ORIGINAL RESEARCH

Experiences and Results of the KANET Test Application in Clinical Practice in Tuzla, Bosnia and Herzegovina

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Abstract

Background: Antenatal neurodevelopmental test (KANET) is a test based on prenatal assessment of the fetal behavior followed by four-dimensional (4D) sonography. The estimation of the fetal behavior has provided a promising ability to understand the hidden function of the fetal nervous system developmental pathway. The test was named after the first author: Kurjak antenatal neurodevelopmental test (KANET).

Materials and methods: The KANET test was administered to 141 pregnant women in single pregnancy between the 28th and the 38th weeks of pregnancy. The fetal behavior was assessed using 4D ultrasound.

Results: The 3D/4D ultrasound allowed the study of the fetal behavior which directly reflects the development and maturation processes of the central nervous system (CNS) of the fetus, the distinction between normal and abnormal brain development as well as prenatal neurological damage diagnosis. From 141 patients, 69% patients had a normal KANET score, 27% had borderline KANET score, and only 4% had abnormal KANET score. The results of the KANET screening showed that only high-risk pregnancies with intrauterine growth restriction (IUGR) and diabetes mellitus type I showed abnormal results for 5 patients (41%).

Conclusion: This is a method that has been applied over the past 10 years and studies show that it is a powerful diagnostic tool and can be introduced into everyday clinical practice. The KANET test is able to evaluate the fetal neuroanatomy and detect neurological disorders based on the fetal behavior assessment using 4D ultrasound in the same way that the newborn is assessed postnatal.

Keywords: 4D ultrasound, Fetal neurological development, KANET.

Donald School Journal of Ultrasound in Obstetrics and Gynecology (2019): 10.5005/jp-journals-10009-1595

Introduction

The introduction of 4D ultrasound technology in fetal medicine, besides extensive and detailed examination of fetal anatomy, has also enabled something that was not possible until then, which is a direct assessment of the fetal behavior in real time.[1–3] The fetal behavior reflects the development of the fetal CNS, which has a specific evolutionary pattern. The type of fetal movement and the overall behavior of the fetus can be studied in a similar way as the newborn who develops and whose the motor system is growing. For example, a newborn born of 30 weeks definitely does not have the same behavior as a newborn born of 40 weeks, and a newborn on the first day of life has a different pattern of behavior than a month later. Similarly, the fetus in 14 weeks has a different fetal behavior in 26 or 36 weeks. By a certain moment, the behavior corresponding to each week of pregnancy was identified.[3] One very important aspect is that the process of human brain development that is very sensitive is not predetermined, so it can be influenced by genetic and epigenetic factors and can be affected by incidents that can occur at any time during pregnancy. Another worrying point is that the degree to which brain development will be affected by external factors that cannot be predicted prenatally. The brain development begins in the third gestational week and depends from the molecular events of gene expression and the early environmental input.[4,5] Also exposure to excess stress during intrauterine life may affect the fetal neurological development and lead to mental health disorders in childhood and even in adult life.[6–10] Therefore, the assessment of the fetal neurological status remains one of the biggest challenges in perinatal medicine, and as a low-risk pregnancy test for pregnancy but also for cases that can be prematurely suspected of a certain degree of neurological damage.[11]

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How to cite this article: Tinjić S. Experiences and Results of the KANET Test Application in Clinical Practice in Tuzla, Bosnia and Herzegovina. Donald School J Ultrasound Obstet Gynecol 2019;13(3):94–98.

Source of support: Nil

Conflict of interest: None

Materials and Methods

Study Design

In the period from May 2015 to April 2018, the KANET test was administered to 141 pregnant women in single pregnancy between the 28th and the 38th week of pregnancy. The gestational age was assessed by the first day of the last period and confirmed by the ultrasound assessment. The fetal behavior was assessed using 4D ultrasound. The examination was used by Voluson E6 and S10 (ultrasound of GE Healthcare, USA), with a volumetric transabdominal probe of 5 MHz. The examinations were performed by one doctor. All pregnant women signed an informed consent to the study. The study was conducted in the private Gynaecological Polyclinic "Korak do Života" in Tuzla, Bosnia, and Herzegovina, including 12 high-risk and 129 low-risk pregnancies as controls. The inclusion criteria for high-risk and low-risk pregnancies were as follows:

