ± 8.67	15.78 ± 2.1	0.484
T0otal_platelet	262.22 ± 100.45	323.53 ± 84.38	0.043
Total_ALT	257.61 ± 277.74	54.13 ± 55.07	0.000
Total_AST	641.91 ± 563.42	101.49 ± 119.94	0.000
Total_PT	19.31 ± 9.65	15.21 ± 7.04	0.003
Total_PTT	46.05 ± 22.02	36.53 ± 11.05	0.000
Total_PH	7.1 ± 0.14	7.21 ± 0.07	0.003

The results in the table above show that there are significant differences at 0.05 level between Experimental group and Control group in: SBP At Admission, SBP After 6 hr from admission, Total SBP, DBP After 6 hr from admission, Total DBP, TEMP At Admission, TEMP After 6 hr from admission, TEMP 2nd day, TEMP 3rd day, and Total TEMP (the P-values less than 0.05).

Regarding SBP At Admission, After 6 hr from admission, and Total SBP, the results exhibit that the mean values of SBP in the Experimental group (69.4, 72.28, 72.07) respectively, are significantly higher than the mean values of SBP in the control group (60.64, 65.15, 67.54).

Regarding DBP After 6 hr from admission and Total DBP, the results exhibit that the mean values of DBP in the Experimental group (42.66, 41.66) respectively, are significantly higher than the mean values of DBP in the control group (35.7, 37.72).

Regarding TEMP At Admission, After 6 hr from admission, TEMP at 2nd day, TEMP at 3rd day, and Total TEMP, the results exhibit that the mean values of TEMP in the Experimental group (36.28, 33.97, 33.73, 33.74, 34.43,) respectively, are significantly lower than the mean values of TEMP in the control group (36.58, 36.33, 35.61, 35.56, 35.97).

On the other hand, the results in the table above show that there are no significant differences at 0.05 level between Experimental group and Control group in: SBP 2nd day, SBP 3rd day, DBP At Admission, DBP 2nd day, DBP 3rd day, and all HR values (P-values are higher than 0.05)The results in the table above show that there are significant differences at 0.05 level between Experimental group and Control group in: Platelet At Admission, Platelet After 6 hr from admission, Total platelet, and all values of ALT and AST (the P-values less than 0.05).

Regarding Platelet At Admission, After 6 hr from admission, and Total platelet, the results exhibit that the mean values of Platelet in the Experimental group (320.45, 314.38, 323.53) respectively, are significantly higher than the mean values of Platelet in the control group (242.82, 235.13, 262.22).

Regarding ALT At Admission, After 6 hr from admission, on 2nd day, on 3rd day, and Total ALT, the results exhibit that the mean values of ALT in the Experimental group (74.23, 61.39, 58.15, 32.13, 54.13) respectively, are significantly lower than the mean values of ALT in the control group (229.95, 262.63, 295.28, 304.92, 257.61).

Regarding AST At Admission, After 6 hr from admission, on 2nd day, and 3rd day, and Total AST, the results exhibit that the mean values of AST in the Experimental group (146.09, 127.72, 94.06, 73.95, 101.49) respectively, are significantly lower than the mean values of AST in the control group (440.14, 533.15, 849.76, 763.78, 641.91).

On the other hand, the results in the table above show that there are no significant differences at 0.05 level between Experimental group and Control group in: all Hemoglobin values and in Platelet at 2nd and 3rd day (the P-values are higher than 0.05).

The results in the table above show that there are significant differences at 0.05 level between Experimental group and Control group in all PT and PTT values (the P-values less than 0.05).

Regarding PT At Admission, After 6 hr from admission, on 2nd day, and on 3rd day, and total PT, the results exhibit that the mean values of PT in the Experimental group (18.46, 15.9, 12.96, 11.62, 15.21) respectively, are significantly lower than the mean values of PT in the control group (23.35, 19.77, 18.98, 16.28, 19.31).

Regarding PTT At Admission, After 6 hr from admission, at 2nd day, at 3rd day, and Total PTT, the results exhibit that the mean values of PTT in the Experimental group (45.36, 37.67, 31.16, 27.91, 36.53) respectively, are significantly lower than the mean values of PTT in the control group (55.64, 48.4, 41.76, 37.68, 46.05).

The results in the table above show that there are significant differences at 0.05 level between Experimental group and Control group in all PH values (the P-values less than 0.05).

Regarding PH At Admission, After 6 hr from admission, on 2nd day, and 3rd day, and Total PH, the results exhibit that the mean values of PH in the Experimental group (7.02, 7.28, 7.39, 7.38, 7.21) respectively, are significantly higher than the mean values of PH in the control group (6.76, 7.17, 7.29, 7.28, 7.1).

5.11 Age that infants who underwent therapeutic hypothermia had feed introduced

Table 5.11: Frequencies and percentage of differences between the Experimental and the Control in which day they start feeding.

Start feeding	Control	Experimental	P value
Up to Day 3	0(0%)	3(9.1%)	0.108
Day 4	0(0%)	5(15.2%)	0.035
Day 5	0(0%)	15(45.5%)	0.000
Day 6	0(0%)	6(18.2%)	0.020
Day 7+	15(55.6%)	4(12.1%)	0.000

5.12 follow up assessment finding between the Experimental and the Control groups.

Table 5.12: Follow up assessment finding between the Experimental and the Control groups.

Result		Group	
		Control	Experimental
		Count	Count
CT	Normal	6	21
	intracranial hemorrhage	3	0
	subcutaneous hematoma	1	0
	brain edema	12	12
	subglual hematoma	1	0
	Not done baby death	4	0
TFU	Normal	12	33
	bulging fontanel	1	0
	Brain edema	4	2
	not done baby death	7	0
	not documented	3	0
Echo	Normal	14	33
	not done baby death	7	0
	not documented	6	0
Vision test	Normal	10	33
	Vision loss	1	0
	not done	2	0
	not done baby death	7	0
	not documented	7	0
Hearing test	Normal	10	33
	hearing loss	1	0
	not done	2	0
	not done baby death	7	0
	not documented	7	0
EEG	Normal	5	30
	changes on wave	8	0
	not done baby death	7	0
	Not documented	7	3

Chapter Six

Discussion

6.1 Introduction

In this current study, all patients were divided into two groups, 27newborn in control and 33 experimental. Discussion it was built on answering hypothesis which were presented earlier in this thesis.

