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CASE STUDY

INTRAUTERINE DIAGNOSED CONGENITAL DIAPHRAGMATIC HERNIA OUR EXPERIENCES IN FAMILY PLANNING

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ABSTRACT

Congenital diaphragmatic hernia is a condition in which a birth defect occurs on the diaphragm. This is a very serious, life threatening state which requires many measurements to be taken for its prevention, treatment, therapy and long term observation. This article presents our experiences with a patient born with congenital diaphragmatic hernia followed intrauterine, after his birth and until his 12 months of age. The baby (patient) born with congenital diaphragmatic hernia was diagnosed intrauterine in the 32 week of pregnancy with ultrasonographic examinations. The diagnosis was confirmed by magnetic resonance. After the established diagnosis, the mother and the baby were treated properly in terms of using the world established protocol for treatment of CDH babies and followed for a monitoring period. Babies born with congenital diaphragmatic hernia have a difficult beginning in life followed by many diagnostic and therapeutical treatments. A major surgery for closure of the birth defect is of great importance for the life saving of these babies. Sometimes additional treatments and paediatric care are necessary like other multiple surgeries, depending on the problem indicated.

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INTRODUCTION

Congenital diaphragmatic hernia (CDH) is an embryological, developmental defect of the diaphragm when parts of organs or entire organs from the abdominal viscera herniate in the thoracic cavity. Thus the abdominal organs pressure the lungs and push the heart on the contra lateral side (https://en. wikipedia.org/wiki/Congenital_diaphragmatic_hernia)). CDH can be a component of Pallister-Killian, Fryns, Ghersoni-Baruch, WAGR, Denys-Drash, Brachman-De Lange, Donnai-Barrow or Wolf-Hirschhorn syndromes. Some chromosomal anomalies involve CDH as well. The incidence is < 5 in 10,000 of live-births (Tovar, 2012). The first description of CDH derives from many years ago, but survival rate after repairing the defect was not achieved until the 20th century (Irish *et al.,* 1996; Golombek, 2002). The first paediatric surgeons reported amazingly low mortalities until the actual severity of the condition surfaced when abortions, stillbirths and pre-hospital deaths were considered, adding a "hidden mortality" to operative and postoperative demises (McNamara *et al.,* 1965; Harrison *et al.,* 1978). Lung insufficiency and persistent pulmonary hypertension with their pathophysiology threaten and the survivals of these children are currently better understood. The results still remain disappointing since mortalities near 50% are still reported worldwide when all deaths are taken into account in population-based series (Stege *et al.,* 2003). The composition of the herniated organs can vary depending on the size of the defect. In some studies the stomach consists of 60 % of the cases, the large intestines and the spleen are present in 54 % of the cases, the pancreas in 24 %, and the kidneys in 12 % of the cases, then the adrenal glands and liver (Stefanović *et al.,* 2013). When these abdominal organs enter in the thoracic cavity they influence negatively on the development on the lungs. The earlier the herniation develops the bigger the hypoplasia of the white lungs is. There is a great damaging on the ipsilateral lung. The lung parenchyma is changed in terms of its development when an early defect of the diaphragm develops, because of the pressure of abdominal organs. The number of bronchi and bronchiole is decreased, also the number of sacci and alveoli and the number of preacini and intraacini blood vessels (which wall is of thickened structure). The hypoplasia (picture 1) itself influences on increasing of the resistance and reactivity of the lung and vascular system. Persistent lung hypertension is one of the most common preoperative and postoperative problems in babies with CDH. Because of the above statements the hypoplasy of the lungs in patients with a consecutive respiratory distress and insufiention is the main purpose of

