

Detection of Fetal Spinal Congenital Malformations

הצעה למחקר רב תחומי ורב מרכזי

תודה, ליאנה

נושא המחקר:

אבחנה בעובר של מומים מולדים של חוט שידרה, וקורלציה עם צריכת מוצרי חלב, סוגי לחם, וחומצה פולית של האם – מחקר פרוספקטיבי ישראלי, רב-תחומי ורב-מרכזי.

נושא המחקר באנגלית:

Detection of Fetal Spinal Congenital Malformations and correlation with maternal consumption of milk products, breads and Folic Acid. A multi-disciplinary multi-center Israeli study.

מילות מפתח:

מומים מולדים, מערכת עצבים מרכזית, אולטרה סאונד עוברי, עגינת חוט שידרה, צריכת מוצרי חלב, חומצה פולית.

Key words:

Congenital malformations, central nervous system, Fetal Ultrasound, tethered cord, spina bifida, milk products, Folic Acid.

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Abstract

Objectives:

1. Tethered cord syndrome (TCS) is commonly found in infancy and childhood and rarely diagnosed in Fetuses. Thus the goal is to increase detection rate of spinal dysrhaphism (SD) and associated anomalies in the fetus.
2. To evaluate the additive value of Fetal detection of SD to postnatal management of the baby.
3. To study possible protective role of FA and other nutrients in prevention of SD in Fetus.

Background:

Modern Fetal imaging has revolutionized Fetal and pediatric medicine, improved fetal diagnosis, management and identification of risk factors for congenital malformations. One of the most important entities of congenital malformations in the central nervous system (CNS) is the group of Spinal Dysrhaphism. This group includes two main entities: Open Spina bifida (i.e. meningomyeloceles- MMC) and Closed Spina Bifida (Tethered cord syndrome –TCS, that include lipomas, split cord malformations, and dermal sinuses). Thanks to prenatal screening tests and quality of fetal US, most of the MMC cases are detected prenatally, but some are still misdiagnosed. For the TCS and closed spinal defects, the majority is not diagnosed during Fetal life but after birth – if suspected by the neonatologist because of associated skin stigmata, or in late infancy or childhood when ***clinical deterioration*** of a previously normal child occurs. The clinical spectrum of the child with TCS may vary from normal (at birth) to severe neurological deficit including leg weakness and deformity, urinary incontinence and progressive scoliosis.

Because TCS is a congenital malformation, increasing Fetal detection rate can also help in understanding risk factors, and maybe prevent or minimize the pathology. Consumption of Folic Acid (FA) plays a major role in decreasing risk for congenital malformations, including MMC and orofacial defects. However the role of FA and other nutrients has not been studied in association to TCS. In the cognitively normal child, the importance of avoiding such complications can have the major impact on quality of life, as well as change the natural history of untreated children with TCS.

Methods: A multi-center, multi-disciplinary prospective study. During Fetal detailed routine US (before 23w) or Nuchal Thickness exam (15-17w), in addition to the standard parameters, the level of Conus Medullaris will be determined. The fetuses with normal level of conus and spinal canal will provide the control arm. Conus below L3, "spinal tails" and abnormal spinal canal (bony spur, lipoma), and open spina bifida will be enrolled into suspected SD group. All babies will be evaluated by neonatologists. Fetuses suspected for SD will be followed by pediatric neurosurgeon and postnatal US by 2 months of age. For all pregnant mothers of enrolled fetuses, the nutritional data including consumption of FA, milk products and breads will be registered prospectively and analyzed in association to pre and postnatal findings.

Importance:

In the potentially normal baby with TCS, Fetal diagnosis may minimize possible clinical deterioration by enabling focused postnatal follow-up and early un-tethering. Association with consumption of foods may indicate dietary and nutritional recommendations focused to prevent SD, and in particular TCS - which is a rather common congenital malformation.