The result of this study showed the presence of relationship between therapeutic hypothermia and reducing mortality rate and a relationship between therapeutic hypothermia and reducing seizure also with reducing staying a day in MV and reducing neurodevelopment defect (hearing, vision), improving in primitive reflexes (sucking, Moro) and these benefit were harvested when TH implemented in NICU in Jenin hospital.

6.1.1 The first hypothesis:

The first hypothesis: The relationship between therapeutic hypothermia and reduce mortality rate.

The percentage of mortality for infants HIE in the control group 4(14.8%) was significantly higher than that in the experimental group 1(3%), while the percentage late neonatal death 0(0%) in the experimental group was significantly lower than that in the control group 7(25.9%) with P value 0.002. The previous study results consistent with current study that the risk

for death or disability estimated nearly half of newborn who have moderate to severe HIE (Jacobs et al.2013).

Infants treated with cooling experienced significantly decreased mortality and improved neurodevelopmental outcomes (Azzopardi et al, 2009) A randomized clinical trial was done by (Abbot. Laptook et al,2017) in April 2008 to June 2016 among infants with moderate or severe hypoxic-ischemic encephalopathy divided to experimental group and control group. Showed that the percentage of death or disability in was experimental group at least 1-3% less than non-cooled infants at age 18-22 month.

6.1.2 The second hypothesis: The relationship between therapeutic hypothermia and reduce seizure.

Regarding Seizures at the second and third day, the percentages of Non Seizures are 27(81.8%) and 28(84.8%) which significantly higher than that in the control group 8(29.6%) and 7(25.9%), while the percentage of Present Seizures in the experimental group are 6(18.2%) and 5(15.2%) which significantly lower than that in the control group 17(63%).

On the other hand, the results show that there are **no** significant differences at 0.05 level between the Control group and the Experimental group in Seizures 1in the first day (the P-value is less than 0.05).

Study by Dawn Gano et, al 2015 Among 224 newborns, divided to two group experimental group, control group showed the newborn in moderate encephalopathy were less likely to have seizures compared with control group (experimental : 26% vs. control : 61%, P<0.001), but in severe HIE there no difference in the risk of seizures both group.

6.1.3 The third hypothesis: The relationship between therapeutic hypothermia and reduce staying day on MV.

Regarding MV after 6 hr from admission, the percentage in the experimental group17 (53.1%) was significantly higher than that in the control group 7(25.9%). In the second day, the percentage in the experimental group 7(21.9%) was significantly higher than that in the control group 3(11.1%). And in the third day, the percentage in the experimental group 6(18.8%) was significantly higher than that in the control group 17(63%).

And this approval by (Lopez Laporte MA et al,2019)in his study Approximately 50–70% of HIE infants need to mechanical ventilation during cooling therapy.

6.1.4 The fourth hypothesis: The relationship between therapeutic hypothermia and reduce neurodevelopment defect (hearing, vision).

Many problem in visual and hearing occurs in infant who suffer from moderate and sever HIE 25% and 18% respectively.(Lindström K ,et al.2006).

In my study good outcome found, hearing and vision are normal in all experimental group, but with one baby loss of vision and hearing as a case of sever HIE.

6.1.5 The Fifth hypothesis: The relationship between therapeutic hypothermia and improve in primitive reflexes (sucking, Moro).

Sucking: Regarding Suck at the second day, the percentage of Weak Suck in the experimental group 25(75.8%) was significantly higher than that in the control group 7(25.9%), while the percentage of Absent Suck in the experimental group 7(21.2%) was significantly lower than that in the control group 18(66.7%).

Regarding Suck at the third day, the percentage of Weak Suck in the experimental group 19(57.6%) was significantly higher than that in the control group 6(22.2%), and the percentage of Normal in the experimental group 13(39.4%) was significantly higher than that in the control group 0(0%), while the percentage of Absent Suck in the experimental group 1(3%) was significantly lower than that in the control group 18(66.7%).

From the other hand, the results in the table above show that there are **no** significant differences at 0.05 level between the Control group and the Experimental group in Suck in the first day (the P-values are higher than 0.05).

Moro: there are significant differences at 0.05 level between the Control group and the Experimental group in Moro on the three days (the P-values are less than 0.05).

Regarding Moro on the first day, the percentage of Weak Moro in the experimental group 29(87.9%) was significantly higher than that in the control group 15(55.6%), while the percentage of Absent Moro in the experimental group 4(12.1%) was significantly lower than that in the control group 11(40.7%).

Regarding Moro on the second day, the percentage of Weak Moro in the experimental group 25(75.8%) was significantly higher than that in the control group 11(40.7%), and the percentage of Normal Moro in the experimental group 6(18.2%) was significantly higher than that in the control group 0(0%), while the percentage of Absent Moro in the experimental group 2(6.1%) was significantly lower than that in the control group 13(48.1%).

Regarding Moro on the third day, the percentage of Weak Moro in the experimental group 10(30.3%) was significantly higher than that in the control group 5(18.5%), and the percentage of Normal Moro in the

experimental group 21(63.6%) was significantly higher than that in the control group 1(3.7%), while the percentage of Absent Moro in the experimental group 0(0%) was significantly lower than that in the control group 17(63%).

6.1.6 The sixth hypothesis

The benefit from implementation therapeutic hypothermia in HIE newborn in Jenin Hospital?

added to all benefit mentioned previously in this study also in:

- Feeding: HIE babies in experimental group started feeding too early than control group who started at and above day 7 of finished cooling, but other started at day 3 of finished cooling in 9.1% , 4 day 15.2% ,5 day 45.5%, 6 day 18.2%, 7+ day 12.1%.

- The improvement on baby health status on HIE grade when compared the first HIE degree before cooling and when cooling finished in the first day 30 baby in experimental group found in moderate HIE at day 3 the number decreased to 9 baby , but the babies who found in control group 13 in moderate and 12 in sever grade the health status became more worst and without cooling increased to 24 babies in sever stage oh HIE

- Mortality: the mortality rate in cooling therapy is lower than the control group.

- Also the follow up assessment results showed in vision test there is no any vision loss on all babies who underwent cooling therapy compared with one vision loss on control group, the same matter in hearing test one hearing loss on control group with no losing in experimental group.