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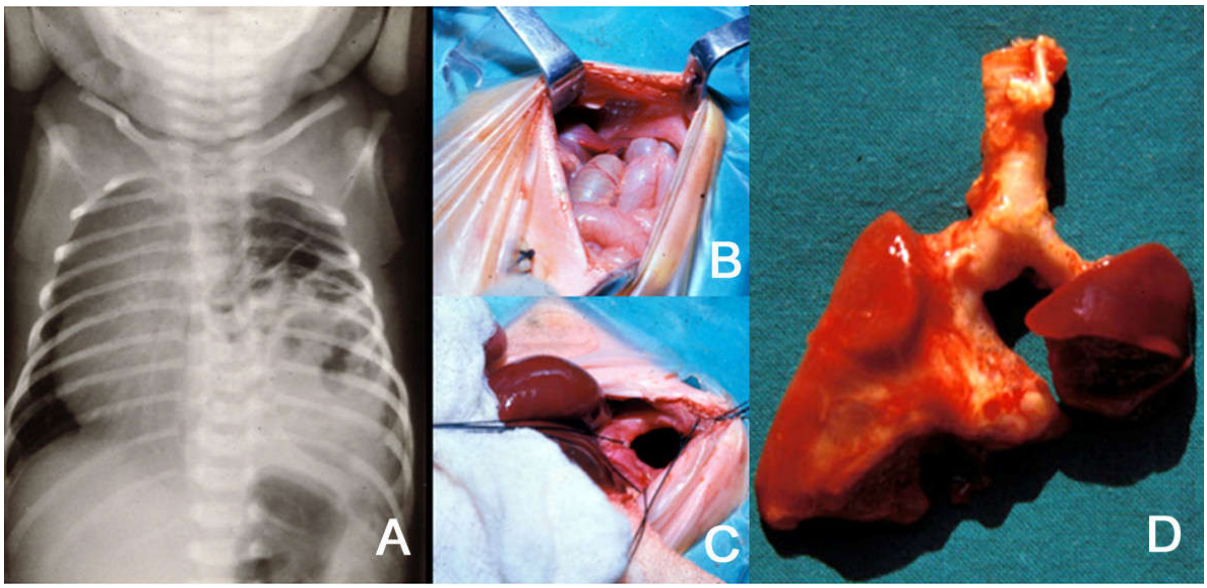


Picture 1, Congenital Diaphragmatic Hernia, Juan A Tovar, Orphanet Journal of Rare Diseases 2012 7:DOI: 10.1186/1750-1172-7-1 Tovar; licensee BioMed Central Ltd. 2012

prenatal and neonatal death even sometimes despite the successful surgical correction of the birth defect. The detection of CDH can be obtained during fetal life when screening ultrasonography demonstrates herniation of the intestine and/or the liver into the thorax. Antenatal diagnosis in some severe cases can be done with the knowledge that the mother has polyhydramnios (Sinha *et al.,* 2009). When the fetus is in the womb it does not require breathing with his lungs. The placenta is capable of compensating this function. In terms of seconds after coming to this world the newborn baby needs his lungs, this is usually when the dramatic outcomes can occur. That is why it is of a such a great importance for the intrauterine diagnoses to be obtained so that the baby and his mother can be prepared for the great struggle ahead of them - the operation of the diaphragmatic hole and postoperative management with possible respiratory distress syndrome. That means medical planning of the newborn, instant hospitalization after delivery and preparing for operation. After operating the transportation of the baby in the paediatric intensive unit, intubation of the baby, planning of the operative and even more important post-operative plan are also of great importance. A whole team of medical specialists must act together in the medical treatment. These involve gynaecologist, paediatrician neonatologist, thoracic surgeon, abdominal surgeon, paediatric cardiologist and anaesthesiologist. In treating patients with CDH sometimes the use of ECMO (extracorporeal membrane oxygenation) is inevitable. Not all patients are indicated for ECMO, but it is good when treating and saving the lives of these children they are hospitalized in an institution that is equipped with ECMO apparatus.

