Final Master Thesis


LSMU, Clinic of Neonatology, Medicine Faculty
Kaunas, 2018

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3. SUMMARY

Comparative study of neonatal operations’ epidemiological and clinical trends in 2004-2005 and 2014-2015, by Maria Trigo Seguin. The purpose of this study is to compare and determine epidemiological and clinical trends in neonatal operations during two different periods; 2004-2005 and 2014-2015, in a tertiary level hospital in Kaunas, Lithuania (Kaunas Clinics).

The aim of the study is to detect, compare and determine epidemiological and clinical trends in neonatal, during 2004-2005 and 2014-2015 in a tertiary level hospital, Kaunas Clinics. The objectives are:

1. To detect and compare general rate of operations.
2. To detect and compare patients; gender, birth weight and gestational age.
3. To detect and compare; age at time of operation (day of life), time of stay in NICU.
4. To detect and compare structure of the following operations; Retinopathy of prematurity, Patent Ductus Arteriosus, Necrotizing enterocolitis, Ventriculoperitoneal shunt implant and Myelomeningocele.

The methodology of the study consists in retrospectively collect data, using the database system of neonatal intensive care unit (NICU) and archive of the hospital. Then select the study participants, which were all the patients from NICU who underwent surgery during the years 2004-2005 and 2014-2015, and relevant demographic data; gender, birth date, gestational age (GA), birth weight (BW), days of stay in NICU, date of operation, type of operation, was collected. Statistical analysis using Microsoft excel and SSPS to find the relevant statistical significant differences on the incidence of surgery in new-borns of this particular NICU and in these two periods of time.

Significant statistical differences were shown during the analysis. From the first period to the second female patients, which already were a minority kept decreasing, the average GA of operated patients was smaller, the length of stay in NICU and the age at time of surgery on the contrary became larger. In particular patients of ROP have shown a lower GA and an older age at surgery, patients of PDA have shown a lower GA as well as in BW and also longer length of stay in NICU, patients treated for NEC had a lower BW and were older at the time of surgery, patients who required VPS implant showed no significant changes and patients that needed MMC repair demonstrated a significant difference in gender, which switched from majority of female to majority of male.
4. ACKNOWLEDGEMENTS

The author wants to express her gratitude towards the supervisor of the work, professor Rasa Tamelienè, for the opportunity to learn about such an interesting topic, discover how research is the pillar of medical practice and for being so patient. Special thanks to the doctors and nurses of the hospital’s NICU that made the data collection as easy and effective as possible. Also to mention Carlos Trigo, the statistic consultant, and Susana Seguin for their support during this project.

5. CONFLICTS OF INTEREST

The author reports no conflicts of interests.
6. PERMISSION ISSUED BY THE ETHICS COMMITTEE

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2018-05-15 Nr. SEC-MF-408

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*Pastaba: šis pritarimas neatliekia tyrojų nuo atsakomybės ir prievoles gauti nacionalinio arba regioninio bioetikos komiteto leidimą pagal LR Biomedicinių tyrimų etikos įstatyme numatytas nuostatas.

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7. ABBREVIATIONS

ROP- Retinopathy of prematurity
NEC- Necrotizing enterocolitis
PDA- Patent ductus arteriosus
VPS- Ventriculoperitoneal shunt
MMC- Myelomeningocele
NICU- Neonatal intensive care unit
GA- Gestational age
BW- Birth weight
LBW- Low birth weight
VLBW- Very low birth weight
ELBW- Extremely low birth weight
EXIT- Ex-utero intrapartum treatment
FETO- Fetal endoluminal tracheal occlusion
MIS- Minimally invasive surgery
OR- Operation room
CDH- Congenital diaphragmatic hernia
ECMO- Extracorporeal membrane oxygenation
ICROP- International classification of retinopathy of prematurity
APROP- Aggressive posterior retinopathy of prematurity
Anti-VEGF- Anti-vascular endothelial growth factor
IGF-1- Insulin-like growth factor 1
PG- Prostaglandins
PUFA- Polyunsaturated fatty acids
CVS- Cardiovascular system
P/IHT- Pulmonary idiopathic hypertension
BPN- Brain natriuretic peptide
HF- Heart failure
hsPDA- Hemodynamically significant patent ductus arteriosus
NSAID- Non steroidal anti-inflammatory drug
FIP- Focal (isolated) intestinal perforation
NPO- Nils per os (nothing by mouth)
MRI- Magnetic resonance imaging
CT- Computed tomography
DHM- Donor human milk
CSF- Cerebrospinal fluid
ETV- Endoscopic third ventriculostomy
US- Ultrasound
ICP- Intracranial pressure
IVH- Intraventricular hemorrhage
PHH- Posthemorrhagic hydrocephalus
VSGS- Ventriculostubgaleal shunt
CPC- Choroid plexus cauterization
8. TERMS

Gestational age- Term used during pregnancy to describe how far along the pregnancy is. It is measured in weeks, from the first day of the woman's last menstrual cycle to the current date. A normal pregnancy can range from 37-42 weeks.

Term birth- Childbirth at the normal duration of the pregnancy.

Prematurity- Infants born before 37 weeks of gestation are considered premature and may be at risk for complications.

Birth weight- Weight at term delivery, normal is 2500–4200 g.

Low birth weight- Birth weight less than 2500 g, regardless of gestational age.

Very low birth weight- Birth weight which is less than 1500 g, regardless of gestational age.

Extremely low birth weight- Birth weight less than 1000 g, regardless of gestational age.

Neonate- Also called newborn infant, is a child under 28 days of age. During this period the child is at highest risk of dying. It is thus crucial that appropriate feeding and care are provided during this period, both to improve the child’s chances of survival and to lay the foundations for a healthy life.

Foetal surgery- Act of opening the gravid uterus, surgically correcting a fetal abnormality, and returning the fetus to the uterus for postoperative recovery and continued gestational development.

Minimally invasive surgery- Minimally invasive surgery is a surgery minimizing surgical incisions to reduce trauma to the body. It is usually performed using thin needles and an endoscope to visually guide the surgery.

Parenteral nutrition- Feeding technique in which nutrients are taken intravenously, bypassing the usual process of eating and digestion.

Human milk bank- Service which collects, screens, processes, and dispenses by prescription human milk donated by nursing mothers who are not biologically related to the recipient infant.
9. INTRODUCTION

Neonatal surgery is the most complex part of pediatric surgery, and there are very few studies on newborns’ incidence of diseases and trends of treatment, specifically over the long term in a single country. None of them has yet been made in Lithuania, that’s why these findings are of great relevance. Evidence based medicine together with a good information system are the way towards optimization of neonatal care, and should therefore be fomented. For example, Japan has a national survey of neonatal surgery program, that commenced in 1964 and has been carried out every 5 years, collecting extremely valuable data for understanding the development and progression of neonatal surgery, and has now lower mortality than European countries and United States [1], [2].