6.2 Study limitation

1. Transfer the baby to another hospital (five babies)
2. Miss diagnosis (one baby).
3. Baby died (three babies).
4. Baby who has congenital problem.
5. Baby who has chromosomal anomalies.

6.3 Strength point of the study

1. This study is the first study in NICU in Jenin hospital.
2. Therapeutic hypothermia protocol implemented newly in Jenin hospital so the research result will give the encouragement.
3. Used the Quiz experimental design which gives the strength of the research.
4. Taken the ethical part in consideration by using historical information in control group.

6.4 Conclusion

HIE is one of the most serious birth complications affecting full term infants with few preventive treatment modalities available. The hypoxic-ischemic event can be caused by multiple events, but ultimately brain injury occurs because of impaired cerebral blood flow and oxygen delivery to the brain. TH is a standard care for newborn 36 week GA who are depressed at birth should be assessed to determine whether they meet the criteria for cooling. TH may be achieved by either total body or selective head cooling. while closely monitoring infants temperature to maintain core temp 33-34 c for 72 hours, followed by rewarming of 6 to 12 hours.

This potential neuroprotective intervention to treat neonatal HIE. In this study therapeutic hypothermia was associated with a highly reproducible reduction in the risk in neurodevelopmental disability in vision and hearing and reducing the risk of seizure. also Infant with HIE who were treated with TH shortly after birth were significantly more likely to survive with zero % in mortality among TH group compared with who not underwent TH. TH shown by significant improvement in sucking by started feeding early that control group.

6.5 Recommendation

- Therapeutic hypothermia should be excluded for the following baby: Baby (<36 weeks), Baby WT <1800, HIE baby admitted after 6hr , Lethal congenital and chromosomal anomalies.
- Current hypothermia protocol is starting treatment within golden hours in the first 6 hrs of life, by systemic cooling to 34.5 ± 0.5°C for head cooling, for (surface cooling) or whole-body cooling(33.5 ± 0.5°C) and continuing for 72 hrs.
- Rewarming phase recommended that temp should increase 0.2-0.5 degree Celsius per hour to reach 36.5 need to 6-12 hour to reach it .
- More researches needed on passive cooling and active cooling .
- More researches needed included HIE babies who pass the first six gold hour and do TH in also first 12 hours.
- More researches needed on HIE babies who underwent TH but in wide sample size and observed the developmental defect later on like, school age.

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Appendix

Appendix 1

Hypothermia protocol

Therapeutic hypothermia protocol in NICU in Jenin Hospital

Eligibility criteria for therapeutic hypothermia (Refer to Cooling guidelines):

The following criteria will be used as a guide when choosing to provide neonatal hypothermia.

Inclusion Criteria: A. Infants ≥ 35 completed weeks gestation admitted to the NICU with at least one of the following:

(1) Apgar score of ≤ 5 at 10 minutes after birth

(2) Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth

(3) Acidosis within 60 minutes of birth (defined as any occurrence of umbilical cord, arterial or capillary pH < 7.00)

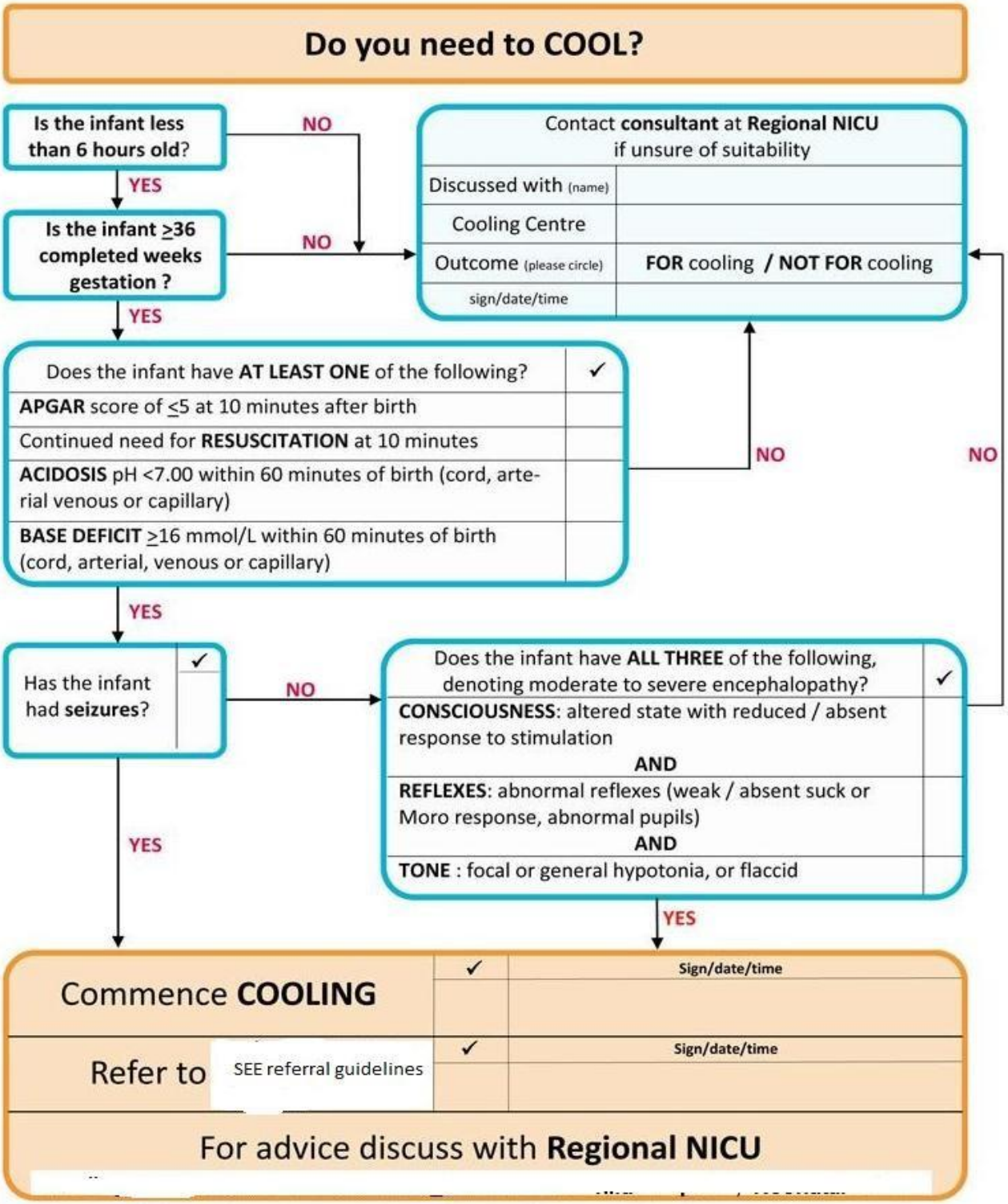
(4) Base Deficit ≥ 16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth.