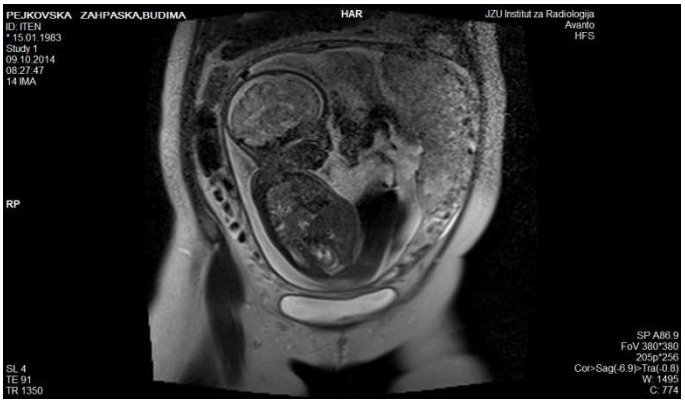
Extra-corporeal membrane oxygenation (ECMO) may be needed in severe CDH cases as a useful adjunct in the treatment. Both the right carotid artery and jugular vein need to be cannulated and connected to a circuit with a membrane gas exchange chamber which allows oxygenation and CO_2 disposal without participation of the lung which is preserved from any pressure insult (Bartlett *et al.,* 1986). The etiology of congenital diaphragmatic hernias is idiopathic; the reason of its intrauterine forming is unknown. However, chromosomal abnormalities have been implicated in about 30 percent of cases.

The modern medicine is still working on discovering on which chromosome exactly the problem appears. Genetics is directly involved in discovering the reason for development of this congenital anomaly as well as for its prevention and transmition to future generations.

MATERIALS AND METHODS

During the pregnancy the mother of the patient was monitored on the ultrasound examinations and until the fifth month was observed to be having a normal pregnancy. At that time only the stomach of the baby was found enlarged and the other measurements were normal. When a control examination was carried out the stomach had normal characteristics, with explanation that the baby emptied its stomach. The mother made biochemical analysis PRISCA 1 was which showed 1:85 risk with the overall risk was 1:600. This was the reason why she made Nifty test in Skopje, Macedonia and in Sofia, Bulgaria. Te test showed low risk with 99,9 % for trisomia 13, 18 and 99,6% for 21 chromosomes. The 46 XY chart discovered that the baby is male. The blood tests and microbiological tests from the cervix and vagina were made. Also urine was checked. Blood results were in average measure and the microbiological tests were all negative. Microbiological tests were made from nose and throat. The results were negative. Test PRISCA 2 was performed on the mother which showed low risk. Overall the mother had normal health and no additional medical problems and conditions. Then at gestational week 30 the mother was feeling very tired, with problems breeding, heartburns, heart racing, dizziness and sudden increase in weight. At the gynaecological examination in the week 32, the only thing that was discovered was a suspection in the stomach of the baby which was again enlarged. A second opinion was asked by a doctor who observed changes in the heart of the baby which were described as dilatation; the stomach was strange also in description. The mother was diagnosed with polyhidramniosis. The placenta had lacunas and the patient was sent for a third opinion in her country the Republic of Macedonia in Skopje in another hospital where she was sent primarily for the baby's heart. There the report of the gynaecologist stated that from the morphological aspect, the heart is normal, the stomach is

normally filled in the abdomen, above it in the thoracal cage there is a content probably intestines, which raises the probability of diafragmal hernia left sided. A single umbilical artery was discovered and also a confirmation of the polyhidramnion. The mother was advised to perform amniocentesis and the results showed that everything is normal in terms of chromosomal abnormalities. The mother also did a magnetic resonance (MR) (picture 2) examination in many slides.



