10.5005/jp-journals-10009-1548

ORIGINAL ARTICLE

Clinical Experience with Kurjak Antenatal Neurodevelopmental Test in Low- and High-risk Pregnancies

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ABSTRACT

Introduction: To assess whether there is a difference in the behavior of fetuses from high-risk pregnancies compared with fetuses from low-risk pregnancies.

Materials and methods: We applied the Kurjak antenatal neurodevelopmental test (KANET) in high-risk (n = 65) and low-risk (n = 119) pregnancies and compared the results. High-risk pregnancies included women with threatened preterm delivery (with premature rupture of membranes and without premature rupture of membranes), hypertension, diabetes, intrauterine growth restriction, and Rh isoimmunization.

Results: There was a difference between the results of KANET applied in these two groups; most of borderline and abnormal results were found in high-risk group, especially from pregnancies complicated by threatened preterm labor. The subgroup of pregnant women with premature rupture of membranes had most of the modified KANET scores.

Conclusion: The median values of the movements of fetuses in low-risk pregnancies were different from those in pregnancies threatened by premature birth and from the rest of the high-risk pregnancies. Fetuses from high-risk pregnancies, including threat of premature birth, had a less active fetal behavior than those from low-risk group.

Keywords: Fetal behavior, High-risk pregnancies, Kurjak antenatal neurodevelopmental test.

How to cite this article: Rotaru O, Vladareanu R, Burnei A, Cristea C, Vladareanu S. Clinical Experience with Kurjak Antenatal Neurodevelopmental Test in Low- and High-risk Pregnancies. Donald School J Ultrasound Obstet Gynecol 2018;12(1):17-22.

Source of support: Nil

Conflict of interest: None

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INTRODUCTION

It is known that obstetricians and neonatologists had some hard time over the years studying the fetal nervous system. The major task is the detection and prevention of early neurological damage.[1-3]

In order to better understand the fetal neurological function, the obstetrician needs to better define the normal and abnormal fetal neurological function *in utero* to predict which fetuses are at risk for adverse neurological outcomes.[4,5] Many factors, such as genetic, external, or pathological conditions can affect the fetal human brain up to a degree that is difficult to assess prenatally. Cerebral palsy is one of the many functional neurological abnormalities that is poorly understood and needs further investigation.[6] Further advancement was the introduction of high-quality three-dimensional/four-dimensional ultrasound (3D/4D US), which allowed the observation of dynamic fetal activity with good image resolution.[7] Therefore, it was assumed that the 4D US evaluation of fetal behavior can give the possibility to differentiate the normal from abnormal brain development. The ability of 4D sonography to visualize the fetal face and its movements and study the facial expressions, including grimace, tongue expulsion, isolated eye blinking, mouth movements, yawning, which 2D US does not, achieved the real breakthrough.[8,9]

This new technology made possible the introduction of KANET (Kurjak antenatal neurodevelopmental test) in low- and high-risk pregnancies, distinguishing between normal and abnormal brain development.[10]

The aim of this study was to apply the new antenatal scoring system KANET to fetuses from high-risk pregnancies for neurological disorders and to compare it with fetuses from low-risk pregnancies.

MATERIALS AND METHODS

During a period of almost 12 months, between June 2016 and May 2017, KANET was applied in 184 singleton pregnancies between 28 and 36 weeks of gestation, recruited in the Department of Obstetrics and Gynecology, Elias University Emergency Hospital, Bucharest, Romania. The inclusion criteria were singleton pregnancies considered "normal" after 2D US examination and pregnancies with high maternal and fetal risk, listed in Table 1. The exclusion criteria are prenatally diagnosed fetal chromosomal

Table 1: Inclusion criteria

Maternal disorders	Hypertension, type II diabetes mellitus
Fetal disorders	Intrauterine growth restriction
Pathological conditions related to the pregnancy	Gestational diabetes, Rh incompatibility, threatened preterm delivery

abnormalities and maternal cigarette and/or alcohol consumption during the pregnancy.

Fetal behavior was assessed by 4D US. All the examinations were performed using Voluson E8, with volumetric transabdominal 7 MHz transducer, by doctors trained in KANET, who were informed about the risk of the pregnancy.

Each patient gave her informed consent to the study.

For assessment of fetal neurobehavior, we used the KANET scoring system presented in Table 2.[7]

Table 3 represents the interpretation of the KANET scores, classifying fetuses into three groups after KANET assessment: normal 14 to 20 points, borderline 6 to 13 points, and abnormal 0 to 5 points. The KANET was repeated every 2 weeks until delivery for borderline and abnormal scores.