(5) Infants that meet criteria A will be assessed for whether they meet the neurological abnormality entry criteria

B. Moderate to severe encephalopathy (Seizure, hypotonia, coma)

C. Timing: Initiation of this therapy should begin within 3-6 hours of birth. New data suggest that cooling before 12 hours of age may have benefits.

Identification and selection of patients for cooling flowchart



Appendix 2

Therapeutic hypothermia Check list

If baby has a perinatal event and/or acidosis and meets the criteria below, therapeutic hypothermia may be indicated.

A-Meet criteria

- Gestational age ≥ 36week ☐
- Wt ≥1800: ☐

B-Physiological Criteria (Ethier of two):

- Cord pH ≤7.0 or base deficit ≥−16 ☐
- pH 7.01 to 7.15 or base deficit −10 to −15.9 on cord gas or blood gas within 1 h ☐

AND

- history of acute perinatal event (ex ,uterine rupture) ☐
- Apgar score ≤5 at first 10 minutes or at least 10 minutes of positive-pressure ventilation ☐

C-Neurological Criteria (Ethier of two)

- presence of seizures ☐
- OR at least on sign in three or more of the six categories ☐

Criteria for defining moderate and sever encephalopathy

	Moderate encephalopathy	Severe encephalopathy
1. Level of consciousness	Lethargy ☐	Stupor/coma ☐
2. Activity	Decreased ☐	no ☐
3. Posture	(Distal flexion, full extension) ☐	internally rotated, legs extended with feet in forced plantar flexion ☐

Appendix 3

Observed data sheet

Effectiveness and outcome of implementation therapeutic hypothermia in asphyxiated neonate at Governmental hospital in West bank

Section one : demographic data

1. Study number _____
2. Date _____
3. Mother name _____
4. Baby name _____
5. Age of mother _____
6. City _____
7. Educational level _____
8. Telephone number _____

Section two : about mother and mother delivery

Q1: In complicated deliveries , the staff present in the delivery room included:

1. Pediatrician
2. Pediatrician specialized in neonatology
3. A nurse midwife
4. A nurse from neonatal

Q 2: Onset of labour for mothers whose infants underwent therapeutic hypothermia

1. Spontaneous
2. Induction

Q 3: what is the Distribution of parity, Parity TH ?

1. Nulliparous
2. Para 1
3. Para 2
4. Para 3+

Q 4: Did an acute perinatal event occur?

1. Variable / late foetal heart rate decelerations
2. Prolapsed / ruptured / tight nuchal cord
3. Uterine Rupture
4. Maternal haemorrhage / placental abruption
5. Maternal trauma
6. Other

Q 5: what is the Mode of delivery for mothers whose infants underwent therapeutic hypothermia ?

1. Spontaneous Vaginal Cephalic
2. Vaginal Breech
3. Caesarean section
4. Ventouse
5. Forceps

Q 6 : what is the color of Liquor ?

1. Clear
2. Meconium

Section Three : about baby and TH

Q 1: Is TH standard of care in your institute?

1. Yes
2. No

Q 2: Do you have a written protocol for TH?

1. Yes
2. No

Q 3: What scale do you use to grade the severity of HIE ?

1. Sarnat
2. Garcia –alix
3. Other
4. None

Q 4: How many times do you perform TH in a month?

1. (…….. per month).

Q 5: what is the gender of infants who underwent therapeutic hypothermia ?

1. Male
2. Female

Q 6 : what is the Apgar Scores at 1, 5 and 10 minutes for infants who underwent therapeutic hypothermia ?

Score	1 minute	5 minutes	10 minutes
0-3			
4-7			
8-10			

Q7: Resuscitation for infants who underwent therapeutic hypothermia?

1. Spontaneous breath taken
2. Resuscitation required
3. Intubation required
4. Chest compression required

Q 8: What inducing methods do you use for TH?

1. Head cooling
2. Surface cooling

Q 9: Is cooling preformed before 6hr ?

1. Yes
2. No

Q 10: What is the duration of cooling (hr)?

1. For 72 hours
2. Less than
3. More than

Q 11: Drugs or fluid treatment administered at birth for infants who underwent therapeutic hypothermia ?

1. Adrenaline
2. Dextrose
3. Saline
4. O neg blood
5. Sodium Bicarbonate

Q 12: what is the pH level from cord and initial infant blood gases for infants who underwent therapeutic hypothermia?

pH level	Cord blood Gas	Initial Arterial Blood Gas
6.6-6.7		
6.71-6.8		
6.81-6.9		
6.91-7.0		
7.01-7.1		
7.21-7.3		
7.31-7.4		

Q 13: Assessment for therapeutic hypothermia TH

>36 completed weeks gestational age	
Apgar score ≤ 5 at 10 minutes	
Weight ≥ 1800 grams	
Continued need for PPV or Intubation at 10 mins	
Acidosis present in any blood sample within 60 minutes of birth	
Base Deficit >16.0 mmol/L in any blood sample, within 60 minutes of birth	

Q 14: Drugs and Volume Replacement Day 1, 2 & 3

	Day 1	Day 2	Day 3
Sedation			
Antibiotics			
Anticonvulsants			
Inotropes			
Blood products			
Volume replacement			
Other			

Baby who received cooling therapy	At admission	After 6hr from admission	اليوم الاول	اليوم الثاني	اليوم الثالث
V/S : • BP					
• HR					
• TEMP					
Lab test: • Hemoglobin					
• Platelet					
• BUN					
• Creatinine					
• ALT					
• AST					
• Sodium					
• Calcium					
• Potassium					
• RBS					
• CRP					
Coagulation profile					

• PT					
• PTT					
ABG • PH					
• PCO2					
• PO2					
• HCO3					
MV parameters • FIO2					
• Respiratory rate					
• Pressure support • Pressure limit					
• PEEP					
Seizure					
a cranial ultrasound					
magnetic resonance imaging (MRI)					
Cardiac echo					

Q 15: How do you measure body temperature?