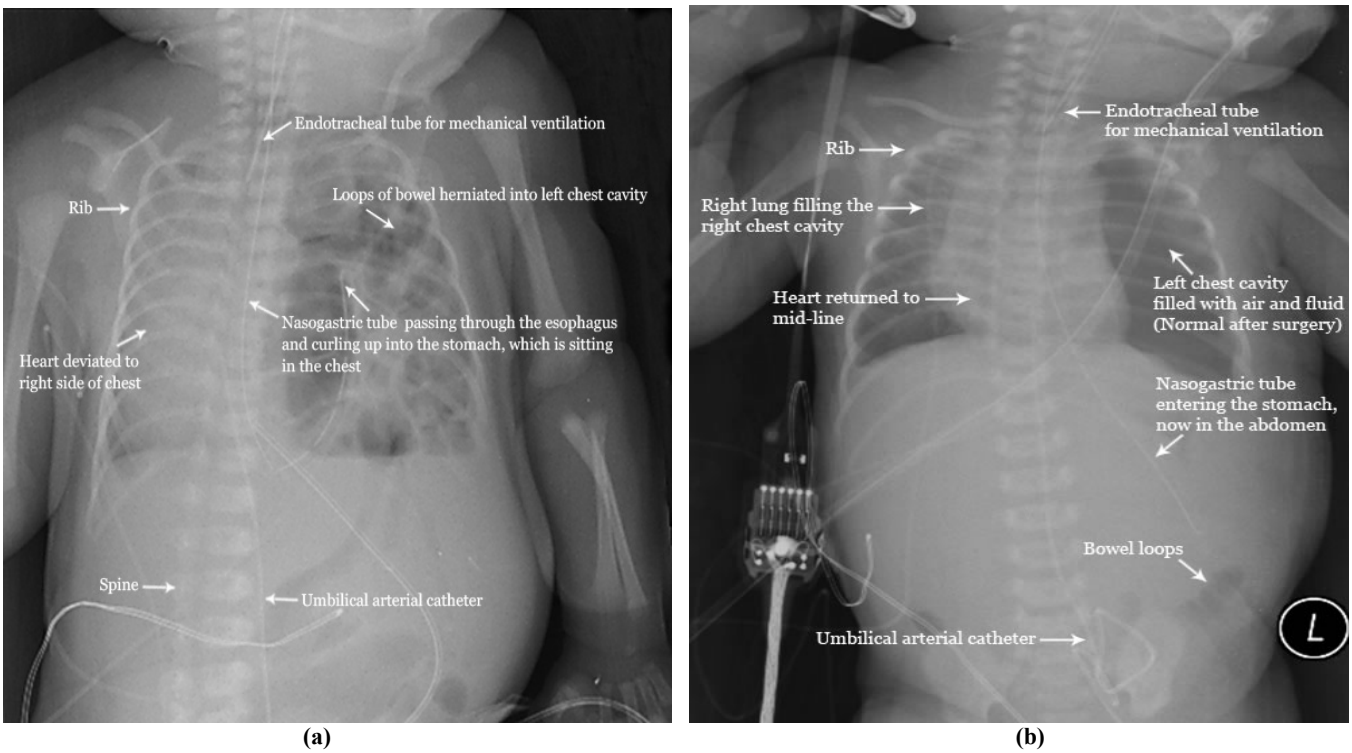
Picture 2. Magnetic resonance at the 32 week of pregnancy showing the babies intestines in the thoracic cavity

From a something what appeared to be a normal pregnancy the mother was advices to be prepared for a surgery of her baby with a high risk pregnancy. The mother had corticosteroids (14 mg ampoule flosteron for each day) administered parenterally for the maturation of the pulmonal tissue, for preparation if a preterm labor occurs. The mother had contractions because of the increase of amniotic fluid and was in a heavy medical condition unable to perform every day activities or even walk without pain. In the Republic of Macedonia 80-90% of these babies die because of very rare prenatal diagnosis, insufficient therapeuticall protocols and lack in experience. The Extracorporal membrane oxygenation (ECMO) system is sometimes life saving for these babies. It is very rarely used in this country and primarily for older patients with heart problems. The nearest country with ECMO apparatus and with an intensive neonative care with the most modern equipment was in Ljubljana, Republic of Slovenia where the mother of the baby had to move, to live for two months. There she stayed together with her mother, the grandmother of the baby and also specialist paediatrician, with help of her entire family, her father, sister gynaecologist and sister ENT specialist. Her 1,5 year old daughter stayed in Macedonia at home with her husband. The daughter didn't have any health problems related to her baby brother.

