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Review Article

A review on Spina bifida

P. Bhavana*, C. Madhavi Latha, K. Lavanyalahari, P. Naga shirisha, D. Madhava Teja, Sk. Masheeha baanu

Ratnam Institute of Pharmacy, Pidathapolur, Nellore, A.P, India

Abstract
Spina bifida is a common congenital abnormality, which cause significant physical and psychological morbidity in affected children and which also affects their career. This small-scale study looked at the health problem of a child with a myelomeningocoele, is also addresses the psychosocial problem that his mother, his main career faced and the social networks involved in his care. the evidence supporting various aspects of spina bifida prevention and management is explored. Furthermore, a literature review is included with regard to physical and psychological issues for child and career. this study aims to raise awareness of the problem faced by children with myelomeningocoele and their families. in particular we aim to educate health care professionals on the important of perceived stress by career of such children, and suggest ways to reduce psychosocial morbidity. Spina bifida is the most common congenital defect of the central nervous system which can portend lifelong disability to those afflicted. While the complete underpinnings of this disease are yet to be fully understood, there have been great advances in the genetic and molecular underpinnings of this disease. Moreover, the treatment for spina bifida has made great advancements, from surgical closure of the defect after birth to the now state-of-the-art intrauterine repair. This review will touch upon the genetics, embryology, and pathophysiology and conclude with a discussion on current therapy, as well as the first FDA-approved clinical trial utilizing stem cells as treatment for spina bifida.

Keywords: Myelomeningocele, neural tube defects, developmental diseases, embryology, spina bifida

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Corresponding Author
P. Bhavana
Ratnam Institute of Pharmacy,
Pidathapolur, Nellore, A.P, India

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Contents

1. Introduction

Spina bifida is a birth defect that occurs when the spine and spinal cord don't form properly. It's a type of neural tube defect. The neural tube is the structure in a developing embryo that eventually becomes the baby's

brain, spinal cord and the tissues that enclose them. Typically, the neural tube forms early in pregnancy and it closes by the 28th day after conception. In babies with spina bifida, a portion of the neural tube doesn't close or develop properly, causing problems in the spinal cord and in the bones of the spine. Spina bifida can range from mild to severe, depending on the type of defect, size, location and complications. When necessary, early treatment for spina bifida involves surgery — although such treatment doesn't always completely resolve the problem. Spina bifida is the most common birth defect affecting the central nervous system (CNS) and is often characterized as the most complex birth defect compatible with survival. Because of its complexity, the diagnosis and treatment of infants born with spina bifida begins before birth and through adulthood, involving multiple disciplines. Not surprisingly, research has flourished across several domains over the past decade. The purpose of this special issue of Developmental Disabilities Research Reviews is to systematically review research on spina bifida within different domains in an effort to promote integration and awareness of this research across disciplines involved directly with spina bifida, necessary strategies for researchers and practitioners involved with other developmental.

Types

Spina bifida occulta

Spina bifida occulta is the most common type of spina bifida and the least likely to cause symptoms that require treatment. In fact, the term “spina bifida occulta” is being used with less frequency as it seldom causes developmental problems, and is rarely diagnosed. Babies with spina bifida occulta have a gap in the vertebrae, but the meninges and spinal cord are contained within the spinal column and the skin grows normally on the back. Most children experience no symptoms, and if they are diagnosed, it’s often because he or she has an X-ray or other diagnostic test for unrelated reasons. Sometimes a child may have a dimple, dark spot, or tuft of hair on the lower back, but these signs almost never cause physical discomfort.

Meningocele

Meningocele occurs when the meninges covering the spinal cord—but not the spinal cord itself—emerges from an opening in a baby’s spine, forming a fluid-filled sac, or cyst. Pediatric surgeons usually close this opening in the first days after birth. Because this type of spina bifida doesn’t usually damage the spinal cord, a meningocele does not normally cause sensory or motor problems in the legs and feet, nor does it cause significant cognitive problems. However, children with a lesion located in the upper part of the spine are at increased risk of nerve damage and muscle or organ dysfunction.