During ten years, advances in management of newborns has been wide, the development of NICUs with full-time neonatologists, refinement of surgical techniques, specially in foetal surgery and minimally invasive surgery, better cardiorespiratory support, total parenteral nutrition and management protocols, have shown an improvement in survival rates, and even extremely low birth weight (ELBW) patients survive now [3].

The purpose of this study is to analyze retrospectively how these innovations in management of newborn patients has affected the incidence of different type of operations and the incidence of these surgeries in different groups of patients divided according type of operation and demographic characteristics; gestational age, birth weight, gender, length of stay in NICU and age at the time of surgery. The data needed was collected from the hospital database, and clinical cases were reviewed. The participants of the study are all the patients that underwent a surgical procedure during their stay on NICU in the years 2004-2005 and 2014-2015. Then data was analysed using Microsoft excel and SSPS; percentages, mains, histograms and standard deviations were calculated, and statistical analysis using Pearson Chi-square test and T-tests, always with a p=0.05, to compare the demographic characteristics of the population and their rates, to detect significant differences in the two groups, also more specifically in five types of operation; ROP, PDA, NEC, VPS and MMC. Results were compared with other current research data. Conclusions and recommendations were made from a logic and evidence based point of view.
10. AIM AND OBJECTIVES

There is very little knowledge related to neonatal surgery incidence and mortality in Lithuania, no big scale researches have been published or proper statistical data has been collected. Therefore, it is of great relevance to start analysing this field, and more studies like this one should be made.

In this study data from patients who underwent surgery in the selected periods (2004-2005, 2014-2015) was collected and analysed to compare and analyse significant difference in epidemiological and clinical trends. Hopefully this small contribution, will be of use for further investigation on the topic.

The aim of this retrospective study is to detect, compare and determine epidemiological and clinical trends in neonatal, during 2004-2005 and 2014-2015; both periods of two years, in a tertiary level hospital, Kaunas Clinics.

The objectives are:

5. To detect and compare general rates of operations.
6. To detect and compare patients; gender, birth weight and gestational age.
7. To detect and compare; age at time of operation (day of life), time of stay in NICU.
8. To detect and compare structure of the following operations; Retinopathy of prematurity, Patent Ductus Arteriosus, Necrotizing enterocolitis, Ventriculoperitoneal shunt implant and Myelomeningocele.

11. LITERATURE REVIEW

Babies in the NICU are usually very sick, and the majority presents with associated conditions such as; preterm birth, low birth weight (LBW), chromosomal defects, genetic syndromes or serious illness, therefore management in highly dedicated neonatal intensive care units is required. These conditions, specially prematurity and LBW, present independent risk factors for the patients’ increased morbidity and mortality [4].
It was not until 1950s that the first NICU appeared and neonatal surgery became a subspecialty of pediatric surgery. Since its appearance until today neonate surgical mortality has been decreasing, although most of the procedures in use were developed in 1960s. The decrease in mortality also includes premature and extremely low birth weight (ELBW) infants who can now reach adulthood. The main reasons for this improved survival of neonates are; better understanding neonatal physiology, new technologies for disease diagnosis and management such as; imaging techniques like 3D and 4D ultrasound (US) and fetal magnetic resonance imaging (MRI); foetal surgical management for perinatal care with Ex-utero intrapartum treatment (EXIT) or Fetal endoluminal tracheal occlusion (FETO); minimally invasive surgery (MIS) not only referring to laparotomy and thoracotomy but also awake surgery for minor procedures, among others [3].

Nevertheless, there are also complications following neonatal surgery that have a big effect on patients, both in short and long term affecting their development and later life quality. The main goal of perinatal medicine is not only to decrease death but also neurodevelopmental impairment. There is a connection between the effect of anesthesia and surgery during early life and the risk for later neurocognitive deficits and impaired school achievements [5]. This increases in extremely premature but also late premature and LBW [6]. Therefore, the priority should be to try to avoid surgical interventions as long as possible, and focus research on less invasive techniques.

MIS has been a great advance for children less than 1-year-old, although it was a challenge since it requires special equipment and different techniques due to patient’s size. There are available laparoscopic procedures such as; pyloromyotomy, fundoplication, chronic diaphragmatic hernia (CDH) repair, anorectoplasty, inguinal hernia repair, nephrectomy and cystectomy; and also thoracoscopic procedures like; CDH repair, PDA ligation, esophageal atresia repair, lobectomy, cyst excision and mediastinal mass incision [7]. There is a small number of surgeons trained and performing these procedures and it requires specially small instrumentation that was not available, therefore technical development has been slow [8]. The results have given rise to a new generation of MIS instrumentation that leads the way in the field of mini-laparoscopy in children and adults [9].

Another factor that rises the risk of complications, specially for critically ill patients is the transport to the operation room. Patients requiring surgery are usually transferred to the
operating room (OR) or can also undergo bedside surgery. However, some studies show that an OR within the NICU may help reduce the risk of these complications, giving continuity of care to critically ill neonates and reducing the disturbances to other NICU babies in case of bedside operations [10].

The overall mortality rate of neonatal surgical disease has markedly decreased and is now less than 10% [2]. There are several conditions presented on newborns that require surgical treatment. Esophageal atresia is a good example of how a proper and on time diagnosis, improved operative techniques and good perioperative management, can have a survival rate of almost 100%. As well as minimally invasive thoracotomy improves patients’ long-term quality of life. However, not all the conditions that affect newborns have such a safe and successful management. Gastrointestinal perforation in a patient with ELBW still shows high mortality rate. Abdominal wall defects, have poor outcomes because it is usually accompanied by chromosomal abnormalities. Congenital diaphragmatic hernia (CDH), pulmonary hypoplasia as well as pulmonary hypertension often leads acute respiratory and circulatory deterioration right after birth, and yet intensive care including ECMO, nor fetal intervention has neither achieved a good outcome, mortality is high.

One of the objectives of the study is to compare the trends in five particular diseases, focusing on this idea I herein review latest and most relevant literature on the newest ways of treatment for this conditions on; ROP, PDA, NEC, VPS and MMC.

11.1. Retinopathy of prematurity (ROP):

ROP is a disease that affects premature newborns. It is the leading avoidable cause of childhood blindness [11] and has become an increasing problem, there are more number of cases in the last years due to the increased survival rate of premature and LBW infants. After it’s discovery in 1940, the epidemiology of the disease is divided in three parts. Now we are in what is called the Third epidemic (1980-Present) where the neonatal care is excellent and there is very low mortality for premature babies of BW <1000g, becoming the group with higher incidence of ROP, since babies with BW of 1000-1500g do not develop ROP as much, and now the main risk factors are prematurity and LBW [12].
Evidence shows that incidence of this disease varies from country to country, and it is influenced by socioeconomics and health care accessibility [13]. In 2010 just China, India, Brasil, Indonesia, Russia, USA, Mexico, Thailand and Turkey presented with 2/3 of cases of visual problems due to ROP, we can say it is an epidemic in low and middle income countries. Therefore, different techniques of screening shall be used, adapted to the particular population [14], [15].