In the University Medical Centre Ljubljana (UMCL) in the Republic of Slovenia the diagnosis CDH was confirmed definitely to be a left sided diaphragmatic defect with abdominal viscera in the thoracic cavity. A brain-lung ratio formula was calculated in favour of increasing the chances of life of the baby. The baby was given an 80 % chance of survival. From the organs, a part of the stomach was pushing the lungs and a large part of the small intestines. Babies with CDH have to be delivered on time or at 37 or 38 week of pregnancy because the longer of the abdominal organs are in the thoracic cavity the larger defect could appear. For the time being in Slovenia, for the reasons of staying stronger the mother was advised to communicate with other mothers of CDH survivors that were treated in the same hospital. This is a good form of mental preparation of the mother with the specific problem of this disease. The mother was induced to give birth at 38 week of pregnancy. The baby boy was born after 6 hours of labor vaginally and was shown to the mother. A full term baby with beautifully pink reflection with a weight of 3 kg and a 50 cm of length was born. He was struggling for air and was not crying loud. His Apgar score was 9/9. Associated anomalies were vascular, with the presence of only two blood vessels of the umbilical cord with only one vein and one artery and a placenta which was very small. After the examination of the placenta was diagnosed as velamentosa, which can is also a very rare life threatening condition for the baby.

From the external examination of the baby a scaphoid abdomen is seen, barrel-shaped chest and respiratory problems. This baby didn't have respiratory distress (retractions, cyanosis, and grunting respirations) because he was in within seconds intubated and put on a ventilating machine to saturate his oxygen levels. Because this case had left sided posterolateral hernia the heart was pushed and a shift of cardiac sounds over the right chest could be heard. Ultrasound was performed in the delivery room on his head and kidneys which showed normal findings. Almost immediately the baby was endotracheally intubated and a respiratory support with mechanical ventilation was performed. With a small application of oxygen (30%) he was regularly oxygenated. He was soon inserted a nasogastric tube (NGT) and umbilical vein catheter. The status of the baby on his reception in the operation room was the following: Nasal intubation, proper ventilation, moving limbs, plethoric, SpO_2 94 till 100% and FiO_2 0,30. The big fontanel was soft and at the level of his calvarias. The heart action could be heard in the middle of his thorax, tones were clear, with no suspicion of any heart problems. The abdomen was under the level of the thorax, soft and on palpation the liver was found. The femoral pulse was obtained to be symmetrically palpable and tactile.

The baby is of the male pole. The laboratory findings showed at the time of his reception that the CRP is under 5, L 13.7, E 4.83, Hb 172, Ht 0,515, Tr 193. The glucose levels were 4.6, the urea was 2.9, K 4.90, Na 137, Cl 102, Ca 2.18, P1.672, Mg 0.79, creatin 44, proteins 53, albumin 33. Gas analyses were: pH 7.42, p CO_2 4.5, pO_2 16.1, HCO_3 21.0, BE-2.4. After the immediate intubation the baby was sent to the neonatal unit to be cleaned and prepared for operation. X-rays were performed (picture 3), blood and urine samples were taken to be analyzed. Ultrasonography of the heart was done which showed a normal anatomy of the heart which is positioned on the right pushed by the intestines and a part of the stomach (http:// www.cdhgenetics.com/congential-diaphragmatic-hernia.cfm).
In within 18 hours after the birth the baby was operated by a team of specialist consisting of pediatrition neonatologist, thoracic surgeon, abdominal surgeon and anaesthesiologist. The operation was intended to close the diaphragmatic opening which was successfully done and the abdominal organs were returned in the abdominal cavity. In the time of operation the definitive diagnosis was deducted for a left sided CDH. After the operation the baby was transferred to the paediatric intensive unit in the Division of Paediatrics in the UMCL. The mother got to see him after the surgery but could not hold him because he was lying on a Babytherm infant warming system (http://www.draeger.com/sites/en_aunz/Pages/Hospital/Babytherm-8000-8010.aspx) with various tubes inserted in his body.