Myelomeningocele

Myelomeningocele is the most severe type of spina bifida. It occurs when part of the spinal cord and the meninges emerge through an opening in the spine. These tissues are contained within a fluid-filled sac that forms on a baby’s back. Children with myelomeningocele have some spinal cord damage, which may affect nerve function in muscles and organs throughout parts of the body located below the opening in the spine. Depending on the extent of nerve damage, myelomeningocele can cause a variety of symptoms, such as poor control over leg muscles, a loss of feeling in the legs or feet, tightness or uncontrolled movement in joints, misaligned or irregularly positioned bones, and lack of control over the bladder and bowels.

Hydrocephalus

Hydrocephalus—a buildup of excess fluid in the brain—often occurs in babies with myelomeningocele. Without surgical treatment to drain the fluid, it can cause pressure and swelling that may lead to irreversible brain damage.

Bladder and Bowel Problems

Myelomeningocele-related nerve damage commonly affects the bladder, bowel, and kidneys. Some children may be incontinent or have frequent urinary tract infections. Our pediatric urologists are part of a multidisciplinary team that cares for your child.

Orthopedic Conditions:

As a child grows, nerve damage can affect muscle tone, which may lead to changes in the alignment of bones. Weak muscle groups can cause tendons and ligaments in the foot or ankle to tighten, restricting movement. Muscle weakness or tight tendons may also cause bones in different parts of the body to move out of position. As a result, a child may develop orthopedic conditions such as scoliosis or clubfoot, in which the feet are twisted inward at the ankle.

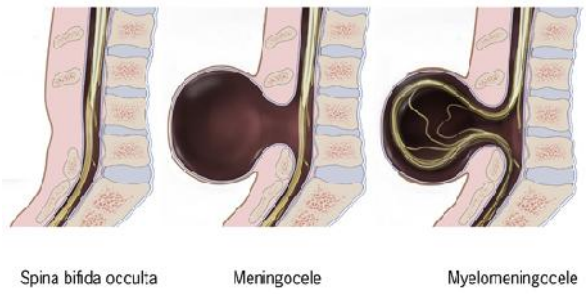

Figure 1

Signs & Symptoms

Signs and symptoms of spina bifida vary by type and severity, and also between individuals. Spina bifida occulta. Typically, there aren't any signs or symptoms because the spinal nerves aren't involved. But you can sometimes see signs on the newborn's skin above the spinal problem, including a tuft of hair, a small dimple or a birthmark. Sometimes, these skin marks can be signs of an underlying spinal cord issue that can be discovered with MRI or spinal ultrasound in a newborn.

Meningocele: This type may cause problems with bladder and bowel function.

Myelomeningocele: In this severe type of spina bifida:
The spinal canal remains open along several vertebrae in the lower or middle back. Tissues and nerves usually are exposed, though sometimes skin covers the sac.

Orthopedic complications:
Children with myelomeningocele can have a variety of problems in the legs and spine because of weak muscles in the legs and back. The types of problems depend on the location of the defect. Possible problems include orthopedic issues such as:

Curved spine (scoliosis)

Abnormal growth: Bowel and bladder problems. Nerves that supply the bladder and bowels usually don't work properly when children have myelomeningocele. This is because the nerves that supply the bowel and bladder come from the lowest level of the spinal cord: Headaches, irritability, vomiting, swelling along the shunt**,** Sleepiness, confusion.