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Scientific background

One of the most important groups of congenital malformations in the central nervous system is the group of Spinal Dysrhapism. This group includes two main entities: Open Spina bifida (such as meningomyeloceles- MMC) and Closed Spina Bifida (Tethered cord syndrome -TCS). Open defects are the rare form (Hoffman 1987; Yen et al. 1992; Olutoye and Adzick 1999; Sutton et al. 1999; Mangels et al. 2000; Suh et al. 2001; Sutton et al. 2003; Nogueira et al. 2004) and are usually found in religious populations that do not perform prenatal screening, or do not accept termination of pregnancy even if severe congenital malformation is diagnosed in the Fetus. Closed Spinal defects are not rare and are usually diagnosed during early infancy or childhood, but *rarely* detected by Fetal US or other fetal screening tests (Hoffman 1987; Yen et al. 1992; Suh et al. 2001; Nogueira et al. 2004). Unlike open spina bifida (such as meningomyelocele), closed spinal dysrhapism is not always evident at birth. Some newborns may have skin stigmata, but if those are not present or under-estimated, children with TC may demonstrate severe clinical deterioration in later life: progressive scoliosis, leg deformities, persistent pressure sores or ulcers in legs, weakness of one or both legs, sensory deficit, pain, urinary incontinence or recurrent urinary infections, and constipation. Some of these manifestations may be irreversible once they appear, even by successful un-tethering surgery (Hoffman 1987; Warf et al. 1993; Prahinski et al. 2000; Suh et al. 2001; von Koch et al. 2002; Lapsiwala and Iskandar 2004; Nogueira et al. 2004; Rosen et al. 2004).

The main pathologies associated with TCS include lipomas, dermal sinuses, thick fatty filum, dermoid cysts and split cord malformations such as diastematomyelia (DSM). Even though the common final pathway may lead to functional deterioration due to the tethering that is present in all these pathologies, the timing of deterioration and degree of neurological deficit vary. It is well accepted that early treatment of symptomatic TCS may improve clinical outcome, yet some damage may be irreversible (Warf et al. 1993; Prahinski et al. 2000; von Koch et al. 2002; Lapsiwala and Iskandar 2004; Nogueira et al. 2004; Rosen et al. 2004). Patients may lose their urinary continence and become catheter dependent for the rest of their lives, or demonstrate progressive motor leg weakness leading in extreme cases to paraparesis and major handicaps (Hoffman 1987; Warf et al. 1993; Prahinski et al. 2000; Suh et al. 2001; von Koch et al. 2002; Lapsiwala and Iskandar 2004; Nogueira et al. 2004; Rosen et al. 2004)

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Significance of prenatal diagnosis of Spinal Dysrhapism (SD)

Both open and closed spinal malformations are extremely important issues from the prenatal diagnosis point of view. Even though most MMC fetuses are aborted, early fetal diagnosis may enable fetal surgery (which is currently performed in some places and is still to be tested by a prospective study). Even if the fetus is not aborted, the parents may prepare themselves for what seems to be one of the most non-fatal severe CNS malformations with impact on the lives of all family members. It is still appreciated that babies with MMC may be misdiagnosed by fetal US, so for those cases – a focused look at level of conus may have led to diagnosis of the MMC which is always associated with a low lying abnormal conus (Quinn et al. 1998; Olutoye and Adzick 1999; Sutton et al. 1999; Mangels et al. 2000; Sutton et al. 2001; Beuls et al. 2003; Sutton et al. 2003).

The importance of diagnosing TCS in fetal life lies in the understanding that late diagnosis of the malformation can cause irreversible morbidity. TCS may be clinically variable from a normal child to a real handicap. It has a major impact on the ***potentially normal child's*** development, since with growth if un-treated on time; the child may develop severe urologic, neurological and orthopedic complications (Hoffman 1987; Yen et al. 1992; Warf et al. 1993; Prahinski et al. 2000; von Koch et al. 2002; Nogueira et al. 2004). A continent child may lose urine continence if a tethered cord is not operated for un-tethering, and progressive leg deformities or scoliosis may lead to multiple surgeries and chronic rehabilitation programs, with clear deterioration in quality of life for the child and family. The social and financial costs are of course a major concern for the whole population in TCS, since the morbidity is present for many years through childhood and adulthood later (Matsuo et al. 1993; Sattar et al. 1998; Levine et al. 1999; Allen and Silverman 2000; Sonigo-Cohen et al. 2003; Wright et al. 2004; Biri et al. 2005).