The examination maximum time was 30 minutes, with fetus awake and mothers who had avoided food, coffee, and tea for 2 hours before the examination.

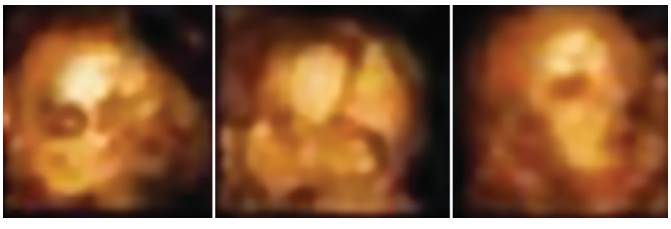
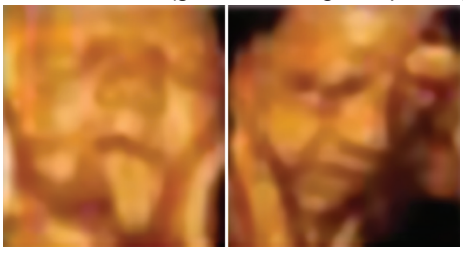
Each parameter of KANET and its meaning is described elsewhere.[11]

The usefulness of KANET to identify fetuses from high-risk pregnancies at neurological risk was the primary outcome.

RESULTS

In this prospective cohort study of 184 singleton pregnancies between 28 and 36 weeks of gestation, 119 are low-risk pregnancies and 65 are high-risk pregnancies.

Table 2: The KANET

Sign	*Score* 0	1	2	*Sign Score*
Isolated head anteflexion 	Abrupt	Small range (0−3 times of movements)	Variable in full range, many alternation (> 3 times of movements)	
Cranial sutures and head circumference 	Overlapping of cranial sutures head circumference below or above the normal limit (-2SD) according to GA	Normal cranial sutures normal head circumference		
Isolated eye blinking 	Not present	Not fluent (1−5 times of blinking)	Fluency (>5 times of blinking)	
Facial alteration (grimace or tongue expulsion) 	Not present	Not fluent (1−5 times of alteration)	Fluency (>5 times of alteration)	

(Cont'd…)

(Cont'd…)

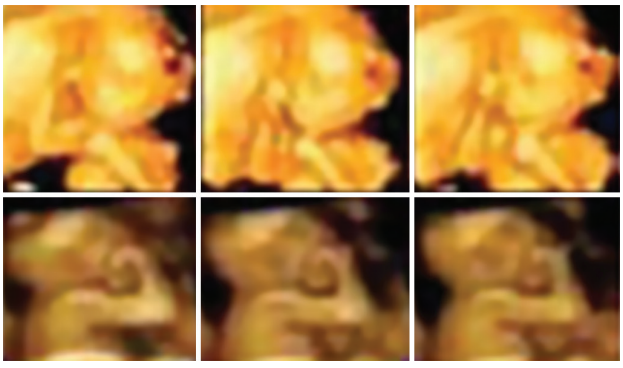
Sign	*Score* 0	1	2	*Sign Score*
Mouth opening (yawning or mouthing) 	Not present	Not fluent (1−3 times of alteration)	Fluency (>3 times of alteration)	
Isolated hand movement 	Cramped	Poor repertoire	Variable and complex	
Isolated leg movement 	Cramped	Poor repertoire	Variable and complex	
Hand to face movements 	Abrupt	Small range (0−5 times of movement)	Variable in full range, many alternation (>6 times of movement)	
Fingers movements 	Unilateralor bilateral clenched fist (neurological thumb)	Cramped invariable finger movements	Smooth and complex, variable finger movements	
Gestalt perception of GMs	Definitely abnormal	Borderline	Normal	
			Total score	

Table 3: Interpretation of the total KANET score

Total score	*Interpretation*
0–5	Abnormal
6–13	Borderline
14–20	Normal

Table 4: Clinical case: Prader–Willi syndrome

KANET: score 6—borderline	
Isolated head anteflexion	2
Cranial sutures and head circumference	0
Isolated eye blinking	1
Facial alterations	1
Mouth opening (yawning or mouthing)	1
Isolated hand movements	1
Leg movements	0
Hand-to-face movements	0
Fingers movements	0
Gestalt perception of general movements	0
Total	6

The final results showed one abnormal score and 5 borderline scores in the low-risk group, one of the five was a Prader–Willi syndrome (Table 4), diagnosed postnatally with methylation-specific multiplex ligation-dependent probe amplification test. The KANET was performed every 2 weeks until delivery and found similar scores.