(a) **(b)**

Picture 3. a, b: An X-ray photograph of a CDH baby before and after the surgery

A nasogastric tube was placed through the nose for feeding of the baby. A constant suction of the mouth was done and cleaning of the nose. He had nasotracheal intubation with suitable ventilation and sufficient oxygenation. To measure continuously the blood pressure and frequent arterial blood gas (ABG) (Steinhorn *et al.,* 2014) monitoring, an indwelling catheter was placed in the umbilical artery which can be done in a peripheral artery (radial, posterior tibial). Placement of a venous catheter was done via the umbilical vein which was made to allow administration of inotropic agents and hypertonic solutions (eg, calcium gluconate). Because of the low blood pressure vasopresor support was given to him. Painkileers like paracetamoll were given to the baby and also antibiotic (for two days) for reducing the risk of bacterial infection due to the seriousness of the condition and age of the baby. The second day he was given mother's milk and adapted milk formula. Because of the small dieresis he was given intermittently a lot of fluid and diuretic. Five days after surgery he had catheter for urination after which he started to urinate by him. He was suitably oxygenated (given nitric oxide). The fifth day after his surgery he was extubated. After the extubation he breathed spontaneously, without effort. He started to feed from a milk bottle. On control radiographies after the surgery the heart from the mediastinum was moved to the medial position, the right lung was fully discovered and the left lung was very hipoplastic and the left part of the hemithorax was mostly empty. Venoarterial or venovenous extracorporeal membrane oxygenation (ECMO) support was in this case unnecessary. His status after his replacement on the semi intensive unit was stable, suitably hydrated, pink complexion, warm skin, capillary return was from 2-3 s. Over the lung the breathing sounds were heard well on both sides, without beeps and noisy sounds. The heart action was rhythmic; the tones were clear without any abnormalities. The stomach was soft with normal palpation findings. The peripheral pulse was symmetrically tactile. His laboratory status was:

CRP under 5, L 12.0, E 3.04, Hb 0.33, MCV 108, MCH 35, Tr 393, glucose 6.0, urea 3.0, K 3.80, Na 142, Cl 108, Ca 2.00, P 1.52, Mg 0.87, creatinin 22, proteins 46, albumin 29. Gas analysis showed pH 7.36, pCO_2 6.5, pO_2 8.8, HCO_3 27, BE 1.2. He was given analgin 50 mg/8h ivpp, paracetamol 20 mg/8h iv pp, chlorhidrat 60 mg/8h to pp, calcium glukonat 100 mg/8h iv. There occurred problems with vomiting of the baby when he was fed through the nasogastric tube when the baby started to feel sick. Then X rays again were performed which showed dilated stomach and a successfully repaired diaphragmatic hernia. He was breathing on his own and was starting to eat slowly small amounts of milk. The paediatrician advice was that he eats 20 ml at every 3 hours. But like many medical problems mathematics can be rarely applied. The baby's mother realized that the baby was hungry and was not putting on weight. She could not breastfeed him, because he had not had the strength for suction. So she started expressing milk and in correlation with the paediatrician to feed him every one and a half hour with small amounts of milk. At day number 8 he was transferred to a half-intensive unit. At the entire time he was also treated by his grandmother (his paediatrician), his mother and the help of the sister's mother. The baby was hospitalized for 15 days. For the entire period blood and urine samples were analyzed. Again cardiatic ultrasonography was performed, which showed normally positioned heart. At the 9 day the baby needed parenteral infusion due to his decrease in weight. After that all the tubes were removed and the stitches were removed, allowing the mother to hold the baby without any tubes. He was not vaccinated because of the very heavy start in his life. He was sent home in a stable condition with 3,090 kg to his country to be treated for a long time by his paediatrician and his mother. His fenilketonuria and thyroxin tests came after his return home which showed normal findings: PKU neo 0.06 mmol/l (normal till 0.12), and TSH 7.00 mE/l (normal till 8). At the first two months return of the baby in his country home, he had to sleep at a high pillow for ease of his breathing.