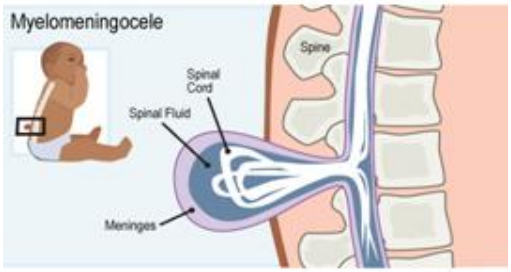

Figure 2

Causes
Not having enough folic acid during pregnancy is one of the most important factors that can increase your chances of having a child with spina bifida. Folic acid (also known as vitamin B9) occurs naturally in some foods, such as broccoli, peas and brown rice. It's also added to foods, such as some breakfast cereals. Folic acid tablets are available from pharmacies and supermarkets, or a GP may be able to prescribe them for you. It's estimated that taking folic acid supplements before you conceive and while you're pregnant may prevent up to 7 out of 10 cases of neural tube defects, such as spina bifida.

Medicine
Taking certain medicines during pregnancy has been linked to an increased risk of having a baby with spina bifida or other birth defects. Valproate and carbamazepine are medicines linked to spina bifida. They're often used to treat epilepsy, and some mental health conditions, such as bipolar disorder. Doctors will try to avoid prescribing these medicines if there's a chance you could get pregnant while taking them, but they may be needed if the alternatives are not effective.

Genetic conditions
If your baby is found to have spina bifida and it's thought they may also have one of these syndromes, you'll be offered a diagnostic test, such as amniocentesis or chorionic villus sampling. These tests can confirm if your baby has one of these genetic conditions.

Other risk factors

Other risk factors for spina bifida include: Obesity – women who are obese (have a body mass index of 30 or more) are more likely to have a child with spina bifida than those of average weight.

Figure 3

2. Pathophysiology
Spinal dysraphism encompasses congenital problems that result in an abnormal bony formation of the spine and the spinal cord. This congenital pathology is caused by the maldevelopment of the ectodermal, mesodermal, and neuroectodermal tissues. The spina bifida is a congenital anomaly that arises from incomplete development of the neural tube. It is commonly used as a nonspecific term referring to any degree of neural tube closure.

The two dominant types of spinal dysraphism are based on the appearance – spina bifida aperta if the lesion is visible and spina bifida occulta if the lesion is not visible. Common manifestations are meningocele, myelomeningocele, lipomeningocele, lipomyelomenigocele, myeloschisis, and rachischisis. Spinal neural tube defects basicaly exist in two forms – open and closed spinal dysraphism.

The simplest form with minimal involvement of nervous tissue is closed dysraphism (spina bifida occulta) where the vertebral defect is hidden. More severe open spinal dysraphisms (spina bifida aperta) mostly represented by meningocele or The most significant amount of financial cost consumpts initial diagnosis and early treatment, inpatient care and the treatment of comorbidities in adult life.

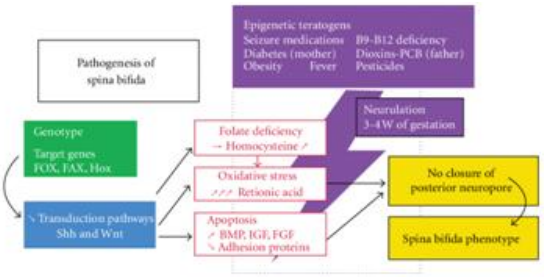

Figure 4

Prevention
Because the neural tube closes 28 to 32 days after conception and before many women are aware they are pregnant, normal development of the brain and spinal cord may be affected during these first three to eight weeks of

pregnancy by the following: genetic problems, lack of proper vitamins and nutrients in the diet, prescription drug and alcohol consumption.

Although many factors related to the development of spina bifida, research has found that folic acid (vitamin B-9), a nutrient found in some green, leafy vegetables, nuts, beans, citrus fruits, and fortified breakfast cereals, can help reduce the risk of neural tube defects. The American College of Medical Genetics (ACMG) and the Centers for Disease Control and Prevention (CDC) recommend that all women of childbearing age take a multivitamin containing folic acid. If a couple has had a previous child with an ONTD, a larger amount of folic acid is recommended and can be prescribed by the woman's physician or healthcare provider. This allows the woman to take it for one to two months prior to conception, and throughout the first trimester of pregnancy, to reduce the risk of another child with ONTD. Current research is focused on looking at how genes control neurulation or the forming of the neural tube. maternal age (spina bifida is more commonly seen in teenage mothers).