1. Rectal probe
2. Axillary
3. Surface

Q 16: SARNAT Scoring on Treatment

		Day 1	Day 2	Day 3
level of consciousness	1. Hyper alert 2. Lethargic or obtunded 3. Stupor or Coma 4. Normal 5. Undocumented			
Activity	1. Normal 2. Decreased 3. Absent 4. Undocumented			
Muscle tone	1. Normal 2. Mild hypotonia 3. Flaccid 4. Undocumented			
Posture	1. Mild distal flexion 2. Strong distal flexion 3. Intermittent decerebration 4. Normal 5. Undocumented			
Stretch reflexes	1. Overactive 2. Decreased or absent 3. Normal 4. Undocumented			
Suck	1. Weak 2. Absent 3. Normal 4. Undocumented			
Moro	1. Strong 2. Weak 3. Absent 4. Normal 5. Undocumented			
Tonic Neck	1. Slight 2. Strong 3. Absent 4. Normal 5. Undocumented			

Pupils	1. Mydriasis 2. Miosis 3. Variable; often unequal 4. fixed 5. dilated 6. Normal 7. Undocumented			
Heart rate	1. Tachycardia 2. Bradycardia 3.Variable 4.Normal 5.Undocumented			
Seizures	1. None 2. Present 3. Undocumented			

Q 17: Grade of Encephalopathy on Treatment

Grade	Day 1	Day 2	Day 3
Moderate HIE			
Severe HIE			

Q 18: Age that infants who underwent therapeutic hypothermia had feed introduced

Up to Day 3	
Day 4	
Day 5	
Day 6	
Day 7+	

Q 19: infant mortality for infants who underwent therapeutic hypothermia

Early neonatal death	
Late neonatal death	

Q 20: Grade of encephalopathy on discharge

Mild-Moderate HIE	
Moderate HIE	
Moderate to Severe HIE	
Severe HIE	
HIE not documented	

Q21: finding after discharge ?

	Result
TFU	
Echo	
Vision test	
Hearing test	
EEG	
Assessment after 6 weeks	

AN-NAJAH UNIVERS

PROTOCOL FOR HUMAN SUBJECTS RESEARCH

NEW PROJECTS ONLY

Investigator's Assurance

By submitting this protocol, I attest that I am aware of the applicable principles, policies, regulations, and laws governing the protection of human subjects in research and that I will be guided by them in the conduct of this research.

To apply for human subjects IRB review:

1. Download this New Projects IRB Protocol and save it on a floppy disk or on your hard drive. You may then open it, type in all requested information, save the file (please use your last name and New Project Protocol as the title: e.g., Musmar New Project Protocol), and send the file as an e-mail attachment, along with your informed consent letter(s), to the Institutional Review Board at

   " irb@najah.edu".

It is essential that you answer all questions on this form since this is the primary source of information used by Board members to make their decisions. Also, only include information necessary to answer the questions. Please keep your responses as free of jargon as possible.

2. Please also send, by campus mail, all supporting materials that cannot be e-mailed (e.g., measures, permission letters from off-campus sites) to the IRB at An-Najah University, Nablus, Palestine. If your research requires review by the full Board, you will be so notified and asked to provide an additional 12 copies of the supporting materials.

PLEASE DO NOT INCLUDE THIS PAGE WITH YOUR SUBMISSION

PLEASE BE SURE TO COMPLETE ALL SECTIONS

Current Date of Submission: _7/7/2020_____

IRB office use only: Date received in IRB office (stamp)_____

If this is a revision in response to an <u>IRB Report of Action (ROA)-approval pending</u>, indicate the date of the ROA: _____

Title of Research: _ Effectiveness and outcome of implementation therapeutic hypothermia in asphyxiated neonate at Governmental hospital in West bank

Principal Investigator: Elham Mahmoud Fayad
Department/School الدراسات العليا
Room # where mail can be sent _____
Phone 0568573458 E-mail turkam.elham2020@gmail.com
Other Investigator: _
Department/School_
Room # where mail can be sent _____
Phone E-mail _
****Faculty Sponsor (for Student Research): Dr Eman Alshawish Jayyose**
Department/School: _faculty of Medicine and Health Sciences
Room # where mail can be sent _____
Phone _0595778058 _E-mail _alshawish@ najah.edu ___
Student Street Address Alzababdah , Jenin
City Jenin State Palestine Zip 00970

Type of Research (please check):

Dissertation _____ (PLEASE NOTE: IRB review of dissertation research requires prior successful proposal defense.)

PhD Defense Date: _____

Master's Thesis _*__

Class project ____

all other projects____

☐ ** If the primary investigator is a student, check here to indicate that your faculty sponsor has read the entire application, including cover letters, informed consents, and data collection instruments, and asserts that this application is accurate and complete.

Dates Human Subjects Portion of Research Scheduled: from: July to December 2020.

Site(s) of Human Subject Data Collection: _in Jenin Govermental Hospital _____

(*NOTE: If sites are administratively separate from the University, please submit approval letters, or indicate when they will be forthcoming.)*

Funding Agency (if applicable):_____NO

I. NATURE OF THE RESEARCH

In the judgment of the Principal Investigator, this research qualifies for which of the following types of review:

Review Type: _____exempt (category*__expedited (category) _full Board[1]

II. PURPOSE OF RESEARCH

Briefly describe the objective(s) of the research (please keep description jargon free and use 100 words or less; the IRB will file this information in our descriptions of approved projects).

- To assess the effectiveness and outcome of implementation therapeutic hypothermia .
- To assess the relationship between therapeutic hypothermia and mortality rate.
- To assess relationship between therapeutic hypothermia and seizure .
- To assess relationship between therapeutic hypothermia and staying day in NICU.
- To assess relationship between therapeutic hypothermia and neurodevelopment defect(hearing, vision).
- To assess relationship between therapeutic hypothermia and improve in primitive reflexes (sucking, Moro).