- Family history: previous child with cerebral palsy;
- Personal pregnancy history: type 1 and 2 diabetes mellitus, hypertension, drug abuse, thrombophilia, anemia, infections

Table 2: Three groups of the KANET's scoring

Total score	*Interpretation*
0–5	Abnormal
6–9	Borderline
10–16	Normal

during pregnancy, first pregnancy after 35 years, and pregnancies after the procedures of medically assisted fertilization;
- Disorders of pregnancy: polyhydramnios, threatening premature birth, intrauterine infections, and viral diseases;
- Fetal state: intrauterine growth restriction (IUGR), abnormal cardiotocography, biophysical profile, and Doppler.

The KANET Score System

To assess the neurological behavior of the fetus, we used the KANET score system shown in Table 1.

After a detailed 2D US measurement of the fetal growth and a review of the volume of the placenta and amniotic fluid, mothers were offered an assessment of the fetal behavior using the KANET scoring system, using 4D ultrasound. The test was carried out while the fetuses were awake. The maximum scanning time was 30 minutes. According to the results of the assessment, the fetal behavior is divided into three groups (Table 2).

The KANET borderline scans were repeated for two weeks until the birth, while patients with abnormal KANET score were hospitalized due to intensive control of pregnancy and time planning and the way to end pregnancy by giving birth.

Results

Diagnosis in the High-risk vs the Low-risk Pregnancy

In this prospective longitudinal study, the KANET test was administered to 141 pregnant women in single pregnancy between 28 and 38 weeks of pregnancy (Tables 3 and 4). In the high-risk group, there were 12 pregnant women and 129 pregnant women with low risk. The primary goal of the study was the importance of the KANET test to identify the fetuses from high-risk pregnancies to neurological risk and then to compare the results between high-risk and low-risk groups.

In the group of high-risk pregnancy women out of total 12 patients, we had 3 diagnosed with IUGR, 2 with diabetes mellitus type 1, 1 with hypertensio arterialis, 1 with hypothyreosis 1, and 2 with cerebral palsy.

In the group of low-risk pregnacy, 45 women (out of 129 of them) went through *in vitro* fertilization (IVF), 29 had first pregnancies after 35 years, 15 had vaginal infection, 5 had premature birth, 18 had anemia, 2 had uterus anomalies, and 15 of them experienced bleeding during the pregnancy.

Table 3: Diagnosis in high-risk pregnancies

Diagnosis	*Number*
IUGR	3
Diabetes mellitus type 1	2
Hypertensio arterialis	1
Hypothyreosis	1
CP	2
Drug abuse and hepatitis C	1
Nuchal cord	1
Polychydroamnion	1
Total	12

The KANET Score Output

Of 141 patients, 69% patients had a normal KANET score, 27% had borderline KANET score, and only 4% had abnormal KANET score (Fig. 1).

The results of the KANET screening showed that only high-risk pregnancies with IUGR and diabetes mellitus type 1 showed abnormal results for 5 patients (41%) (Fig. 2).

Table 4: Diagnosis in low-risk pregnancies

Diagnosis	*Number*
IVF pregnancies	45
First pregnancies after 35 years	29
Vaginal infections	15
Premature birth	5
Anemia during pregnancy	18
Uterus anomalies	2
Bleeding in pregnancy	15
Total	129