In recent years, pioneer surgeons have developed an experimental technique for performing surgery prenatally to correct this condition before birth. Currently, the National Institute of Child Health and Human Development (NICHD), part of the National Institutes of Health (NIH), is conducting a clinical trial to determine whether carrying out the procedure prenatally leads to an overall improvement for these children - with acceptable.

Screening:

If you're pregnant, you'll be offered prenatal screening tests to check for spina bifida and other birth defects. The tests aren't perfect. Some mothers who have positive blood tests have babies without spina bifida. Spina bifida can be screened with maternal blood tests, but typically the diagnosis is made with ultrasound. Maternal serum alpha-fetoprotein (MSAFP) test. For the MSAFP test, a sample of the mother's blood is drawn and tested for alpha-fetoprotein (AFP) — a protein produced by the baby. It's normal for a small amount of AFP to cross the placenta and enter the mother's bloodstream.

Other blood tests:

Your doctor may perform the MSAFP test with two or three other blood tests. These tests are commonly done with the MSAFP test [aminocentesis of the mother amniotic fluid], but their objective is to screen for other conditions, such as trisomy 21 (Down syndrome), not neural tube defects. A screening test is not always 100 percent accurate. The results help your doctor determine whether further testing is needed to obtain more information about the health of an unborn baby. The quadruple screen test is a routine blood test used to screen for certain birth defects, such as Down syndrome and neural tube defects.

It is performed in your obstetrician's office between 15 and 22 weeks of pregnancy. After your doctor draws blood, he or she sends the sample to a laboratory, where technicians measure levels of four substances produced during pregnancy: alpha-fetoprotein, human chorionic gonadotropin, estriol, and inhibin A. Some of these hormones cross the placenta—the organ that delivers oxygen and nutrients to an unborn child—and enter a woman's bloodstream. High levels of these hormones may indicate your unborn child has spina bifida or another type of neural tube defect in which the spinal column does not close completely.

The results of this test are available in about two weeks. Spina bifida may be associated with other malformations as in dysmorphic syndromes often resulting in spontaneous miscarriage.

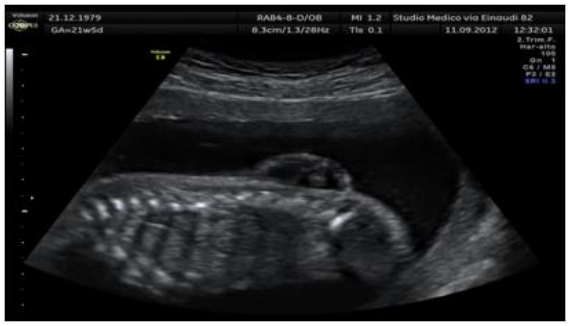

Figure 5

Ultra sound view of the fetal spine at 21 weeks of pregnancy, in the longitudinal scan a lumbar myelomeningoceleis seen.

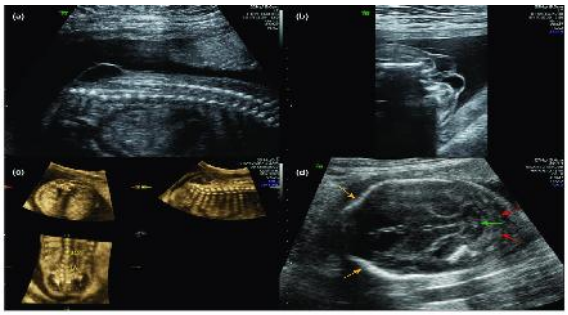

Figure 6

Three dimenshional ultra sound image of the fetal spine at 21 weeks of pregnancy.