Detection of SD by prenatal US

Fetal US policy up to now does not include routine demand for definition of level of Conus medullaris. However, since most patients with TCS and MMC have low lying conus, and sometimes associated intra-spinal pathology at the level of conus – focus on demonstrating the conus and defining the level in the fetus might be the key to early fetal diagnosis of spinal congenital malformations. Some authors have demonstrated the level of conus in fetuses by US and few case reports have been published about fetal diagnosis of TCS associated malformations such as diastematomyelia (DSM) and lipomas (Govender et al. 1989; Robbin et al. 1994; Sattar et al. 1998; Mernagh et al. 1999; Allen and Silverman 2000; Sonigo-Cohen et al. 2003; Wright et al. 2004; Biri et al. 2005). The level of conus in fetus is not supposed to be below L2, so that any

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level below L3 would indicate a possible TCS. Suspected TCS may lead to Fetal MRI that will differentiate possible other pathologies (i.e. teratomas) and coexisting malformations (i.e. chiari), and multi-system involvement (VACTER syndrome) (Levine et al. 1999; Mangels et al. 2000; Suh et al. 2001; Sonigo-Cohen et al. 2003).

It is possible to detect TCS in Fetal Life as early as 19 weeks gestation. The data from literature regards conus lower than L3 as a low lying conus. (Govender et al. 1989; Levine et al. 1999; Allen and Silverman 2000; Biri et al. 2005)

Since routine fetal follow-up in Israel includes detailed US before 24 weeks of gestation, the authors suggest including into the protocol detection of level of conus medullaris. Most of the TCS will have low lying conus, or a fatty filum that restricts motion of cord. Spinal lipomas and dermoid cysts may be easier to detect compared to dermal sinus, but detection of low conus may indicate later fetal US when resolution is better or Fetal MRI that can help diagnose the pathology. (Govender et al. 1989; Levine et al. 1999; Olutoye and Adzick 1999; Beuls et al. 2003; Stiefel et al. 2003; Wright et al. 2004; Biri et al. 2005)

Before offering changes to standard US protocol exams, a pilot of several thousands of Fetal US will help to demonstrate feasibility, sensitivity and yield in diagnosis of SD in the fetus. Such a study is valid only if conducted prospectively by a multi-disciplinary team that will evaluate postnatal clinical and sonographic data in correlation with the Fetal findings.

Nutrition, Folic acid and congenital malformations

Since congenital malformations have multi-factorial risk factors, nutrition may play a major role in fetal normal development. TCS is rarely associated with genetic factors and are not familial in most cases. Environmental factors, including nutrition may thus play an important role.

Maternal consumption of Folic acid (FA), different minerals and vitamin intake have been previously studied in some congenital pathologies (Lindhout et al. 1992; Gil et al. 2000; Krapels et al. 2004). It has been recently shown that periconceptional FA intake prevents orofacial clefts (OFC) (Krapels et al. 2004). The energy adjusted intakes of fiber, vegetable protein, Iron and Magnesium decreased OFC risk. (Krapels et al. 2004). Even though the importance of FA intake is well recognized to minimize risk for neural tube defects, the consumption rate of FA in many populations, including Israel, is not optimal. In a study looking into the consumption rate of FA in pregnant women, Of 221 women interviewed, only 67 (30%) regularly took pills containing 0.4 mg folic acid. Women with higher educational levels were more likely to take multivitamins with folic acid than were the less educated ($p = 0.05$) (Gil et al. 2000).

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The role of FA in prevention of closed spina bifida and TCS is still to be studied. As closure of the neural tube and formation of spinal components are processes that take place early in gestation, nutritional factors may play a role in malformation of spinal canal and its contents. Up to now, no major prospective study has looked into association of milk products and food consumption habits in relation to fetal occurrence of spinal dysraphism, partially because it is hard to detect TCS by fetal US that is not focused at recognizing the level of cord and intraspinal pathologies related to TCS.

This study will thus combine the nutritional aspect as a possible risk factor, with the technical aspect of focused look at fetal spinal canal to evaluate this issue.

This study will look at the incidence of spinal dysraphism (open and closed) in the Fetus and will explore a possible protective role of milk products, different breads and FA by recording dietary information of the pregnant mothers at time of enrollment to study. If any association is found, recommendations about appropriate diet or development of specific foods such as dedicated milk products or incorporation of vitamins and minerals into breads or milk products may be a convenient and feasible way to approach this issue in the wide population of young women at child-bearing age. For the religious population, or in cases where familial pre-planning is not practical, routine consumption of such dedicated food products may be the window of opportunities for the whole society to deal with congenital malformations of the central nervous system, and can allow further studies to evaluate the impact of such practice on other congenital malformations occurring early during fetal development.