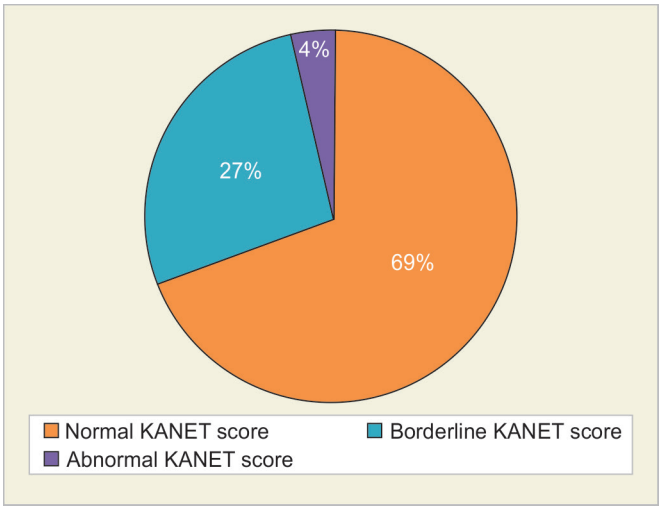


Fig. 1: Results of the KANET's scoring

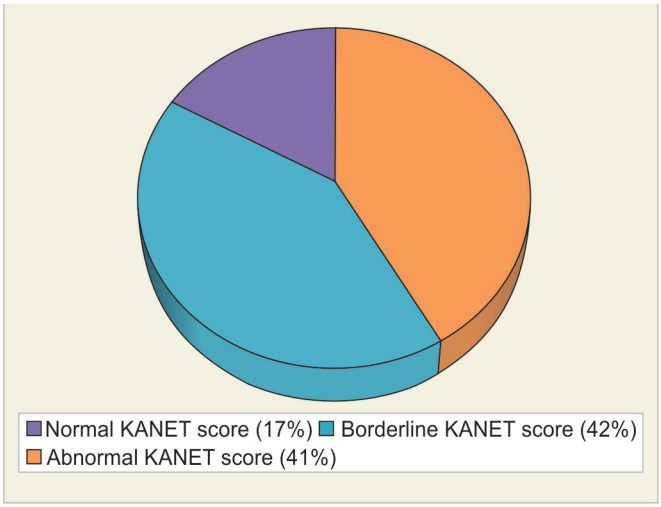
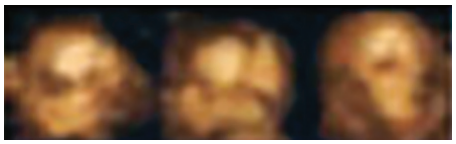
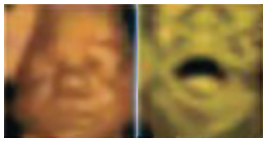
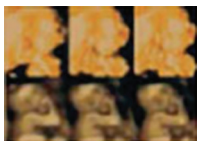


Fig. 2: Results of the KANET test in high-risk pregnancies

Table 1: The KANET score system for the evaluation of the fetal neurological behaviors

	Score			*Sign score*
Sign	*0*	*1*	*2*	
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	Normal cranial sutures with measurement of HC below or above the normal limit (−2SD) according to GA	Normal cranial sutures with normal measurement of HC according to GA	
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)	
Mouth opening (yawning or mouthing) 	Not present	Not fluent (1–3 times of alteration)	Fluency (>3 times or 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 at movements)	
Fingers movements 	Unilateral or bilateral clenched fist, (neurological thumb)	Cramped invariable finger movements	Smooth and complex, variable finger movements	
Gestalt perception of general movements	Definitely abnormal	Borderline	Normal	
			Total score	