Treatment

There are several different treatments for the various problems spina bifida can cause. In babies with spina bifida, nerves and membranes can push out of an opening in the spine and form a sac. This damages the nerves and can lead to serious infections, so your baby will usually have surgery to repair the spine within 48 hours of birth.

During surgery, the surgeon will put the spinal cord and any exposed tissues or nerves back into the correct place. The gap in the spine is then closed and the hole sealed with muscle and skin. Although this will repair the defect, unfortunately it cannot reverse any nerve damage.

Treating hydrocephalus

Surgery is usually needed if your child has hydrocephalus (excess fluid on the brain). The surgeon will implant a thin tube called a shunt to drain away excess fluid to another part of the body, usually the tummy.

Physiotherapy

Physiotherapy is an important way of helping someone with spina bifida to become as independent as possible. The main aim is to help with movement, prevent deformity, and stop the leg muscles weakening further.

This may involve daily exercises to help maintain strength in the leg muscles, as well as wearing special splints to support the legs.

Occupational therapy

Occupational therapy can help people find ways to carry out everyday activities and become more independent.

An occupational therapist can help find practical solutions to problems such as getting dressed. For example, they may provide equipment, such as handrails, to make the activity easier.

Treating bone and joint problems

Further corrective surgery may be needed if there are problems with bone development, such as hip dislocation or club foot (a deformity of the foot and ankle). This type of surgery is known as orthopaedic surgery.

Treating bladder problems

Many people with spina bifida have problems controlling their bladder.

Treatments for bladder problems include:

Antibiotics: lifelong antibiotics are sometimes needed to help prevent kidney and urinary infections

Bladder surgery: may involve enlarging the bladder so it can hold more pee, or connecting the appendix to the bladder and making an opening in the belly so that a catheter can be used more easily.

Treating bowel problems

Bowel problems, particularly constipation, are often a problem for people with spina bifida.

Treatments for bowel problems include:

Laxatives: a type of medicine to help empty the bowels. Suppositories and enemas: medicines put into the bottom to help stimulate the bowels and relieve constipation. Anal irrigation: where using special equipment, you pump water through a tube into your bottom to clean out your bowels; this can be done at home once you've been trained in using the equipment.

Childhood

Neurologists treat and evaluate nervous system issues such as seizure disorders.

Orthotists design and customize various types of technology including crutches, walkers, and wheel chairs.

Medical Management

Medical management of the newly born child with Spina Bifida varies according to the severity of their condition. Those with Spina Bifida Occulta do not usually require any specific treatment. Some people with Spina Bifida Occulta do not exhibit any symptoms and may only discover they have the condition when they are older after having an XRAY.

Children born with myelocoele or myelomeningocoele will require surgery normally within 2-3 days of birth in order to close the gap in the spine and return the spinal cord and nerves to their original place within the spinal column. This aims to prevent infection and further damage to the exposed spinal cord and spinal nerves. Following surgery, the child will be monitored closely for signs of common post-operative problems associated with this type of surgery, namely hydrocephalus and leaking of cerebrospinal fluid. As the infant gets older, management of incontinence will be an important role of the medical team. Effective management strategies include the use of Clean Intermittent Catheterisation (CIC) and certain drugs which can increase the storage volume of the bladder. Children can also develop constipation due to lack of bowel movements and will require the development of a bowel programme that may involve assisted evacuation of stools.

Positioning and Handlings. Following the first few days after surgery, the infant will normally be placed inside or stomach lying. As the infant begins to stabilize and recover from surgery, the physiotherapist will offer advice as to how to hold the newborn child safely. This is incredibly important as the infant will have undergone major surgery which requires careful handling and positioning at all times. It may be advised that parents or careers hold the child underneath the stomach and across their forearm due to the surgical wound that will be present on the infant's back. This handling technique may be used when sitting or walking around. When advised, parents or careers may take the infant for a walk around the hospital resting over the shoulder.