How do we follow the suspected Fetus with TCS and SD

To validate the suspected fetal diagnosis of spinal dysraphism, all fetuses will be evaluated after birth by a pediatric neurosurgeon for potential skin stigmata and neurologic deficit. All babies enrolled to this study (both controls and SD groups) will be evaluated by a neonatologist after birth, and the data correlated with prenatal diagnosis. All fetuses suspected for TCS by prenatal US or by postnatal exam (on routine neonatology exam) will be followed by a pediatric neurosurgeon. Also babies enrolled into control arm, that will demonstrate postnatal signs suspicious of TCS, such as skin stigmata or other deficit that were un-diagnosed during fetal life – will be seen by a pediatric neurosurgeon. A postnatal US early during first month after delivery will evaluate the level of conus medullaris and the low spinal canal to correlate with the prenatal findings of both groups (A and B). It is well established that early postnatal US for the spine may show TC associated pathologies and is a good screening imaging postnatally (Azzoni et al. 2005).

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The benefits of the proposed study may include:

1. Improve the diagnosis of TSC and MMC in Fetal life.
2. Study the immediate clinical outcome of a prospectively enrolled population of spinal dysrhaphism.
3. Study the pattern of folic acid (FA) consumption and its importance to TCS and MMC.
4. Identify possible risk factors regarding food consumption (vitamins, milk products, different breads) in the pregnant women for development of fetal congenital spinal malformation, and look into a possible protective role against spinal congenital malformations.

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Specific Research objectives & Expected significance

1. To explore the possibility that there is different food product consumption in the mothers with congenital spinal malformations as compared to controls.
2. Hypothesis that specific detection of level of conus medullaris as an integral part of the detailed US performed before 24 weeks of gestation will increase the diagnosis rate of TCS.
3. To prospectively evaluate Fetuses with diagnosed TCS and check reliability of prenatal diagnosis with postnatal imaging.
4. To see if early fetal detection or suspicion of TCS enables focused follow up and early treatment that reduce the rate of progressive postnatal deterioration.

Working hypothesis

* Food consumption patterns may be associated with rate of congenital malformations. Milk products and Folic acid consumption may decrease the risk for open and closed spinal malformations.

*Since it is not feasible to screen every newborn by postnatal US, the authors propose to use the major screening opportunity for congenital malformations, which is during fetal life- the detailed Fetal US PERFORMED ROUTINELY by 24 weeks, to detect spinal open and closed malformations. Early detection or suspicion may lead to focused postnatal follow-up in the affected babies, may enable early surgery before clinical symptoms or signs appear and may lead to lesser morbidity in the childhood from TCS.

*It is possible to improve diagnosis of TCS and spina bifida in fetuses by a focused examination of level of conus medullaris, and evaluation of low spinal elements during fetal US performed for NT and for detailed Prenatal US.

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Methods:

1. Multi-disciplinary multi-stage assessment of each Fetus and born baby.
2. Fetal detection by obstetrician (US mandatory, MRI as indicated – as detailed above).
3. If the obstetrician accepts parental consent (consent form 1): enrollment.
4. The consent form 1 includes:
 - Fetal data registry anonymously
 - Postnatal clinical data (within 1 month of age)
 - Post natal radiological data
 - Tentative agreement for follow up until age of 3m by pediatric Neurosurgeon if TCS is suspected.
5. If the fetus is born – Clinical FU as by protocol.
6. If parents/obstetrician chooses termination of pregnancy: ask for informed consent to collect data from pathology report (consent form 2).
7. If Fetal MRI was indicated – data incorporated. **The study does not imply performing Fetal MRI if so was not advised by the common practice** of the gynecologist / pediatric neurosurgeon if Fetal counseling was performed.
8. All born babies will be evaluated by Neonatologists and postnatal forms will be filled up and sent to headquarters.
9. All babies suspected in fetal life for SD will be seen by a pediatric neurosurgeon by age 3m.
10. All babies suspected in fetal life for SD will undergo postnatal US by a pediatric Radiologist within 1 month.
11. All babies will be seen by Urologist and Orthopedic surgeon as indicated by clinical status.
12. **No change will be performed from the standard treatment given by the centers** involved, so that the study does not imply new or different treatment protocols in each center. However the recommendations and the treatment if performed during the study period will be registered as extra clinical data.
13. Collection of data: by a research coordinator blind to identity of participants (mothers or babies).
 - The data will be transferred with number codes and not names.
 - The statistical analysis will be performed by a specialist in Statistics.
 - For fetuses enrolled into study outcome versus suspected Fetal pathology, correlation between prenatal and postnatal imaging (when available), and correlation between prenatal and postnatal diagnosis will be performed.
 - For fetuses enrolled only to Registry part, without clinical outcome arm (parents do not agree to FU) – Fetal US data will be used to study technical aspects such as: yield for detection of conus, incidence of TCS etc.