Pathogenesis of ROP is still undergoing investigation and new associated factors are being studied with the purpose of knowing how to stop the development of the disease. As Rivera et al. published in 2017 [16], inflammation is a key factor in ROP progression, he also introduced choroidal degeneration, affecting retinal pigmented epithelium and photoreceptors, as one of the reasons for visual impairment later in life for ROP patients. The process is divided in two phases; premature babies lack enough amount of omega-3-PUFA and IGF-1, which are needed for normal development of blood vessels, it leads to the Initial phase where oxidant stress, suppression of oxygen-regulated pro-angiogenic factors, and an excessive production of pro-inflammatory factors leads to vascular obliteration and arrest in progression of vascularization. In compensation the Second phase hypoxia-induced angiogenic factors start pathogenic neovascularization, which can lead to retinal detachment, causing irreparable visual impairments [16], [17]. Recent studies show more independent factors predisposing to ROP in premature babies of different gestational age groups, such as; Sepsis, NEC, PDA and prolonged mechanical ventilation [18].

International Classification of ROP (ICROP) most recent actualization is from 2005. It divides ROP based on the severity (stage), antero-posterior location (zone), circumferential extent and presence or absence of plus disease. Generally, ROP passes through five stages (1–5). Late stages of ROP may present with leucocoria (white re- flex), falciform fold and pthisis bulbi. Aggressive Posterior ROP (APROP) can progress directly to Stage 5 without passing through the intervening stages. It is characterized by posterior location (Zone I or posterior Zone II), rapidly evolving plus disease, flat intraretinal neovascularization and vascular loops. Plus, disease is at least 2 quadrants (6 or more clock hours) of dilation and tortuosity of the posterior retinal blood vessels. It may be associated with a rigid pupil, vitreous haze or neovascularization of the iris [19].
Treatment for ROP rely on invasive procedures, such as laser photocoagulation; where affected areas of the peripheral retina are cauterized, to stop progression of uncontrolled neovascularization, or cryotherapy; using an instrument that generates freezing temperatures briefly touching spots on the surface of the eye that overlie the periphery of the retina, to produce the same effect. Both of this techniques are used for ROP Stage III with plus disease. The problem is that after this treatment some peripheral vision will be lost permanently [20]. Other treatments, that would not lead to vision loss, including anti-VEGF therapy, as well as IGF-1 and omega-3, are currently being already used and more thoroughly evaluated. In addition, the development of anti-inflammatory drugs as well as, future regenerative therapeutic interventions involving stem cells are also being explored and considered for the treatment of ROP [16].

11.2. Patent ductus arteriosus (PDA):

Fetal circulation differs from circulation at any other age; childhood or adulthood. When babies are born preterm (<32wog) their cardiovascular system (CVS) is still under development. Physiologically there are alterations in: preload, contractility, afterload, diastolic filling and intra-cardiac flow patterns. This changes are normal in fetal circulation, but at birth they cause persistence of the fetal shunt pathway connecting the pulmonary artery to the aorta, this condition is called Patent Ductus Arteriosus (PDA). During this transition there is constant change in the regulators; increased levels of prostaglandins (PG), decreased levels of oxygen in blood and immature muscular wall of the heart; which will cause a delay in ductal closure. If there is no closure of the ductus, reverse flow from left-to-right side could develop, leading to pulmonary hypoperfusion and in some cases even systemic hypoperfusion [21].

Incidence increases with decreased gestational age. It is the most common CV disease in preterm babies. PDA is also associated with birth weight; it develops in 33% LBW infants and 65% of ELBW [22]. Recent studies using ultrasonography (US) suggest that PDA hemodynamic impact starts at the early time after birth, during the first hours, not later as it was previously believed. It remains a conundrum when to treat it or even if to treat it at all, 60% achieve closure within 24hs. There are almost no studies that made trials involving a study group of non treated babies [23].
Several outcomes are associated with PDA; pulmonary or idiopathic hypertension (P/IHT), pulmonary hemorrhage (or more accurately hemorrhagic pulmonary edema), chronic lung disease (CLD), NEC, hypotension and ventilator dependency among others. The problem is that P/IHT, CLD and NEC are independently associated also with prematurity itself. Therefore, there is no clear evidence that allows us to say if persistent PDA is a normal process of neonatal physiology of a premature baby or a pathological one [24].

Definition of the disease is not yet clear, but hemodynamically significant PDA (hsPDA) can be diagnosed with clinical (murmur, hyper-dynamic precordium, bounding preductal pulses, worsening respiratory status, wide pulse pressure, hypotension, metabolic acidosis) or echocardiographic features (increased left atrium to aortic root ratio, cardiomegaly, left-to-right shunting, large open ductus, reversal of flow in postductal major arteries) [22]. To detect the persistence of the shunt before birth, we can use fetal assessment of circulation; or birth imaging like echocardiography, MRI and spectroscopy among others [21].

Some biomarkers, specially BPN and NT-proBPN, which are adult and children markers of heart failure (HF), are released when there is stress of the myocytes. They could help determining a threshold for when to treat PDA, but it needs further study to arrive to a consensus on how to use them [25].

There are different options on how to manage PDA, the treatment can be: symptomatic (treating when there is hsPDA), pre-symptomatic (treat when detecting the persistent duct, usually up to 3 days old), prophylactic (treat all the babies of a certain GA and BW, which was testes and proved to have higher side effects and increase bad outcomes, so it is not recommended) or no treatment [22].

Treatment consists first in proper care of the newborn following the recommendations of restricted fluid administration (not too high, not too low), treat surgically (PDA ligation or percutaneous closure) only when there are hemodynamic or clinical symptoms. Conservative treatment with intravenous NSAID’s (indometacin or ibuprofen or paracetamol, there is not much difference in results so all of them could be used) continuous infusion and repeat twice if needed. Early treatment with NSAID’s is not indicated for early routine, but has shown in a study less need for ligation of PDA compared to children that were just discharged. There is also a possibility that this therapy on the days 1 to 5 could be protective for ROP [24], [26], [27]. Although studies have show that early treatment does not improve long term respiratory outcomes [28].
11.3. Necrotizing enterocolitis (NEC):

NEC is the most common neonatal surgical emergency and the leading cause of mortality in NICU [29], and has remained without variations on it’s incidence in the past decade [30]. With a high morbidity and mortality between 30-40% NEC has a greater incidence in premature babies corresponding to 90% of the cases of NEC, also babies weighting less than 1000g and less than 28 wog are at highest risk [29]. Up to ten percent of patients with NEC will develop recurrent disease and it can develop weeks to months after the initial episode.

NEC’s pathophysiology is multifactorial and it involves the immaturity of the gastrointestinal tract; enteral feeding, usually symptoms start during the first feeding; pathogenic bacterial colonization; can become abnormal due to prematurity and also if formula or cows milk feeding; abnormal intestinal blood flow/ ischemia, inflammatory cascade which leads to necrotic process. The disease leads to mucosal or trans-mucosal necrosis and eventually to perforation. The most affected parts of the intestine are the terminal ileum and colon. It manifests with clinical symptoms of decreased feeding tolerance, abdominal distention, vomit and diarrhea that can become bloody.