3. Epidermology

Spina bifida is a condition in which the neural tube, a layer of cells that ultimately develops into the brain and spinal cord, fails to close completely during the first few weeks of embryonic development. As a result, when the spine forms, the bones of the spinal column do not close completely around the developing nerves of the spinal cord. Part of the spinal cord may stick out through an opening in the spine, leading to permanent nerve damage. Because spina bifida is caused by abnormalities of the neural tube, it is classified as a neural tube defect. Children born with spina bifida often have a fluid-filled sac on their back that is covered by skin. If the sac contains part of the

spinal cord and its protective covering, it is known as a myelomeningocele. In a milder form of the condition, called spina bifida occulta, the bones of the spinal column are abnormally formed, but the nerves of the spinal cord usually develop normally. Unlike in the more severe form of spina bifida, the spinal cord does not stick out through an opening in the spine. Spina bifida occulta most often causes no health problems, although rarely it can cause back pain or changes in bladder function.

Parental Age and Birth Order

In a meta-analysis study of maternal age as risk factor for NTDs, the authors found increased risk associated with mothers of 40+ years and mothers younger than 19 years.

The detected effect was stronger for SB than for anencephaly. Perhaps somewhat related to maternal age, in a meta-analysis of birth order as a potential risk factor for NTDs, children with higher birth order were more likely to have SB.

Parental Race

Recent estimates for the period of 2003–2005 in the United States found that the birth prevalence for NTDs per 1,000 births was 2.0 for non-Hispanic whites, 1.96 for Hispanics, and 1.74 for non-Hispanic blacks. Thus, there appears to be a slightly reduced risk for NTDs among non-Hispanic blacks in the United States. Among sub-Saharan blacks, the birth prevalence is 1.99 per 1000 births, which is higher than that observed for blacks in the United States. Immigrants from Ireland have a higher incidence of spina bifida than do natives .highest rates of the defect in the USA can be found in Hispanic youth.

Embryology

The neural tube is a transient structure that is formed during the development of an embryo; it is the precursor to the central nervous system, which is composed of the brain and spinal cord. In human embryos, this entire process occurs between days 17 and 28 after fertilization.

The activities required to form a normal neural tube include apoptosis, neural crest migration, neuroepithelial proliferation, contraction of apical cytoskeletal microfilaments, and flexing at dorsolateral bending points. Any aberration during embryogenesis can result in neural tube failure and a resultant NTD. Neural tube closure can be succinctly summarized by sequential folding, elevation, closing, and fusing of the neural tube along the dorsal midline, allowing for functional separation of non-neuronal tissue from the neural tube itself. This entire process and sequence of events is termed neurulation, which can be further subdivided into primary and secondary neurulation.

During primary neurulation:

The brain and spinal cord are formed, specifically the segments extending from the medulla to the mid-lumbar enlargement. Primary neurulation is responsible for the shaping, folding, and fusing of the neural plate along the midline. In mouse embryos, the act of primary neurulation is initiated at the boundary between the cervical spine and future hindbrain. Closure spreads bi-directionally from this point. A second closure origin site arises at the boundary of the forebrain and midbrain; this closure also spreads bi-directionally. A third closure event originates at the rostral end of the forebrain as well.

Closure between all three of these initiation sites leads to completion of cranial and spinal neurulation, thus providing a closed anterior, posterior, and hindbrain neuropore. These events, as seen in mice, are suggested to be similar in human embryos with some key differences

Secondary neurulation

The secondary neuralation is responsible for the lower portion of the spinal cord, which includes the distal lumbar cord, conus medullaris, and filum terminale. This process is composed of canalization and retrogressive differentiation. Canalization is the process by which the neural tube elongates caudally toward the posterior neuropore. As the notochord and neural epithelium fuse, a caudal cell mass is formed. Within this cell mass, multiple microcysts coalesce and form an ependyma-lined tubular structure, which then fuse with the neural tube from above, creating a continuous primary neural tube. In humans, the development and closure of the neural tube is complete 28 days after conception. After day 38, there is controlled cell necrosis along the caudal neural tube, which results in the formation of distal lumbar cord, conus medullaris, and filum terminale.