[1] All research that is either externally funded or greater than minimal risk must be reviewed by the full Board

III. METHODS

Approximate number of subjects: _30 in each group, to tal 60_____

Subjects will be (check only if applicable):

__*__minors (under 18)

__involuntarily institutionalized

__mentally handicapped

Describe <u>in detail</u> how the subjects will be selected and recruited:

The study will use Quzi experimental design. The study conclude prospective study

experimental group baby who received therapeutic hypothermia and historical study as control

group who not received therapeutic hypothermia . Survey will be carried out at Neonatal

Intensive Care Unit in Governmental Hospital in Jenin

*** Study Population and sampling :** The researcher will target all the newborn who HIE

admitted to intensive care unit at Jenin hospital .

*** Data collection methods and instrument :**the data gathering by check list and

Questionnaire(appendix3) that consists several parts , included socio-demographic characteristic

about the mother and the baby, baby status during and after birth, and question about therapeutic

hypothermia criteria, and baby status during implementation criteria and finding that will be seen

,other investigation.

After obtaining a formal approval from IRP and the ministry of health (MOH) , secondary data

will be collected started through using neonatal register book and the baby file to observe the

result of lab test and some radiology studies (February 2019-June 2020).

*** inclusion criteria**

All baby who have HIE.

- Singleton and twins.
- Baby with gestetional age above 36week.
- Baby wt > 1800
- Primigravida or multigravida .
- HIE newborn from normal delivery, cesarean delivery, instrument delivery.

*** Exclusion criteria**

- All baby admitted to NICU not HIE .
- Baby (<36 weeks)
- Baby wt <1800
- HIE baby admitted after 6hr .
- Lethal congenital and chromosomal anomalies.

Describe <u>exactly what will be done</u> to subjects once they have agreed to participate in the project:

The data gathering by check list and Questionnaire(appendix3) that consists several parts , included socio-demographic characteristic about the mother and the baby, baby status during and after birth, and question about therapeutic hypothermia criteria, and baby status during implementation criteria and finding that will be seen ,other investigation.

After obtaining a formal approval from IRP and the ministry of health (MOH) , secondary data

will be collected started through using neonatal register book and the baby file to observe the

result of lab test and some radiology studies (July 2020- december 2020)

What incentives will be offered, if any? Nothing

IV. RISKS/BENEFITS TO PARTICIPANTS

Identify possible risks to subjects:

(NOTE: These may be of a physical, psychological, social or legal nature. If subjects are vulnerable populations, or if risks are more than minimal, please describe what additional safeguards will be taken.) no risk

What are the benefits and how will they be optimized?

This study will support the use of therapeutic hypothermia in treatment newborn who have HIE

and harvesting the benefit that return the baby and family and to hospital and society by reduce

the complication of birth asphyxia .

So the Study is important for several reasons. First, a lack of Palestinian studies that can support

the implementation of cooling therapy .Second ,this research will be the first study that deal

with this type of treatment in Jenin Governmental Hospital .Third, to increase the

awareness of health team in the neonatal intensive care unit to the advantage of this treatment .

Fourth , decrease the cost of HIE treatment because the cooling therapy will be offer benefit

when decrease the severity of HIE complication.

Do benefits outweigh risks in your opinion? Yes ✓

------ NO

Are there potential legal risks to the Principal Investigator or University? Yes----- No - ✓

V. INFORMED CONSENT

Describe how participants will be informed about the research before they give their consent. Be sure to submit with this protocol a copy of the informed consent/assent letter(s) you will use. Please prepare your informed consent letter at the 8th grade reading level or lower as dictated by the needs of the subjects. (See IRB website for required elements of an informed consent.)

Dear Parents:
To participate in a research project being conducted in the department; your participation is entirely voluntary. It is up to you to decide whether or not to take part in this study.

Before you decide, it is important for you to understand what the research involves. This consent form will tell you about the study, why the research is being done and the possible benefits, risks and discomforts.

If you wish to participate, you will be asked to sign this form. If you decide to take part in

this study, you are still free to withdraw at any time and without giving any reasons for your decision.

If you do not wish to participate, you do not have to provide any reason for your decision. You will not lose the benefit of any medical care to which you are entitled or are presently receiving.

Please read this form carefully and feel free to discuss it with your family, friends and doctor before you decide.

And the data gathering by check list and Questionnaire

Benefits:

This study will support the use of therapeutic hypothermia in treatment newborn who have HIE

and harvesting the benefit that return the baby and family and to hospital and society by reduce

the complication of birth asphyxia .

Risks and discomforts:

There are no physical risks associated with this study.

Costs and reimbursements:

There is no cost to you for participating in this study. You will not be paid for your participation.

Who to contact for questions about this study:

If you have any questions about this study, you can contact The Principal Investigators,

Elham Mahmoud Fayad (0568573458)

Consent:

I, _____, have read and

Understand the above information and agree to participate in the study entitled:

Effectiveness and outcome of implementation therapeutic hypothermia in asphyxiated neonate at Governmental hospital in West bank .

I understand that my participation is voluntary and that all the information collected will be kept confidential and used only for scientific objectives.

I am not waiving any of my legal rights by signing this consent form. I freely consent to

Participate in this study.

Signature of parent_____
Date_____

V. INFORMED CONSENT

Describe how participants will be informed about the research before they give their consent. Be sure to submit with this protocol a copy of the informed consent/assent letter(s) you will use. Please prepare your informed consent letter at the 8th grade reading level or lower as dictated by the needs of the subjects. (See IRB website for required elements of an informed consent.)

بِسْمِ ٱللَّهِ ٱلرَّحْمَٰنِ ٱلرَّحِيمِ

موافقة للإشتراك في البحث العلمي

جامعة النجاح الوطنية –كلية الطب وعلوم الصحيه \دائرة التمريض والقبالة

أخي المشارك / أختي المشاركه

السلام عليكم ورحمة الله وبركاته

تحية طيبة وبعد ، ،

أنت مدعو(ة)ك أم أوأب للمشاركة ببحث علمي سيجرى في جنين في فلسطين . الرجاء أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بتأن قبل أن تقرر(ي) إذا كنت تريد(ي) مشاركة طفلك أم لا. بإمكانك طلب إيضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الإستمارة أو عن هذه الدراسة ككل من الباحث.