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Control Arm:

Inclusion Criteria:

- * Fetuses examined routine detailed US (weeks 20-24) or N Thickness (15-17w).
- * No Spinal abnormalities suspected or found.
- * Single fetus pregnancies
- * Parents agree (informed consent) to participate in study.
- * All Prenatal data forms will be filled up and sent by neonatologists.
- * Babies born Term (not premature babies).

Informed consent for Control arm will include:

1. Brief description of Study Goals
2. Importance of study
3. Agreement to register data anonymously into to pool for statistical analysis
4. Agreement to send discharge letter from after birth to evaluate post natal clinical data.
5. Agreement to present for FU examination at 6 months and at 2 years after birth for clinical FU.

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Study arm:

Inclusion Criteria:

- * Fetuses with suspected low lying conus (L3 and below) by Fetal US at any stage of pregnancy.
- * Fetuses suspected for MMC, Meningocele, suspected TCS: intraspinal masses : i.e. lipoma, Split cord malformations, dermal sinus, "tails", spinal soft tissue masses.
- * Fetuses suspected for spinal vertebral anomalies.

Informed consent for study arm will include:

1. Brief description of Study Goals
2. Importance of study
3. Agreement to register data anonymously into to pool for statistical analysis
4. Agreement to send discharge letter from after birth to evaluate post natal clinical data.
5. Agreement for FU by postnatal US within 1m after birth, and clinical FU by pediatric Neurosurgeon within 3m.

Exclusion criteria:

- * Fetuses born premature suffering from major complications related to prematurity:
 - * IVH (Intra ventricular hemorrhage)
 - * Infection
 - * Long term ventilation

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Study design:

- I. Enrolment by registry: How to keep both Confidentiality and Accuracy:
- Registry is anonymous
 - Number of fetus enrolled is included by using the date/serial number per day of enrolled fetus in the specific center/number of center provided by headquarters.

For example:

F01012006/01/a

The data provided by the obstetrician is delivered to the headquarters in this manner using no names of parents. This number will be provided to the parents who agree to participate in the study on the documents they will receive from their obstetrician – "**registry for parents form**"(appendix 1).

This form will be provided to the neonatologists when the child is born to fill the postnatal data. The neonatologist will deliver the filled form to the headquarters after adding the postnatal number:

When the child is born the number at follow up will remain the same, however in case of multiple fetus pregnancies the additional letters will follow: for example:

B01012006/01/a/II/III meaning: Born, second of triplets.

Both numbers must follow the child until end of follow up.

The data provided to the headquarters will thus have no direct access to patient's identity, apart from the treating physician, as usual.

Thus each fetus enrolled will have 2 identification titles: for example -

F01012006/01/a - until birth

B01012006/01/a/II/III – after birth

II. Imaging (Attachment 1):

- Fetal US is the first and obligatory diagnostic tool to enroll patients.
- Fetal MRI will be considered for SD either by the obstetrician or after Fetal Neuro-counseling, that will be performed by communication between Obstetrician and Pediatric Neurosurgeon.
- Post natal US will be performed at least once within 1 month after birth. If clinical condition necessitates MRI – this will be performed according to clinical judgment as would have been done without the study.
- All Fetal MRI or post natal imaging studies will be reevaluated by an expert pediatric Radiologist or Neuro-radiologist.

III. Post Natal follow-up will be performed at the following time points (attachment 1):

- At the immediate post-natal period (age 1-3 days) – by Neonatologist.
- Pediatric neurosurgeon by 1 month of age.
- Pediatric urologist, orthopedic surgeon, neurologist if indicated.