Folate Metabolism

Folates are folic acid compounds that refer to a class of essential water-soluble vitamins, mainly found in fruits and green leafy vegetables. Folic acid is a synthetic compound, mostly used in pharmaceuticals and dietary supplements, owing to its chemical stability. The umbrella term “folate” refers to all these compounds, be they natural or synthetic. Folic acid (pteroylglutamate) is the most oxidized form of folate, and it must undergo reduction to be biologically active. This process occurs in two steps via the same enzyme (dihydrofolate reductase), first to dihydrofolate, then its active form, tetrahydrofolate. All proliferative cells utilize folate in this manner. The addition of a single carbon unit and reduction steps produces 5-methyltetrahydrofolate (5-MTHF), which is the predominant form found in plasma.

4. Conclusion

Prenatal detection will undoubtedly become more refined, and may well continue to reduce the incidence of meningomyelocele. Another possible advancement that is often discussed concerns intrauterine surgery (surgery on the fetus while still in the womb) to close a meningomyelocele prior to birth. Experimental work has clearly demonstrated that the exposed neural elements are vulnerable to damage from contact with amniotic fluid. There may in fact be progressive loss of lower extremity function during the latter part of gestation. Since this is the

case, it would seem reasonable to close the back as early as possible.

This is certainly attractive from a theoretical point of view. However, in light of the present state of the surgical art, there is, unfortunately, little likelihood that this sort of procedure will be feasible in the foreseeable future. The incidence of meningomyelocele has declined as a result of prenatal testing. At the present time virtually all children born with this affliction are treated, irrespective of the magnitude of neurological deficit. This is done because there is simply no way to arrange for future care if the back is open and the head growing. It is essential that there be a continuing interchange between parents and physicians to avoid misunderstandings about the complexity of the problem and the necessity of future treatment. But with the assistance of a multitude of specialists, social workers and psychologists, many of these children will have the potential for enjoying an excellent quality of life.

5. References

[1] Canfield MA, Mai CT, Wang Y, O'Halloran A, Marengo LK, Olney RS, Borger CL, Rutkowski R, Fornoff J, Irwin N, Copeland G, Flood TJ, Meyer RE, Rickard R, Alverson CJ, Sweatlock J, Kirby RS., National Birth Defects Prevention Network. The association between race/ethnicity and major birth defects in the United States, 1999-2007. Am J Public Health. 2014 Sep, 1(2): 78-89.

[2] Trudell AS, Odibo AO. Diagnosis of spina bifida on ultrasound: always termination? Best Pract Res Clin Obstet Gynaecol. 2014 Apr,2(3): 98-100.

[3] Martínez-Lage JF, Moltó MA, Pagán JA. [Latex allergy in patients with spina bifida: prevention and treatment]. Neurocirugia (Astur). 2001, 3(4); 38-45

[4] Biggio JR, Owen J, Wenstrom KD, Oakes WJ. Can prenatal ultrasound findings predict ambulatory status in fetuses with open spina bifida? Am J Obstet Gynecol. 2001 Nov,5(6);55-60

[5] Appasamy M, Roberts D, Pilling D, Buxton N. Antenatal ultrasound and magnetic resonance imaging in localizing the level of lesion in spina bifida and correlation with postnatal outcome. Ultrasound Obstet Gynecol. 2006 May;27,2(3);65-69

[6] Levin-Decanini T, Houtrow A, Katz A. The Evolution of Spina Bifida Treatment Through a Biomedical Ethics Lens. HEC Forum. 2017 Sep, 4(5): 78-80