Bell Classification divides it into: Stage I (Clinical findings suspicious for NEC but no definitive criteria); Stage II (definitive NEC without indication for surgical intervention e.g. abdominal radiograph with with pneumatosis intestinalis); Stage III (evidence of perforation e.e. pneumoperitoneum). When 75% of the intestines are affected it’s called NEC totalis [31].

It is important in case of perforation to differentiate between a focal (isolated) intestinal perforation (FIP) and NEC. FIP can be treated by primary peritoneal drainage, but NEC may more radical operation with laparotomy and bowel resection with the creation of a stoma [32]. There are no clear specific criteria to determine when is the best time to operate, the only absolute criteria for surgery are: pneumoperitoneum on X-ray (unfortunately one third of NEC patients with perforation will not display free air on radiograph); positive paracentesis (containing intestinal contents such as stool, cloudy fluid, bile, bacteria); worsening of the clinical condition despite maximal treatment (abnormal blood work, thrombocytopenia, neutropenia and metabolic acidosis).

Treatment of NEC when there is no indication for surgery consist in supportive care (hypothermia, intravenous fluids, broad spectrum antibiotics, NPO with gastric
decompression) and also screening for progression of disease (abdominal exams, radiographs, WBC and platelet count, blood gases) [33].

Surgical treatment may be either exploratory laparotomy or peritoneal drain placement; used when the babies have too small weight (less than 1000g) or those with poor condition that could not take the stress of the surgical intervention. It has been compared the efficiency of laparotomy vs peritoneal drainage, some studies show no significant difference in survival, but worse neurodevelopmental outcomes for peritoneal drainage. The goal of laparotomy is to resect the necrotic bowel and preserve the maximal intestinal length, with likely ostomy and possible temporary abdominal wall closure. There may be a need for a second operation 48 or 72 hours after [34] [35].

Possible complications for this disease can be abdominal compartment syndrome, sepsis, death, short gut syndrome, intestinal stricture (common in the ileum and colon although this is more common after medical management) [35].

The major improvements in management of patients with NEC are feeding techniques, anti-inflammatory therapies and probiotic use. This last one has show the biggest effect in prevention of NEC. Human trials have shown that probiotic administration to very low birth weight premature infants reduces the incidence of severe NEC and mortality, and also the benefits of breast feeding, specially for premature and extreme low birth weight, but still more research is needed to ensure the safety and efficacy of these treatment. It is recommended for patients less than 37 wog or under 2500g (although not for under 1000g) at birth to undergo prophylactic treatment with probiotics since the first feed (<48hs) until there is no risk of NEC. [36], [37].

Breast feeding and donor human milk (DHM) are preferred for multiple of NICU patients including ELBW and premature, and specially for NEC. The mothers milk compensates the immaturity of the GI system and immune system, also avoiding cow’s proteins [38]. Genetic predisposition has been recognized for NEC, more understanding in this field could help us to detect and target care to the infants at highest risk [39].
11.4. Ventriculoperitoneal shunt:

Hydrocephalus is the most common neurological problem in infants and it is possible to correct with surgery. There are multiple reasons for a newborn to develop this condition: genetic causes such as X-linked aqueductal stenosis which has been linked to genes that regulate brain growth and development [40]; congenital causes including myelomeningocele where the cerebellum blocks the flow of cerebrospinal fluid (CSF) in a development of Chiari Malformation II; and acquired causes such as intraventricular hemorrhage (IVH), trauma, tumors that also block the CSF, and infection [41]. Also several medications have been associated with infantile hydrocephalus if taken during pregnancy, including misoprostol, metronidazole and antidepressants [42].

Excess cerebrospinal fluid (CSF) can increase intracranial pressure (ICP) resulting in progressive ventricle dilatation which can lead to: herniation, intracranial hematoma, cerebral edema, or crushed brain tissue. In pediatric patients, untreated hydrocephalus can lead to many adverse effects including increase irritabilities, chronic headaches, learning difficulties, visual disturbances, and in more advanced cases severe mental retardation [43].

The need for and timing of surgical intervention in patients with hydrocephalus is determined by the severity of symptoms and the neuroimaging findings. In most cases it is progressive, so drainage of the CSF its needed to prevent ventriculomegaly and compression of brain structures.

Intraventricular hemorrhage (IVH) in preterm infants is one of the major causes of hydrocephalus in developed countries. The incidence of IVH in premature and VLBW babies it is approximately 15%–20%. The incidence of hydrocephalus in patients with IVH of prematurity is reported to be approximately 25%–30% [44].

Standard treatment of symptomatic PHHP is VP shunt placement. Many studies have shown that the complication rate of VP shunts in the PHHP population is higher than other hydrocephalus etiologies. Another treatment techniques such as; ventriculas access device (VAS), external ventricular drains (EVD), lumbar puncture (LP) or ventriculosubgaleal (VSG) shunt are recommended as surgical temporizing measures. There are new studies that have
proven endoscopic third ventriculostomy (ETV) and choroid plexus cauterization (CPC) is a safe initial procedure for hydrocephalus in premature infants with IVH and hydrocephalus, to avoid shunt in selected patients [45].

Although VPS has been the most widely used treatment for hydrocephalus in the twentieth century, it is unclear whether the outcomes have improved significantly up to this day, despite better understanding of CSF physiology and the technological advancements in valve devices [44].

Since they were first invented, shunt systems and especially valves, have evolved offering now flow-regulating, anti-siphon and gravitational characteristics to avoid the over-drainage that can be caused by changes in patient position [46]. This approach has good early results relieving the symptoms, resolving the problem of ventricle enlargement and reducing ICP, but it still requires lifelong monitoring, and surgical revisions are common to resolve infections or shunt failure [47].

Outcomes after shunt implant have a wide range from almost a normal life, to others with physical, cognitive, social and emotional impairments associated with disability. The cause of these results is not only the hydrocephalus but also treatment-related complications. They may appear shortly after surgery, and generally within six months of shunt implantation or revision [48], [49]. There are various intra-abdominal complications seen on abdominopelvic CT, of which, shunt infection was the most common, followed by CSF pseudo-cyst, abscess, and infected fluid collection [50]. There is an increasing number of older children admitted with shunt malfunctions, and when hydrocephalus treatment and its complications were compared with other chronic illness, such as cystic fibrosis, the use of inpatient service was higher for hydrocephalus [46].

Another problem of this intervention it’s that the follow up for complications of shunt malfunction and repeated surgeries increase medical cost, and expose patients to unnecessary radiation and mayor and minor procedures [51].
11.5. Myelomeningocele:

Neural tube defects (NTD) like spina bifida are associated with significant neonatal and childhood morbidity and mortality. MMC is the most common as well as severe type of open spina bifida, in which neural tissue is visible and it is often associated with CSF leakage. On the contrary, closed spina bifida, has no visible neural tissue and there is no CSF leakage.