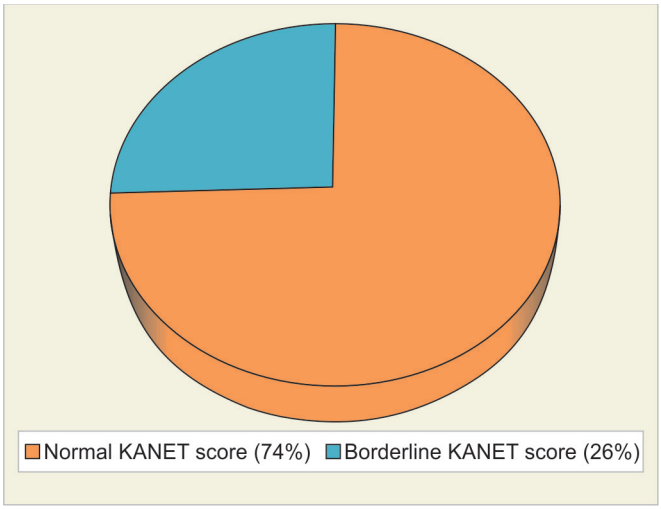


Fig. 3: Results of the KANET test in low-risk pregnancies

Table 5: High-risk group pregnancies and the KANET score

		KANET results		
High-risk group	*Total*	*Normal*	*Borderline*	*Abnormal*
IUGR	3	0	0	3
Diabetes mellitus type 1	2	0	0	2
Hypertensio arterialis	1	1	0	0
Hypothyreosis	1	0	1	0
CP	2	1	1	0
Drug abuse and hepatitis C	1	0	1	0
Nuchal cord	1	0	1	0
Polyhydramnios	1	0	1	0
Total	12	2	5	5

Of 129 patients with low-risk pregnancies, 96 of them (74.42%) had a normal KANET score and 33 (25.58%) of them had a borderline KANET score (Fig. 3).

In the high-risk group of 12 women, three were with IUGR and had abnormal KANET score, two were diagnosed with diabetes mellitus type I and also had an abnormal KANET score, one patient with hypertensio arterialis had a normal KANET score, and one with hypothyreosis had borderline KANET score. Of two patients with cerebral palsy (in previous pregnancies), one had borderline and the other had normal KANET score. One patient who abused drugs had hepatits C and had a borderline KANET score, one with nuchal cord had a borderline KANET score, and the patient with polychydroamnion had a borderline KANET score (Table 5).

Antenatally in one newborn (with IUGR), there is a slowed psychomotor development. Pregnancy ended with cesarean section in July 2017, five weeks after the abnormal KANET test IUGR was diagnosed.

In the low-risk group of 129 patients, 45 of them had IVF and 36 had a normal KANET score, and 9 had borderline KANET score. In the pregnancies after 35 years, we had 29 patients: 23 of them had normal KANET score and 6 of them had borderline KANET score.

Of 15 patients with vaginal infections, 11 of them had normal and 4 of them showed borderline KANET score. Of 5 patients who gave birth prematuerly, 2 of them had normal and 3 of them had borderline KANET score. Of two patients with uterus anomalies, 1 had borderline and 1 had normal KANET score, and of 15 patients who experienced bleeding during pregnancy, 10 had normal and 5 had borderline KANET score (Table 6).

Table 6: Low-risk group pregnancies and the KANET score

		KANET results		
Low-risk group	*Total*	*Normal*	*Borderline*	*Abnormal*
IVF pregnancy	45	36	9	0
First pregnancy after 35 years	29	23	6	0
Vaginal infections	15	11	4	0
Premature birth	5	2	3	0
Anemia during pregnancy	18	13	5	0
Uterus anomalies	2	1	1	0
Bleeding in pregnancy	15	10	5	0
Total	129	96	33	0

Table 7: Total score interpretation of the KANET test

Total score interpretation	*High risk (n = 12)*	*Low risk (n = 129)*
0–5 abnormal	5 (41.67%)	0
6–9 borderline	5 (41.67%)	33 (25.58%)
10–16 normal	2 (16.67%)	96 (74.42%)

The total score of high-risk and low-risk pregnancy groups with the KAANET score interpretation is presented in Table 7.

Discussion

Conditions during early brain development, besides genetic inheritable factor, are decisive in directing cellular proliferation and differentiation to normal structure and function or to some pathologic brain condition.[4–12] The development of novel intrauterine diagnostic approaches for real-time monitoring of the fetal brain development is highly needed and would be of great help in establishing an early diagnosis. The KANET test presents such a novel approach and is the first method for which 4D ultrasound is used in estimating the fetus in the same way as the newborn is neurologically assessed after the birth by neonatologists. It presents a significant diagnostic tool for the detection of neurological damage and evaluation of the fetal neurology for conditions that have been unavailable in traditional prenatal diagnostic methods so far. At least two years of postnatal monitoring should be available and documented for all the fetuses to which KANET has been applied, in order to make conclusive conclusions.[3] Using KANET in pregnant women, with high and low-risk pregnancy, will give more knowledge about early detection of the risk for the fetal neurological damage, in order to allow accurate prenatal diagnosis and enable early treatment. The outcome of neurological development in these newborns can be improved.[3]

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