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Attachment 1: Data collected:

1. To be filled by the pregnant woman:

age mother: _____ age father: _____ Children at home: _____

previous congenital malformation in family: yes/no

If yes: child / sibling / parent / grand parent

Maternal disease: _____

Paternal disease: _____

Pregnancy nutritional details:

Mother's folic intake:

- Regularly before pregnancy
- Irregularly before pregnancy
- Regularly during pregnancy
- Irregularly during pregnancy
- After third trimester
- Not at all

Milk products: free text:

- Yogurt: 1% / 3% detailed type: _____
quantity/day _____
- Milk: less than 1 glass / more than 1 glass/ none
- Soy products instead of milk: yes/no why: _____
- Other milk products on daily basis:
- Other milk products on weekly basis:

Bread consumption:

- White
- Full wheat
- Other:
- Free text:

How much bread do you eat per day?

Is economic condition a consideration in bread consumption?

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2. To be filled by the Obstetrician:

2.1. Demographic Details

Male / Female Fetal No.: _____ Birth No.: _____
Gestational Age AT ENROLLMENT (W+days): DLP: _____ By US: _____
Type of US: Early screening/ Late screening

- Level of conus on Fetal US: Above L2 / L2-3/ Below L3
- Contents of spinal canal: normal / abnormal
- Detail: bony spur / lipoma/ cyst/ other: _____
- Associated spinal abnormalities: vertebra / scoliosis / other:
- Chiari 2: yes / no * open spinal dysrhapsism: yes / no
- Other CNS malformation yes/no *other malformations: yes/no

*** Tethered cord diagnosed with pre natal in imaging: Yes / No

Other positive findings in Fetal imaging:

Suspected diagnosis: DSM/ Deramal sinus / Lipoma / Low lying conus only/ other

- Technical problems : obese mother / no _____
- Sent for Fetal MRI: YES/NO
A: Age at Fetal MRI (GA – weeks)
B: MRI findings: In agreement with US / Not in agreement with US
C: MRI findings: text _____

2.2 In case a repeat US is performed:

- 1) Date of US examination: ____/____/____ 2) Age at US examination (GA): _____
- 3) Previous Fetal US : normal/abnormal/not performed
- 4) Assessment of skeletal structure: Normal / Abnormal 5) Detail: _____
- 6) Height of conus medullaris: L2 & above / L2-L3 / L4 & below
- 7) Filum terminale thickness: thick/normal

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- 8) Presence of dermal tract: Yes / No
- 9) Mass within spinal canal: Yes / No 10) Mass location (vertebrate): _____
- 11) Tissue characterization of mass: Lipoma External Cyst
 Hemorrhage Cartilage Bar
 Calcification Internal Cyst
 MMC
 Sacrocoxygeal teratoma
- 12) Overall assessment: Normal / Abnormal / Inconclusive
- 13) Diagnosis, combined pathology: Yes / No
- 14) Gynecologists evaluation of US technical quality: Very good / Good / Poor
- 15) Sent for Fetal MRI: YES/NO
- 15 A: Age at Fetal MRI (GA – weeks)
- 15 B: MRI findings: In agreement with US / Not in agreement with US
- 15 C: MRI findings: text _____

2.3 Pregnancy:

- * Spontaneous / fertility treatment / IVF
- * singleton / multiple _____
- * Pregnancy Uneventful / Events: trauma/ documented infection / other:

- * Medical treatment during pregnancy: _____
- * Name regular drugs/medications (for chronic illness): _____ yes/no
- * Name temporary treatment (antibiotics for UTI): _____ yes/no
- * Prenatal imaging: US / MRI / both

2.4 pregnancy screening tests:

- Full, as recommended
- Not at all
- Irregular
- Bloods exams, AFP, BHCG: yes, normal/yes abnormal not performed
- Early US : detailed / regular / Nuchal Translucency exam
- Amniosentesis yes / no if yes, which week of pregnancy:

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3. To be filled by Neonatologist:

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3.1 Birth:

Delivery: CS / VAGINAL remarks: GA at delivery:

APGAR: 1min: 5m:

Dysmorphism : yes/ no

Skin stigmata: Yes / no detail:

Congenital malformation suspected: heart / lungs/ GI /GU/ CNS/ none

Hospital stay days:

Weight at birth: HC at birth: length:

Remarks:

Postnatal US if performed before discharge:

Yes/ no

Details:

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4. To be filled by a Pediatric Radiologist

B01012006/01/a/II/III

- 1) Date of US examination: ____ / ____ / ____ 2) Age at US examination (d): ____
- 3) Previous Fetal US : normal/abnormal/not performed
- 4) Assessment of skeletal structure: Normal / Abnormal 5) Detail: _____
- 6) Height of conus medullaris: L2 & above / L2-L3 / L4 & below
- 7) Filum terminale thickness: thick/normal
- 8) Presence of dermal tract: Yes / No
- 9) Mass within spinal canal: Yes / No 10) Mass location (vertebrate): _____
- 11) Tissue characterization of mass: Lipoma External Cyst
Hemorrhage Cartilage Bar
Calcification Internal Cyst
MMC
Sacrocoxygeal teratoma
- 12) Overall assessment: Normal / Abnormal / Inconclusive
- 13) Diagnosis, combined pathology: Yes / No
- 14) Radiologist evaluation of US technical quality: Very good / Good / Poor
- 15) Sent for POST-NATAL MRI: YES/NO
- 15 A: Age at MRI (weeks)
- 15 B: MRI findings: In agreement with US / Not in agreement with US
- 15 C: MRI findings: text _____

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5. To be filled by Pediatric Neurosurgeon – postnatal before 3m

Date of birth: _____

B01012006/01/a/II/III

Age at exam1: _____

1) Neurological Assessment: Normal / Abnormal

2) skin stigmata: yes/no

if Presence of Dermal Lesions:

I) Mongolian Spot / Light down

II) Simple Dimple

III) Non simple dimple / Deviated gluteal fold

IV) Discoloration patch / Hypertrichoses

V) Midline masses / Tags

3) motor hands / legs: _____

4) sensory hand/ legs: _____

5) leg deformity: _____

6) spine deformity: _____

7) urinary / stools anamnesis:

IF Orthopedic Examination:

1) Hip joint assessment: Normal / Abnormal

2) Hip joint findings:

3) Ankle and feet assessment: Normal / Abnormal

4) Ankle and feet findings:

5) Scoliosis: Yes / No

6) Additional orthopedic findings:

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B01012006/01/a/II/III

IF Urology Examination:

1) Assessment: Normal / Abnormal / NA

2) Urology findings:

3) US assessment: Normal / Abnormal / Irrelevant 4) US findings:

URINOMETRY:

CYSTOGRAPHY:

BLADDER US:

PRESENCE OF hydronephrosis:

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Preliminary results:

- * Fetuses were diagnosed with TCS.
- * Early surgery was possible due to prenatal diagnosis in early infancy in few cases.
- * These babies develop well clinically.
- * These were only pilot cases to demonstrate feasibility and significance of the proposed work.

Research Plan:

Time table: Study planned for 3 years.

Enrollment of Fetuses: 2006-2008 (3 years).

Collection of postnatal data : until June 2009

Statistical and Database analysis: end of 2009

Number of Fetuses expected to be enrolled: 1000 in the control group.

100 in the Study group.

Informed consent: Form for Control arm (Group A):

Form for Study arm (Group B):

Helsinki for the study submitted.

Budget requested:

- **manpower:**
 - **3 Research coordinators: collecting data from all centers, delivering to headquarters, building Database**
 - **computer assistant for troubleshooting**
 - **Statistics**
- **Equipment:**
 - **Software for Database – Filemaker**
 - **Software for US and possible MRI pictures- Adobe Photoshop.**
 - **Software for statistics – SPSS**

Detection of Fetal Spinal Congenital Malformations

- **Portable computer to feed Data and Images of Fetal US and OTHER relevant images**
- **Office equipment and photocopies: Forms to fill for informed consent, forms for Gynecologist, Forms for neonatologist, and other photocopies.**
- **Postal expenses: to provide stamped envelopes to families or the neonatologist who decide to send the postnatal follow-up forms by mail, and other postal expenses.**
- **Photography**
- **Literature**
- **Publication fees**
- **Communication services**

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CV OF PI:

HELSINKI:

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