D vitamin was subscribed and vitamin supplements. He drank expressed mother's milk because again he did not have the strength to breastfeed. After the second month he had his first infection on throat which immediately spread on his lungs. He has taken antibiotics and was cured for 3 weeks. He was rapidly putting on weight until the infection. At the 4 months of age he was taken to an orthopaedist where he had ultrasound tests on his hips which were normal. At that time he has a strawberry haemangioma rapidly growing on the upper left side of his back. He also developed a mobile testicle on the left side. He had his first tooth at 7 months of age. And at the same age he had his second very serious infection. He was breathing with difficulty, with distended abdomen and for 10 days was in a heavy condition. After that his symptoms improved and he started to breathe normally, still couching but much less. He was starting to eat solid foods and he loved homemade meals with baby beef meat. He was growing into a very dear, happy laughing baby boy. He was beginning to crawl and at the same time beginning to speak. His first word was grandma at 7 months of age. When he was one year old he was making mild attempts to walk. He wanted to stand on his own. He was taken to a routine examination and blood analysis, urine samples were taken. X-rays pictures were made and ultrasound examination. The results came back showing a normal development of a one year old CDH survivor. His lungs were normal except for the base of the lowest lobus of the left lung which is still developing. He has a normal appetite and in paediatric and psychological tests he doesn't show any difference from any one year old child.

RESULTS AND DISCUSSION

Every child born with a congenital diaphragmatic hernia is a case for itself. There are no two cases alike. Every condition depends on the severity of the defect and the accompanying abnormalities. Medical anamnesis should be concentrated on the cases from the past, on previous and present members of the family (transgenerationally) (Kjaeva Pejkovska, 2008; Kjaeva-Pejkovska Mirjana, 2002). Genetic examinations need to be carried out. The presented experiences in this research study is about patient, baby born at term vaginally with a short period of preparation and with urgent determination about the actions that are necessary for successful results for the health of the baby. The baby had to travel intrauterine from his country Macedonia to Slovenia. His mother had to make many crucial decisions for saving his life. She had to undergo many examinations for the confirmation of the diagnosis of the baby. In the amniocentesis results shows that the baby has normal cariotype. He had a single isolated anomaly only CDH. CDH occurs as an isolated anomaly in 60 % of the cases. One of things that were seen was the development of an abnormal placenta and the presence of only one umbilical vein and one artery. Later in his life he was diagnosed with undescended testicle and strawberry haemangioma. There is no evidence that these diagnosis are linked with CDH. The baby boy was born in the intensive paediatric unit where he stayed for 15 days. At the time being he was also diagnosed with the most contemporary equipment which not every county has. He was intubated, operated, medically treated 18 hours after he was born. He was on oxygen supply for 5 days when he started to breathe by himself. Glucose and ionized calcium concentrations should be maintained in babies with CDH within reference range. Medications should be used for stabilization of the blood pressure and circulating of the volume for alleviating pulmonary distress and correct hypoxemia. From vasoactive agents dopamine, dobutamine, milrinone can be administered for regulation of the blood pressure. Neuromuscular relaxing agents like pancuronium and vecuronium can be given so the baby can be calm while lying on the Babytherm intensive warming system intubated. Vasodilating pulmonary agent nitric oxide was applied in the treatment of the baby. Also opioid drugs can be administered postoperatively for sedation and relaxation of the muscle preoperative and postoperative. The baby was extubated and the nasogastric tube was taken out the 5 day at the intensive unit and the baby was fed with a bottle through his mouth with expressed mother's milk. The management of the medical therapy in patients with congenital diaphragmatic hernia is directed toward optimizing oxygenation while avoiding barotraumas (Steinhorn *et al.,* 2014). The management includes placement of a vented orogastric tube and connecting it to continuous suction to prevent bowel distention and further lung compression. Mask ventilation must be avoided and the trachea must be intubated immediately.