[7] Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. Lancet. 2010 Feb 20,3(4);66-69

[8] Houtrow AJ, Thom EA, Fletcher JM, Burrows PK, Adzick NS, Thomas NH, Brock JW, Cooper T, Lee H, Bilaniuk L, Glenn OA, Pruthi S, MacPherson C, Farmer DL, Johnson MP, Howell LJ, Gupta N, Walker WO. Prenatal Repair of Myelomeningocele and School-age Functional Outcomes. Pediatrics. 2020 ,3(4);45-48

[9] Binks JA, Barden WS, Burke TA, Young NL. What do we really know about the transition to adult-centered health care. A focus on cerebral palsy and spina bifida. Arch Phys Med Rehabil. 2007 Aug,4(5);67-70

[10] Khan F, Amatya B, Ng L, Galea M. Rehabilitation outcomes in persons with spina bifida: A randomised controlled trial. J Rehabil Med. 2015 Sep2(3);28-30

[11] Dicianno BE. 21st century challenges to the provision of health care to adults with spina bifida: a rehabilitation approach. Arch Phys Med Rehabil. 2014 Sep4(5);40-43

[12] Cohen AR, Robinson S: Myelomeningocele and Myelocytocele in Yeomans (ed), Neurological Surgery Philadelphia PA, 2012 pp 2507-2012.1(2);55-58

[13] Garceau GJ: The Filum Terminal Syndrome (the cord traction syndrome), J Bone and Joint Surgery Am, 711-716, 1953.2(3);60-63

[14] Hoffman HJ, Hendrick EB, Humphreys RP: The Tethered Spinal Cord: its Protean Manifestations, Diagnosis and Surgical Corrections. Childs Brain 2:145-155, 1976.4(5);34-36

[15] von Recklinghausen F : Untersuchungen uber die Spina Bifida. Arch Pathol Ana 105: 243-330, 373-255, 1886. 2(3);42-46

[16] Yamada S, Zinke DE, Sanders D: Pathophysiology of “tethered cord syndrome”. J Neurosurg 54: 494-503, 1981 3(4): 67-69.

[17] Lichtenstein BW. “Spinal dysraphism: ”Spina bifida and myelodysplasia. Arch Neurol Pyschiat 44: 792-810, 1940 2(1): 70-73.

[18] McClone DG, Herman Jm, Gabrieli AP, Dias L: Tethered Cord as a Cause of Scoliosis in Children with a Meningocele. Ped Neurosurg 16:8-13, 1990/1991.3(4): 58-62.

[19] Eubanks JD, Cheruvu, VK: Prevelance of sacral spina bifida occulta and its relationship to age, sex, race, and the sacral table angle: An Anatomic osteologic study of three thousand one hundred specimens. Spine, 2009, 2(3): 64-67.

[20] Conley A, Tye GW, Ward JD, Myseros JS: Occult Spinal Dysraphism and the Tethered spinal Cord in Benzel EC (ed): Spine Surgery: Techniques, complications avoidance, and management, third edition. Philadelphia PA, 2012, 4(5): 89-92.

[21] Guerra LA, Pike J, Milks J et al: Outcome in patients who underwent tethered cord release for occult spinal dysraphsim. The Journal of Urology. 176:1729-1732, 2006, 3(4): 32-37.

[22] Tredway TL, Musleh W, Christie SD, Khavkin Y, Fessler RG, Curry DJ. A novel minimally invasive technique for spinal cord untethering. Neurosurgery. 60; 2007 2(3): 52-55.
[23] Bassett RC. The neurologic deficit associated with lipomas of the cauda equine. Ann Surg 1950; 131: 109–16.
[24] Schmidt DM, Robinson B, Jones DA. The tethered spinal cord. Etiology and clinical manifestations. Orthop Rev 1990, 2(3): 58-64.