The Prader–Willi syndrome is a neurogenetic disorder, caused by chromosomal deletion on chromosome 15q11.2-q13, uniparental disomy for chromosome 15, or imprinting center defects affecting the gene expression in this region. It is characterized at the molecular level by abnormal methylation of imprinted regions at 15q11.2-q13 and it is associated in newborns with hypotonia, feeding problems, developmental delay, and/or mental retardation.[11] In this particular case, the prenatal US findings did not reveal any abnormalities, and the KANET score was the sole parameter that was modified.

The high-risk group was divided into two subgroups: 39 pregnant women with threatened preterm delivery (with or without preterm premature rupture of membrane) and 26 pregnant women with other high-risk conditions: hypertension, diabetes, intrauterine growth restriction, and Rh incompatibility. If premature rupture of membranes occurred in a patient included in another subgroup of high-risk pregnancies, she was still evaluated as belonging to the initial subgroup.

The results of p-value of chi-square test for each parameter are shown in Table 5. Highly significant p-values are observed for isolated blinking, facial alterations, isolated hand movements, hand-to-face movements, and finger movements; meanwhile, significant p-values are noted for cranial sutures and mouth opening. Statistical analysis showed a significant p-value for cranial sutures and head circumference for the group of threatened preterm delivery, considering that there were two cases with preterm premature rupture of membranes

Table 5: Application of KANET in low-risk and high-risk pregnancies

		KANET score			
Sign	*Risk*	*0*	*1*	*2*	*p-value*
Head anteflexion	High	1	16	48	0.081
	Low	9	23	87	
Cranial sutures	High	2	16	47	0.036
	Low	10	30	79	
Isolated blinking	High	9	25	31	0.000006
	Low	7	27	85	
Facial alterations	High	10	44	11	1.42×10^{-11}
	Low	10	23	86	
Mouth opening	High	6	32	27	0.00198
	Low	5	28	86	
Isolated hand movements	High	4	32	29	0.000091
	Low	5	24	90	
Isolated leg movements	High	0	17	48	0.265
	Low	6	20	93	
Hand-to-face movements	High	13	34	18	3.62×10^{-9}
	Low	5	22	92	
Finger movements	High	10	35	20	1.65×10^{-10}
	Low	5	16	98	
General movements	High	0	16	49	0.308
	Low	4	19	96	

Red: statistically highly significant (p-value < 0.001); Violet: statistically significant (p-value < 0.05); Black: statistically insignificant

which had a score of 0 for this parameter and severe oligohydramnios (amniotic fluid index score under 5). Overall, in this subgroup, we observed a reduced volume of amniotic fluid and less active fetal movements.

We compared the distribution of KANET scores in the three groups: low-risk pregnancies, threatened preterm delivery, and other high-risk depending on the classification of the results (abnormal, borderline, and normal), and we noticed highly significant differences between them. The chi-square test p-value was $p = 0.00000106 < 0.001$. The analysis of variance (ANOVA) also showed significant differences between the mean values of KANET. Because the ANOVA test result was significant, we used a *post hoc* Tukey honest significant difference test to identify the two groups between which differences are observed. Thus, we found that the mean values of the low-risk group are higher than the other two groups. In the threatened preterm delivery group, we compared the distribution of two subgroups (with and without preterm premature rupture of membrane) and we had no significant differences (chi-square test p-value $= 0.525 > 0.005$), although an abnormal or borderline KANET score is higher in the subgroup with preterm premature rupture of membrane.

The median values of movements of the fetuses in low-risk pregnancies were different from those in pregnancies threatened by premature birth and from the rest of high-risk pregnancies.

Fetuses from high-risk pregnancies, including threat of premature birth, had a less active fetal behavior than those from the low-risk group.

CONCLUSION

In recent years, it has been attempted to create a diagnostic test for the assessment of fetal behavior. The KANET is the first 4D US prenatal neurological screening test with encouraging results.[12-15]

Our study shows that some prenatal conditions are temporarily affecting the fetal neurological status and that the KANET might be useful for neurobehavioral assessments. The KANET appears to be able to differentiate fetuses with normal and abnormal neurological development and this gives major contribution to understanding more about functions and development of fetal central nervous system.[5,16-19] Neurological disability is one of the most feared complications in perinatal medicine and its diagnosis antenatally is one of the greatest challenges in obstetrics.[20,21]

In Romania, the KANET is used as an evaluation test in clinical practice, but in order to introduce it as a screening tool, more research is needed in our department of materno-fetal medicine. Until now, we observed the great potential for the antenatal detection of serious neurological problems.

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