MMC consists on a protrusion of the meninges and spinal cord as a sac through a defect in the spinal column that failed to close during embryogenesis. If left untreated complications such as motor and sensory dysfunction, difficulty learning, orthopedic deformities, and urinary and fecal incontinence may occur [52]. MMC is also associated with hindbrain herniation, where the hindbrain, including the cerebellum, protrude into the foramen magnum.

In majority of patients with MMC hydrocephalus develops, varying with the level of MMC and requiring surgical intervention [53]. At least 80% of spina bifida patients need the placement of shunts apart of the plastic reconstructive closure of the defect, to prevent the neurologic and intellectual compromise that accompanies significant ventriculomegaly caused by hydrocephalus, and 46% have complications of shunts within the first year of placement [54]. Shunt implant has shown improvement in revision free survival rates for infants with a MMC-related hydrocephalus in comparison to other etiologies of hydrocephalus in infants [55]. Studies have shown no association between MMC closure and development of infection, as well as antibiotic prophylactic use did not reduce the infection risk in MMC repair surgery. Thus, antibiotics should not be used if there are no risk factors predisposing to infection [56].

The two-hit hypothesis explains the damage associated with spina bifida as a combination of exposure of the neural tissues to amniotic fluid and ongoing intrauterine trauma leading to secondary damage throughout gestation, therefore prenatal treatment is indicated to reduce further intrauterine damage, however, surgery cannot reverse nerve damage that already has occurred [52], [57].

Conventional treatment was to undergo a postnatal repair within two days of birth, and inserting a VPS for hydrocephalus. Nowadays it is possible to diagnose this condition prenatally, as early


as the first trimester of pregnancy, with prenatal US, maternal serum alpha-fetoprotein levels or amniocentesis, used to detect fetal chromosomal abnormalities. So it is not necessary to wait until delivery to treat this condition. In a large scale study, it was proved that prenatal repair of MMC reversed or corrected hindbrain herniation and reduced the need for VPS placement at 12 months of age (82%) [58].

Prenatal repair exposure of the fetal spine via laparotomy and uterine hysterotomy, also known as open fetal surgery, followed by dissection of the neural placode and closure of the overlying dura mater and skin, rapidly became the standard of treatment. Although this approach is associated with significant neonatal benefit, uterine entry via hysterotomy carries maternal and obstetric risks, especially preterm labor. Recently novel fetoscopic surgical approaches to decrease maternal morbidity and reduce obstetric risks are being developed [59]. MOMS trial suggests the neonatal benefits of in-utero repair, fetoscopic spina bifida repair as a promising technique to improve maternal and obstetric outcomes, at the same time as maintaining the benefits of less hindbrain herniation, reducing the need for neonatal ventricular shunt placement, and maintaining lower motor neuron, bladder, and gastrointestinal function. However, fetoscopic techniques should still be optimized to overcome the high rate of dehiscence and leakage at the MMC repair site. A fetoscopic approach via maternal laparotomy reduces the risk of preterm birth [60].

With an appropriate campaign reinforcing the beneficial effects of folic acid supplementation during gestation and appropriate guidelines on required doses, substantial progress could be made in preventing this disorder [61].

There are also novel stem cell therapies together with in-utero medical approaches that target the pathophysiological pathways associated with spina bifida, these new techniques are likely to make significant impact. The effective differentiation of CSF-derived neural progenitor cells from MCC-affected fetuses suggests great potential for future stem-cell-based therapeutic approaches [62].
12. RESEARCH METHODOLOGY AND METHODS

On the beginning of 2017, the research was organized. During the first six months of work (semester IX) a theoretical investigation on the most recent updates on general neonatal surgery was done, and another most specially focusing on ROP, PDA, NEC, VPS and MMC. On the next six months (X semester) selection of literature was performed, including articles less than 10 years old (2008-2018). Out of 300 only 75 were used, taking into consideration for selection the most updated version if research over the same topic, the broadness of the study favouring the ones with most reliable evidences and the ones covering the relevant objectives of this research.

The object of study is to detect and compare surgical trends in neonates between the years 2004-2005 and 2014-2015. Patients from NICU who underwent surgical treatment during those years were included in the study. The inclusion criteria were to be a patient from NICU and to have needed a surgical procedure. The exclusion criteria were non operated patients. Demographic data including the gender, birth date, gestational age, birth weight, duration of stay in NICU, date of operation, age at date of operation were collected for further analysis.

The participants of the study are all the patients from NICU that underwent a surgical procedure during their stay on the years 2004, 2005, 2014, 2015.

To collect the data for the study, surgical journals, NICU database and patients’ case histories have been revised. The information obtained from each patient was; date of operation, date of birth, gender, gestational age, birth weight, diagnosis, type of procedure and length of stay in NICU.

Literature review has been made using three different data bases PubMed, NCBI and Medline, to find the latest and most up to date publications on neonatal surgery. Searching for the key words: “neonatal surgery”, “rates of neonatal surgery”, “incidence neonatal surgery”, “mortality neonatal surgery”, “NICU”, “retinopathy of prematurity”, “patent ductus arteriosus”, “necrotizing enterocolitis”, “hydrocephalus”, “ventriculoperitoneal shunt”, “myelomeningocele”, “spina bifida” to find articles less than 10 years old, that would cover information on rates of neonatology operations in different populations and their reasons, also further more specific research on the selected main type of operations mentioned above.
Statistical analysis from those retrospective charts has been performed using Microsoft excel and SSP, to calculate the total number of operations, number of operations divided by types, the number of female and male, the average GA, the average BW, the average length of stay in NICU and the average of age at the time of operation, for the two different year periods (2004-2005, 2014-2015). The chi-square test was used to examine the relationship or association between two categorical variables; gender and type of operation. Independent Samples t-test compare the means and standard deviations for demographic characteristic of the two year periods, 2004-2005 and 2014-2015. All given values are presented as mean ± standard deviation (SD). The level of statistical significance (p) of 0.05 was selected for all variables.

When determining type of operations, the list of the total 377 procedures have been divided into 10 different groups according to their discipline and separating those selected for further more detailed investigation. The classification goes as follow: ophthalmological (ROP), cardiovascular (PDA), gastrointestinal (NEC), gastrointestinal (others), neurosurgery (VPS), neurosurgery (MMC), neurosurgery (others), hernia repair, others and minor surgeries.

It is important to remind that in Lithuania neonatal care is regionalized, the hospital in which this research was performed is a tertiary level hospital were all the neonatal neurosurgery procedures for the country are performed, and only one cardiovascular procedure is done, PDA closure, this will affect the results of the study.
13. RESULTS AND THEIR DISCUSSION

Of the total 377 patients included in the study, 167 (44.3%) have undergone surgery during their stay in NICU in Kaunas clinics on the first period; from January 1st 2004 to December 31st 2005, and 210 (55.7%) on the second period; from January 1st 2014 to December 31st 2015.