يقوم البحث بالأساس على دراسه فعالية استخدام نظام خفض الحرارة والنتائج المرجوة عند الاطفال الذين يعانون من نقص الاكسجين عند الولادة.

التأثيرات السلبية او ردات الفعل التي يمكن ان يسببها الإشتراك في هذا البحث :

لا يوجد أي تأثيرات سلبية من هذا البحث.

الفوائد الناتجة عن البحث:

أولاً : معرفة الفوائد المرجوة من استخدام نظام خفض الحرارة.

ثانياً : معرفه العلاقة بين استخدام نظام خفض الحرارة و انخفاض نعدل الوفيات

ثالثا: معرفه العلاقة بين استخدام نظام خفض الحرارة وانخفاض معدل التشنجات عند حديثي الولاده

رابعا: معرفه العلاقة بين استخدام نظام خفض الحرارة و مجدة المكوث في قسم العناية المكثفه الخاصه بالخدج وحديثي الولاده

خامسا: معرفه العلاقة بين استخدام نظام خفض الحرارة والتقليل من مشاكل السمع والنظر.

في حال وافقت على مشاركة طفلك في هذه الدراسة، ستبقى المشاركة في غاية السرية والكتمان . لا يحق لأي شخص كان الإطلاع على الأستبانة الخاصة بالمشارك بالبحث باستثناء الباحث المسؤول عن الدراسة ومعاونيه، ولجان الأخلاق المهنية المستقلة، و مفتشين من الإدارات الحكومية المنظمة.

موافقة المشترك:

لقد قرأت استمارة القبول هذه وفهمت مضمونها. تمت الأجابة على أسئلتي جميعها. وبناء عليه فأنني، حرا مختارا، أجيز إجراء هذا البحث و أوافق على الإشتراك فيه، وإني أعلم ان الباحث او مساعديه سيكونون مستعدين للإجابة على أسئلتي، وأنه باستطاعتي الإتصال بهم على الهاتف. واذا شعرت لاحقا ان الأجوبة تحتاج الى مزيد من الإيضاح فسوف أتصل بالباحث , كما أعرف تمام المعرفة بانني حر في إنسحاب طفلي من هذا البحث متى شئت حتى بعد التوقيع على الموافقة دون ان يؤثر ذلك على العناية الطبية المقدمة لطفلي.

التوقيع _____
التاريخ _____

إسم الباحث: الهام محمود فياض

رقم هاتف الباحث:0568573458

مشرف البحث: د .ايمان الشاويش (جامعة النجاح الوطنية/ كلية الطب وعلوم الصحيه /دائرة التمريض والقبالة/ رئيسة قسم القبالة وتمريض الاطفال والمراهقين).

عنوان البحث**:**

دراسه فعالية استخدام نظام خفض الحرارة والنتائج المرجوة عن الاطفال الذين يعانون من نقص الاكسجين عند الولادة في مستشفى جنين الحكومي- فلسطين

مكان إجراء البحث: جنين.

VI. PRIVACY/CONFIDENTIALITY

Please describe whether the research would involve observation or intrusion in situations where subjects have a reasonable expectation of privacy. If existing records are to be examined, has appropriate permission been sought; i.e. from institutions, subjects, physicians? What specific provisions have been made to protect the confidentiality of sensitive information about individuals?

Every participant in the study will receive an explanation about the purpose, confidentiality of the study. Participation in the study will be voluntary and based on the ability to give an informed consent, all data and information's gathered is strictly confidential and is not to be accessed by any other without prior permission from the participants, moreover, the participant had the right to withdraw at any time if they can't complete the questionnaire.

Data confidentiality: Participants will be informed that data will be treated with absolute confidentiality, and that data will be used exclusively for the objectives of the study.

جامعه النجاح الوطنية

كليه الدراسات العليا

فعالية ونتائج إستخدام نظام خفض الحرارة لدى أطفال حديثي الولادة الذين يعانون من نقص الأكسجين في مستشفيات الحكومية في الضفة الغربية

إعداد

الهام فياض

إشراف

د. إيمان الشاويش

قدمت هذه الأطروحة إستكمالاً لمتطلبات الحصول علي درجه الماجستير في برنامج تمريض العناية المكثفة، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

2021

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اعداد

الهام فياض

اشراف

د. إيمان الشاويش

الملخص

مقدمة: اختناق الولادة هو حالة طبية ناتجة عن نقص الأوكسجين للرضيع لفترة طويلة من الوقت أثناء عملية الولادة، ونتيجة للعديد من المسببات يصبح الطفل عادة ازرق اللون ويحدث تباطأ بضربات القلب ،وتكون درجة أبغار APGAR منخفضة في أول 5 دقائق.

ترتبط درجات الاختناق الشديدة بارتفاع معدلات الوفيات في جميع أنحاء العالم. هناك حاجة ملحة لتحسين النتائج عند الرضع المصابين، فقد أصبح انخفاض حرارة الجسم العلاجي ((TH مثل الجسم بالكامل أو التبريد الانتقائي للرأس علاجًا قياسيًا لـ HIE المعتدل والشديد في العديد من البلدان المتقدمة لتقليل الضرر العصبي خلال الساعات الست الأولى من الحياة، عن طريق خفض درجة الحرارة إلى 34.5 ± 0.5 درجة مئوية لتبريد الرأس، لتبريد الجسم (33.5 ± 0.5 درجة مئوية) والاستمرار لمدة 72 ساعة.

هدف الدرسة: لتقييم فعالية ونتائج تنفيذ انخفاض حرارة الجسم العلاجي والعلاقة بين انخفاض حرارة الجسم العلاجي ومعدل الوفيات والتشنجات ومدة مكوث الطفل على جهاز التنفس الصناعي والعلاقة بين انخفاض حرارة الجسم العلاجي وخلل النمو العصبي وردود الفعل البدائية.

تصميم الدراسة وطريقتها: اعتمدت الدراسة التصميم التجريبي. Quazi ضمنت الدراسة دراسة مستقبلية لمجموعة من الاطفال الذين سيتلقو انخفاضًا في درجة الحرارة العلاجي ودراسة تاريخية كمجموعة ضابطة لم يتلقوا انخفاضًا علاجيًا في درجة حرارة الجسم، وسيتم إجراء المسح في وحدة

العناية المركزة لحديثي الولادة في المستشفى الحكومي في جنين. الفترة هي عام واحد من فبراير 2020 إلى سبتمبر 2020.