Continuous monitoring of oxygenation, blood pressure, and perfusion must be followed 24 hours until improvement of the clinical picture (Ramadani, 2001). The baby was given opioid analgesics diazepam to relieve the muscles so that the surgical repair can heal fast. After 15 days of hospitalization he was sent home for a long term neonatal care. For the period of 12 months of age he was observed, controlled, followed and treated. His anatomy external and internal developed well like every normal child his age. He had 4 serious conditions of bronchopneumonia which were treated. His lungs are very sensitive and he needs to avoid bacterial and viral infections as much as he can in life. The infection material in this child spreads very fast from his throat to his lungs which is very important to know for prevention of future bronchopneumonia as much as possible. He had two additional surgeries which lead to the possibility that because they are also left sides, there might be a connection to the general condition, CDH. Also delay in speech is something he developed later, leading to the connection again of genetics. The most important link in the chain of the entire process is intrauterine, prenatal diagnostic of the condition. Pregnant woman must be followed with a great deal of attention to details, because sometimes ultrasound examination can mislead. Sometimes the position of the baby, inadequacy of the apparatus, inexperience of the medical personal can lead to misdiagnosis which often times can have fatal results even in patients that have CDH as an isolated anomaly, which can be operated successfully.

Early intrauterine diagnostic of the condition CDH is of extreme importance. It is of great significance to mention cases with CDH to learn how to recognize them prenatally. Thus parents can learn their conditions, can plan their family, can plan treatment of their children and prepare themselves mentally, physically and financially. All efforts are directed at enhancing antenatal lung growth in prenatally diagnosed cases and at protecting the lung during the intensive care in pre and post-operative phases in all cases[2]. CDH is a condition which many people haven't heard about. Worldwide standardized protocols are developed for its treatment and therapy and many things are taken step by step. Every day is a new learning as every child is not a book. Children with CDH need to be treated with proper care, slowly, step by step, with a lot of attention, with everyday learning, like the child in this case study. Also finances must be taken in consideration. People pay a great amount of money and move to other countries to

save the lives of their beloved little ones. Much information cannot be obtained through the internet, but through observing the baby, by spending everyday a lot of time with him, to understand his needs, his behaviour and his health and to act to improve his physical and mental health condition. Most cases of CDH are sporadic but there are some reports of familial clusters that suggest multifactoral (Crane, 1979; Wolff, 1980; Norio *et al.,* 1984; Mishalany and Gordo, 1986; Frey *et al.,* 1991) rather than autosomal recessive (Hitch *et al.,* 1989; Gibbs *et al.,* 1997) patterns of inheritance. Genetic aspects of CDH were recently addressed (Pober *et al.,* 2005; Pober, 2007; Bielinska *et al.,* 2007; Pober, 2008).

Conclusion

Congenital diaphragmatic hernia as a birth defect needs to be taken with a great deal of seriousness. It is a life threatening condition in which it usually takes a part of a second to save a baby's life. Every aspect must be taken with a great amount of care, for the prenatal and neonatal procedures, therapies in the direction of positive thinking for the best possible results. Often times a second, third, even fourth opinion must be obtained for the definitive diagnosis. Everyone can learn in this entire process, because there are not two patients same and alike. Every patient is unique for himself. The state of CDH is something that affects not only the family that is planning to have children but also a serious thought must be made for the future generations, because of the possibility of genetic transmition. Every procedure, every detail is important for improving the health of the patient. The procedures that are presented in this articles can give the impression about the complicated nature of CDH which the mother and the baby have experienced by themselves. This also shows how much effort must be given by the medical team which have multidimensional approach that is needed for solving such kind of problems. Also only equipped institutions and well trained professionals could deal with CDH. Medical professionals must be well educated for the diagnosis and treatment protocols of congenital diaphragmatic hernia. Parents of these children should be familiar when planning a family for the prevention modalities and possibilities of therapy for the wellbeing of their babies. That is why medical staff and patients must be well informed of the conditions that occur in the womb. The possibilities and modalities of treatment must be analyzed with meticulous attention to details from every aspect, from every point of view, for the wellbeing of these beloved children.

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