13.1 General rates of operations and patient characteristics

(Table 1 and 2) The total amount of 377 operations performed during the two periods covered by the study were divided into ten categories according the procedure type. The rates on the first (2004-2005) and second period (2014-2015) respectively were as follows: for cardiovascular PDA (1) remained almost the same from 10.2% to 10%, gastrointestinal NEC (2) has slightly decreased from 13.2% to 11%, meanwhile “other” gastrointestinal surgeries (3) have increased from 16.8% to 30.5%, ophthalmological ROP (4) also minimally decreased from a 6% to a 5.2%, neurosurgery MMC (5) have decreased from 7.8% to 3.3%, neurosurgery VPS (6) also was also performed less from 12.6% to 7.6%, “other” neurosurgical procedures (7) remained almost stable from 4.2% to 3.8%, hernia repairs (8) were also stable from 6% to 6.7%, minor procedures (9) were performed for major number of patients on the second period increasing from 4.8% to 10% and other surgeries that do not fit these groups are classified in “others” (10) which was a 18.6% of the operations from the first period and 11.9% of the second.
Table 3. Patient characteristics.

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<tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>167</td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>69 (41.3)</td>
<td>64 (30.5)</td>
<td>0.028*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>98 (58.7)</td>
<td>146 (69.5)</td>
<td>0.028*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>34.3 ± 5.3</td>
<td>32.2 ± 6.3</td>
<td>0.019‡</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>2326 ± 1128.5</td>
<td>2189 ± 1777.8</td>
<td>0.36‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>12.9 ± 16.3</td>
<td>17.2 ± 22.8</td>
<td>0.034‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>27.0 ± 31.2</td>
<td>38.1 ± 47.7</td>
<td>0.006‡</td>
</tr>
</tbody>
</table>

* Using the Pearson chi-square test.
‡ Using the t-test.

(Table 3) On the first period (2004-2005) 69 (41.3%) of the patients were females and 98 (58.1%) were males. Their average gestational age at birth was 34.3 ± 5.3 weeks, the average birth weight was 2326 ± 1128.5 g, the average length of stay in NICU of this babies was 12.9 ± 16.3 days and the average actual age at time of surgery was 27.0 ± 31.2 days. On the second period (2014-2015) there were 64 (30.5%) female patients and 146 (69.5%) male patients. The average gestational age at birth of these babies was 32.2 ± 6.3 weeks, the average birth weight was 2189 ± 1777.8 g, the average length of stay in NICU of this babies was 17.2 ± 22.8 days and the average actual age at time of surgery was 38.1 ± 47.7 days.

Comparing both periods there were found significant differences in gender, GA, the length of stay in NICU and the age at surgery of the patients in the two periods. So patients from the first period who required surgical intervention were older in GA at the time of birth, they had a shorter stay in NICU and they were younger at the time of the surgery than those from the second period. There was no significant difference between the birth weights of the two groups.
The decrease of the mean GA in the second period may be related to the better survival of premature babies, also the mean age at time of surgery on the second period was higher, that can be influenced by the type of procedures performed the most, but since surgery and general anesthesia have been found to be negative for the infant’s neurodevelopment, it is a positive change. The increase in length of stay for the babies operated may be related to a better surgery outcome, with less number of deaths, but another study must be performed to find out.

13.2 Retinopathy of prematurity

*Table 4. ROP characteristics:*

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<tbody>
<tr>
<td>No. of patients</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>4 (40)</td>
<td>2 (18.1)</td>
<td>0.269*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>6 (60)</td>
<td>9 (81.2)</td>
<td>0.269*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>32.2 ± 4.4</td>
<td>25.3 ± 1.8</td>
<td>0.001†</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>1545 ± 759.6</td>
<td>1372 ± 2140.1</td>
<td>0.80‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>5.7 ± 7.8</td>
<td>19.5 ± 31.4</td>
<td>0.18‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>49 ± 19</td>
<td>98 ± 21</td>
<td>0.004‡</td>
</tr>
</tbody>
</table>

*Using the Pearson chi-square test.
†Using the t-test.

(Table 4) On the first period (2004-2005) 10 (6%) patients required ROP intervention; 4 (40%) females and 6 (60 %) males. Their average gestational age at birth was 32.2 ± 4.4 weeks, the average birth weight was 1545 ± 759.6 g, the average length of stay in NICU of this babies was 5.7 ± 7.8 days and the average actual age at time of surgery was 49 ± 19 days. On the second period (2014-2015) 11 (5.2%) patients of which; 2 (3.1%) female patients and 9
(6.1%) male, required surgical treatment for ROP. The average gestational age at birth of these babies was $25.3 \pm 1.8$ weeks, the average birth weight was $11372 \pm 2140.1$ g, the average length of stay in NICU of this babies was $5.7 \pm 7.8$ days and the average actual age at time of surgery was $98 \pm 21$ days.

Comparing both periods significant differences were found in; GA at birth and age at time of surgery. So patients from the first period who required surgical intervention for ROP were older in GA ($32.2 \pm 4.4$ weeks) at the time of birth than patients from the second period ($25.3 \pm 1.8$ weeks) and they were younger at the time of the surgery ($49 \pm 19$ days) than those from the second period ($98 \pm 21$ days). There was no significant difference between the gender, birth weight and length of stay in NICU between the two groups.

The incidence and severity of ROP increases with decreasing GA and BW, therefore since the survival of premature, LBW and ELBW makes sense to see more patients of these characteristics [63], [64], [65].

### 13.3 Patent ductus arteriosus

*Table 5. PDA characteristics:*

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<tbody>
<tr>
<td>No. of patients</td>
<td>17</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>11 (64.7)</td>
<td>11 (52.4)</td>
<td>0.44*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>6 (35.3)</td>
<td>10 (47.6)</td>
<td>0.44*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>28.9 ± 3.9</td>
<td>24.2 ± 2.0</td>
<td>0.001‡</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>1196 ± 542.4</td>
<td>701 ± 195.0</td>
<td>0.001‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>34.6 ± 20.4</td>
<td>53.8 ± 14.9</td>
<td>0.001‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>17.2 ± 7.1</td>
<td>25.8 ± 18.8</td>
<td>0.063‡</td>
</tr>
</tbody>
</table>
*Using the Pearson chi-square test.
‡Using the t-test.

(Table 5) On the first period (2004-2005) 17 (10.2%) required PDA intervention of which 11 (64.7%) were females and 6 (35.5%) were males. Their average gestational age at birth was 28.9 ± 3.9 weeks, the average birth weight was 1196 ± 542.4 g, the average length of stay in NICU of this babies was 34.6 ± 20.4 days and the average actual age at time of surgery was 17.2 ± 7.1 days. On the second period (2014-2015) there were 21 (10%) patients; 11 (52.4%) female and 10 (47.6%) male patients who required surgical treatment for ROP. The average gestational age at birth of these babies was 24.2 ± 2.0 weeks, the average birth weight was 701 ± 195.0 g, the average length of stay in NICU of this babies was 53.8 ± 14.9 days and the average actual age at time of surgery was 25.8 ± 18.8 days.