النتائج: لا توجد فروق ذات دلالة إحصائية عند مستوى 0.05 بين المجموعة التجريبية والمجموعة الضابطة في عمر الأمهات، وفروق ذات دلالة إحصائية في عمر الحمل عند مستوى 0.05 بين المجموعة الضابطة والمجموعة التجريبية في الحاجة المستمرة لـ PPV أو التنبيب عند 10 دقائق (القيمة P أقل من 0.05).

كانت النسبة المئوية للأطفال المحتاجين إلى PPV في المجموعة التجريبية 10 (30.3٪) وهي أعلى بكثير من تلك في المجموعة الضابطة 0 (0٪) ، بينما كانت النسبة المئوية للأطفال الذين يحتاجون إلى جهاز تنفس في المجموعة التجريبية 23 (69.7٪)) وهو أقل بكثير من المجموعة الضابطة 27 (100٪). اليوم الأول في المجموعة الضابطة خفيف 7.4) 2 HIE٪ (معتدل 13 (48.1٪)، فصل 12 (44.5٪)، في المجموعة التجريبية 0 (0٪)، 30 (90.9٪)، 3 (9.1٪) على التوالي.

ولكن في اليوم الثالث من العلاج في المجموعة الضابطة خفيف، متوسط، حاد 0 (0.0٪)، 3 (27.3٪)، 24 (72.7٪) في المجموعة التجريبية 24 (72.7٪)، 9 (27.3) .0 (0.0) على التوالي. كانت النسبة المئوية للوفيات عند الرضع HIE في المجموعة الضابطة 4 (14.8٪) أعلى بكثير من تلك في المجموعة التجريبية 1 (3٪)، بينما النسبة المئوية لوفيات المتأخرة 0 (0٪) في المجموعة التجريبية كانت أقل بكثير من المجموعة الضابطة 7 (25.9٪) بقيمة 0.002 P، وفيما يتعلق بالنوبات التشنج في اليوم الثاني والثالث، كانت نسب عدم وجود تلك النوبات 27 (81.8٪) و28 (84.8٪). أعلى بكثير من المجموعة الضابطة 8 (29.6٪) و7 (25.9٪)، بينما كانت نسبة النوبات الحالية في المجموعة التجريبية 6 (18.2٪) و5 (15.2٪) وهي أقل بكثير من المجموعة الضابطة. المجموعة 17 (63٪).

فيما يتعلق بخضوع الاطفال الى اجهزه التنفس بعد 6 ساعات من الدخول، كانت النسبة المئوية في المجموعة التجريبية 17 (53.1٪) أعلى معنوياً من المجموعة الضابطة 7 (25.9٪). في اليوم الثاني كانت النسبة في المجموعة التجريبية 7 (21.9٪) أعلى معنوياً من المجموعة الضابطة 3 (11.1٪). أما بالنسبةالبلع في اليوم الثاني فقد كانت نسبةالبلع الضعيف في المجموعة التجريبية 25 (75.8٪) أعلى بكثير من تلك في المجموعة الضابطة 7 (25.9٪).

بينما كانت نسبة البلع الغائب في المجموعة التجريبية 7 (21.2٪) أقل بكثير من تلك الموجودة في المجموعة الضابطة 18 (66.7٪) لذلك بدأت عملية التغذية في المجموعة التجريبية بالتغذية في وقت مبكر جدًا عن المجموعة الضابطة التي بدأت في اليوم السابع وما فوق. تم الانتهاء من التبريد، ولكن الأخرى بدأت في اليوم الثالث من التبريد النهائي بنسبة 9.1٪، 4 أيام 15.2٪، 5 أيام 45.5٪، 6 أيام 18.2٪، 7+ يوم 12.1٪، كما أظهرت نتائج تقييم المتابعة في اختبار الرؤية أنه لا يوجد أي فقد في الرؤية لدى جميع الأطفال الذين خضعوا للعلاج بالتبريد مقارنة بفقدان بصر واحد في المجموعة الضابطة، نفس الأمر في اختبار السمع فقد سمع واحد في المجموعة الضابطة مع عدم الخسارة في المجموعة التجريبية.

الخاتمة: يكون انخفاض حرارة الجسم أكثر فائدة عندما يتم تثبيته في أول 6 ساعات عند الرضع الناضجين والخداج المتأخر GA ≥36 أسبوعًا للحد من التلف في الدماغ. يجب أن يستوفي الرضع الذين تعرضوا لانخفاض حرارة الجسم معايير الاشتمال. تشمل معايير الأهلية درجة حموضة 7.0 أو عجز أساسي قدره 16 مليمول / لتر في عينة من دم الحبل السري أو الدم الذي تم الحصول عليه خلال الساعة الأولى بعد الولادة، والاحداث السابقة للولادة ودرجة أبغار لمدة 10 دقائق < 5، أوالحاجة للمساندة بالاكسجين عند الولادة واستمرت لمدة 10 دقائق على الأقل بالإضافة إلى ذلك، من الضروري إجراء فحص عصبي يوضح HIE المعتدلة إلى الشديدة.

التوصية: مستبعدة للطفل التالي في: TH الرضيع (أقل من 36 أسبوعًا)، وزن الطفل أقل من 1800، إدخال الطفل HIE بعد 6 ساعات، التشوهات الخلقية والكروموسومية القاتلة. يبدأ بروتوكول خفض حرارة الجسم الحالي العلاج خلال الساعات الذهبية في أول 6 ساعات من الحياة، عن طريق التبريد النظامي إلى 34.5 ± 0.5 درجة مئوية لتبريد الرأس، من أجل (تبريد السطح) أو تبريد الجسم بالكامل (33.5 ± 0.5 درجة مئوية) والاستمرار لمدة 72 ساعة، هناك حاجة أيضًا لمزيد من الأبحاث التي تضمنت أطفال HIE الذين يجتازون أول ست ساعات ذهبية ويقومون بعمل TH أيضًا في أول 12 ساعة باستخدام حجم عينة واسع ولاحظوا الخلل في النمو فيما بعد مثل سن المدرسة.