Comparing patients who underwent surgical PDA closure in both periods it was found significant difference in GA at birth, birth weight and length of stay in NICU. So patients from the first period were older in GA (32.2 ± 4.4 weeks) at the time of birth than patients from the second period (25.3 ± 1.8 weeks) and they spent less time in NICU (34.6 ± 20.4 days) than those from the second period (53.8 ± 14.9 days). The birth weight of the operated patients was lower on the second period, with a mean ELBW of 701 ± 195.0 g, compared to the first period which was 1196 ± 542.4 g. There was no significant difference in gender and age at surgery between the two groups.

Incidence of PDA has been directly related to increase as gestational age decreases and it is also associated with to low birth weight, specially ELBW [22], [66], [67].
13.4 Necrotizing enterocolitis

**Table 6. NEC characteristics:**

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<tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>22</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>9 (40.9)</td>
<td>7 (30.4)</td>
<td>0.36*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>13 (59.1)</td>
<td>16 (69.6)</td>
<td>0.36*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>30.2 ± 4.2</td>
<td>38.1 ± 4.6</td>
<td>0.12‡</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>1667 ± 693.8</td>
<td>1019 ± 392.1</td>
<td>0.001‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>23.1 ± 9.5</td>
<td>34.1 ± 28.5</td>
<td>0.093‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>16.8 ± 7.1</td>
<td>37.2 ± 40.5</td>
<td>0.03‡</td>
</tr>
</tbody>
</table>

*Using the Pearson chi-square test.
‡Using the t-test.

(Table 6) On the first period (2004-2005) 22 (%) patients required surgical intervention for NEC, of which; 9 (40.9%) were females and 13 (59.1%) were males. Their average gestational age at birth was 30.2 ± 4.2 weeks, the average birth weight was 1667 ± 693.8 g, the average length of stay in NICU of this babies was 23.1 ± 9.5 days and the average actual age at time of surgery was 16.8 ± 7.1 days. On the second period (2014-2015) there were 21 (10%) patients; 7 (30.4%) female and 16 (69.6%) male, who required surgical treatment for NEC. The average gestational age at birth of these babies was 38.1 ± 4.6 weeks, the average birth weight was 1019 ± 392.1 g, the average length of stay in NICU of this babies was 34.1 ± 28.5 days and the average actual age at time of surgery was 37.2 ± 40.5 days.

Comparing the two group of patients who underwent surgical procedures for the treatment of NEC significant difference was found in; birth weight and age at time of surgery. So patients from the first period had a larger birth weight (1667 ± 693.8 g) than the ones from the second period (1019 ± 392.1 g), also they were younger at the time of the surgery (16.8 ± 7.1 days).
than those from the second period (37.2 ± 40.5 days). There was no significant difference in gender, GA, and length of stay in NICU between the two groups.

The benefits of human breast milk have been proven for prevention of necrotizing enterocolitis, in between the two periods the first human milk bank in Lithuania was open in this hospital, the improvements in the rates of operation of this patients, or even only the possibility for the premature and ELBW may be due to a better nutrition for these patients [68], [69], [70].

13.5 Ventriculoperitoneal shunt

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<tbody>
<tr>
<td>No. of patients</td>
<td>21</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>8 (38.1)</td>
<td>4 (26.7)</td>
<td>0.399*</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>13 (61.9)</td>
<td>12 (73.3)</td>
<td>0.399*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>35.5 ± 5.9</td>
<td>33.4 ± 6.6</td>
<td>0.32‡</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>2728 ± 1470.5</td>
<td>2457 ± 1294.6</td>
<td>0.54‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>3.9 ± 7.8</td>
<td>3.0 ± 8.0</td>
<td>0.78‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>50.5 ± 44.6</td>
<td>41.0 ± 37.6</td>
<td>0.48‡</td>
</tr>
</tbody>
</table>

*Using the Pearson chi-square test.
‡Using the t-test.

(Table 7) On the first period (2004-2005) 21 (12.6%) patients required VPS implant; 8 (38.1%) were females and 13 (61.9%) were males. Their average gestational age at birth was 35.5 ± 5.9 weeks, the average birth weight was 2728 ± 1470.5 g, the average length of stay in NICU of this babies was 3.9 ± 7.8 days and the average actual age at time of surgery was 50.5 ± 44.6 days. On the second period (2014-2015) there were 16 (7.6%) patients; 4 (26.7%) female
and 12 (73.3%) male, who required VPS implant. The average gestational age at birth of these babies was 33.4 ± 6.6 weeks, the average birth weight was 2457 ± 1294.6 g, the average length of stay in NICU of this babies was 3.0 ± 8.0 days and the average actual age at time of surgery was 41.0 ± 37.6 days.

Comparing these two groups of patients who underwent VPS implant there was no significant difference found neither in gender, GA, birth weight, length of stay in NICU nor age at time of surgery between the two groups.

The decreased in number of cases has been linked to better folic acid supplementation, early detection during ultrasound screening, proper diagnostic and close monitoring [71], [72].

### 13.6 Myelomeningocele

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<tbody>
<tr>
<td>No. of patients</td>
<td>13</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>8 (61.5)</td>
<td>1 (14.3)</td>
<td>0.042*</td>
</tr>
<tr>
<td>Male (%)</td>
<td>5 (38.5)</td>
<td>6 (85.7)</td>
<td>0.042*</td>
</tr>
<tr>
<td>Mean gestational age at birth ± SD (wks)</td>
<td>38.9 ± 1.6</td>
<td>39.3 ± 0.8</td>
<td>0.50‡</td>
</tr>
<tr>
<td>Mean birth weight ± SD (g)</td>
<td>2974 ± 512.8</td>
<td>3042 ± 904.5</td>
<td>0.83‡</td>
</tr>
<tr>
<td>Mean length of stay in NICU ± SD (days)</td>
<td>1.8 ± 1.3</td>
<td>4.9 ± 10.2</td>
<td>0.29‡</td>
</tr>
<tr>
<td>Mean actual age at surgery ± SD (days)</td>
<td>7.6 ± 16.6</td>
<td>1.4 ± 2.6</td>
<td>0.21‡</td>
</tr>
</tbody>
</table>

*Using the Pearson chi-square test.
‡Using the t-test.
(Table 8) On the first period (2004-2005) 13 (7.8%) patients required surgical intervention for MMC repair; 8 (61.5%) were females and 5 (38.5%) were males. The average gestational age at birth of these babies was 38.9 ± 1.6 weeks, the average birth weight was 2974 ± 512.8 g, the average length of stay in NICU of this babies was 1.8 ± 1.3 days and the average actual age at time of surgery was 7.6 ± 16.6 days. On the second period (2014-2015) there were 13 (7.8%) patients; 1 (14.3%) female and 6 (85.7%) male, who required surgical repair of MMC. Their average gestational age at birth was 39.3 ± 0.8 weeks, the average birth weight was 3042 ± 904.5 g, the average length of stay in NICU of this babies was 4.9 ± 10.2 days and the average actual age at time of surgery was 1.4 ± 2.6 days.

Comparing these two groups of patients who underwent MMC surgical repair it was found significant difference in gender. So patients from the first period were mostly females (61.5%) and on the second period the majority was males (85.7%). There was no significant difference found neither in GA, birth weight, length of stay in NICU nor age at time of surgery between the two groups.

More studies have shown a decrease in incidence of MMC over the past decades due to better public health systems and refinement of surgical techniques [73], [74], [76].

14. CONCLUSION

This study describes population characteristics and incidence of surgical interventions in neonatal patients treated in the NICU of a tertiary level hospital in Kaunas, Lithuania, two periods; 2004-2005 and 2014-2015, were compared.

1. The rate of operations in these two periods was detected and compared, finding out the differences in incidence of 10 groups of operations between the first period (n=167) and the second period (n=210). From the first to the second period the rates of patent ductus arteriosus, retinopathy of prematurity and hernia repairs remained almost stable, there was a decrease in neurosurgery operations specially in ventriculoperitoneal shunt and myelomeningocele. For gastrointestinal diseases there were slightly less cases of necrotizing enterocolitis and an increase in other type of gastrointestinal operations. Minor
procedures not using general anesthesia increased, and “other” surgeries decreased. It must be pointed out the role of the hospitals milk bank, which allows the most needed patients to receive the benefits of breast milk, which has been shown to be protective for newborns.

2. Incidence of surgery depending on gender showed significant differences. During the first period (n=167) there was more males, 58.7%, than females, 41.3%, it significantly kept on increasing this difference in the second period (n=210) where male were 69.6% and female 30.5%. This suggests that females may be born healthier, but a further study must be made to be able to prove that.

3. The mean gestational age of the patients operated on the first period was 34.3 ± 5.3 weeks and on the second period 32.2 ± 6.3 weeks, it is statistically relevant, which shows that in both periods premature babies are at higher risk for surgery, and the more advances in neonatal care the more chance of survival of early premature babies.

4. According to birth weight no significant differences were found, during the first period the mean birth weight was 2326 ± 1128.5 g and during the second 2189 ± 1777.8 g.

5. In terms of general neonatal surgical diseases were compared the age at time of operation (day of life), time of stay in NICU, both of which were significantly different. During the first period the mean age at time of surgery was 27.0 ± 31.2 days, which became bigger on the second period 38.1 ± 47.7 days, the mean length of stay in NICU also increased, it was 12.9 ± 16.3 days on the first period and 17.2 ± 22.8 days on the second.

The study also focused on five neonatal surgical interventions for particular diseases were also compared to determine relevant trends:

6. Patients operated for retinopathy of prematurity remained almost at the same rate in both periods, but they showed significantly differences in gestational age and age at the time of surgery. During the first period (n=10) the mean age of gestation was 32.2 ± 4.4 weeks which decreased on the second period (n=11) to 25.3 ± 1.8 weeks, this might be due to increased survival of early premature patients. Patents of the first period were younger at the time of the surgery (49 ± 19 days) than those from the second period (98 ± 21 days). There was no significant difference between the gender, birth weight and length of stay.
7. The number of operations for **patent ductus arteriosus** in both periods remained almost the same, from 10.2% (n=17) in the first period, to 10% (n=21) on the second. Comparing patients who underwent surgical PDA closure in both periods, significant differences were detected. The mean gestational age became smaller on the second period; from 32.2 ± 4.4 weeks to 25.3 ± 1.8 weeks. The mean birth weight decreased during the second period, with a mean birth weight of 701 ± 195.0 g, while in the first period it was 1196 ± 542.4 g, now affecting mostly ELLBW infants. In length of stay in NICU, and they were younger at the time of the surgery (49 ± 19 days) than those from the second period (98 ± 21 days). There was no significant difference in gender and age at surgery between the two groups. This suggests the possibility that preterm and extremely low birth weight babies have a better survival rate in the second period.

8. There was a decrease in number of surgical interventions for the treatment of **necrotizing enterocolitis** on the second period, moving from 13.2% (n=22) to 11% (n=23). Also patients from the first period had a larger mean birth weight 1667 ± 693.8 g than the ones from the second period 1019 ± 392.1 g, and were younger at the time of the surgery 16.8 ± 7.1 days and on the second 37.2 ± 40.5 days. There was no significant difference in gender, age of gestation nor, length of stay in NICU between the two groups. Extremely low birth weigh babies have the opportunity to be operated, and this might be for the implementation of a DHM bank in the hospital.

9. There was a decrease in cases of **ventriculoperitoneal shunt implant**, accounting for 7.8% (n=21) of the total operations in the first period and only 3.3% (n=15) on the second period. This changes are related to the prevention of infections, obesity, and other risk factors during pregnancy. Demographically the patient characteristics showed no significant differences among the two periods.

10. The reduction in number of **myelomeningocele** repairs from 7.8% (n=13) in the first period to 3.3% (n=7) in the second may be due to a better ultrasound screening program and a good care during pregnancy to avoid risk factors. There was no significant difference between the demographic characteristics of the patients, except for a dramatic switch in gender, on the first period of the operated patients for myelomeningocele repair were; 61.5% females and 38.5% males but during the second period only 14.3% were females and 85.7% were males.
15. PRACTICAL RECOMMENDATIONS

It is important to be updated and implement the latest techniques and tools for neonatal care. The incidence of surgical need in newborns is strongly related to prematurity and low birth weight, neonatologists should therefore team up with obstetricians and try to prevent the risk factors for this conditions and avoid neonatal diseases, therefore surgery as maximum as possible. The milk bank which is already established in this hospital has a very important role for the prevention of surgery in neonatal patients. More retrospective studies must be performed with the data collected from past years, to create a wider evidence based knowledge of the quality of care.

For **retinopathy of prematurity** it is suggested screening in all infants with BW $\leq 1500$ g or GA of $<30$ weeks, focusing on prompt detection of the disease, and treatment based on disease severity; monitoring closely patients that do not reach the criteria for type I and treating the ones with type I or more severe and treatment.

In case of **patent ductus arteriosus** Interventions for ductal closure include percutaneous catheter occlusion and surgical ligation. Once the decision is made for PDA closure, the age and size of the patient, and the availability of experienced clinicians to perform the procedure, dictate the choice of intervention.

For a better management of **necrotizing enterocolitis**, probiotics and breast feeding are indicated, Medical management should be initiated promptly when NEC is suspected and in all infants with proven NEC. Bacterial culture and after antibiotic prophylaxis is recommended. When there is intestinal perforation or worsening of clinical condition it is recommended surgical treatment, primary laparotomy is the initial surgical intervention for NEC, but one can consider PPD at the bedside especially in extremely low birth weight (ELBW) infants (BW $<1000$ g) who are hemodynamically.

For prevention of **ventriculoperitoneal shunt** due to hydrocephalus and neural tube defects such as myelomeningocele; a program to foment folic acid supplementation among woman of reproductive age and a good ultrasound screening during pregnancy are specially pointed out. Also avoiding risk factors for prematurity like obesity, smoking, infections among others. In case of myelomeningocele it is also interesting to implement fetal surgery as a possibility of treatment. Further research should focus on developing ways of reducing disability and improving quality of life for this patients.
16. REFERENCES


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