

EDITORIAL

Precision Medicine: Trends In Perinatal Gynecology

Asim Kurjak^{1,2,3} 

¹Department of Obstetrics and Gynecology, Clinical Hospital "Sveti Duh", Zagreb, Croatia

²Sarajevo School of Science and Technology, Sarajevo, Bosnia and Herzegovina

³International Academy of Science and Art in Bosnia and Herzegovina

Corresponding Author: Asim Kurjak MD, PhD. Department of Obstetrics and Gynecology, Clinical Hospital "Sveti Duh", Zagreb, Croatia; E-mail: asim.kurjak1@yahoo.com; Phone: +387 33 569 540; ORCID ID: <https://orcid.org/0000-0002-1680-3030>.

Pages: 1-4 / Published online: 19 August 2024

Cite this article: Kurjak A. Precision Medicine: Trends In Perinatal Gynecology. Sar Med J. 2024; 1(1): Online ahead of print.  DOI: 10.70119/0001-24

Original submission: 14 March 2024; **Revised submission:** 06 June 2024; **Accepted:** 10 July 2024

Abstract

The Kurjak Antenatal Neurodevelopmental Test (KANET) has revolutionized prenatal care and fetal neurology by providing a non-invasive method to assess fetal neurodevelopment using four-dimensional ultrasound (4D US). Over the past ten years, KANET has been widely implemented across various clinical settings, enabling the early detection of neurodevelopmental disorders. This early identification is crucial for timely intervention and improved long-term outcomes. KANET standardizes the assessment of fetal neurological function, offering a structured and objective approach that enhances our understanding of fetal behavior and its implications for postnatal development. While KANET demonstrates high specificity and a low false-negative rate, its sensitivity in detecting specific conditions like cerebral palsy (CP) remains limited. The test's widespread use has not only informed clinical management strategies but also promoted further research into prenatal neurodevelopment and potential prenatal interventions. Recent studies highlight differences in fetal behavior in pregnancies complicated by gestational diabetes, suggesting the potential for KANET to inform future neurodevelopmental outcomes. Continued research and refinement of KANET are essential to enhance its predictive accuracy and ensure comprehensive postnatal follow-up.

Keywords: fetal development, screening, prognosis.

Significance of the Kurjak Antenatal Neurodevelopmental Test

The introduction of the Kurjak Antenatal Neurodevelopmental Test (KANET) has significantly impacted clinical practice, particularly in prenatal care and fetal neurology (1-8). According to our opinion, the key aspects of its significance and importance are (1):

- early detection of neurodevelopmental disorders
- non-invasive assessment,

- enhanced understanding of fetal behavior,
- standardization in fetal neurology,
- guidance for clinical management,
- promoting research and innovation.

KANET has enabled healthcare providers to detect potential neurodevelopmental disorders much earlier than by traditional methods. By using four-dimensional ultrasound

(4D US) to assess fetal behavior and movements, KANET offers a window into the developing fetal nervous system, allowing clinicians to identify abnormalities that could indicate future neurological issues (1-8). This early detection is crucial for timely intervention and management (7).

As a non-invasive procedure, KANET provides a safe way to assess fetal development without posing risks to the mother or fetus (4-6). This aspect is particularly valuable in prenatal care, where minimizing risks is a priority.

KANET has contributed to a deeper understanding of fetal behavior and its correlation with postnatal neurodevelopment (9). It has highlighted that certain patterns in fetal movements and behavior can be early indicators of conditions like developmental delays (among them cerebral palsy) (1-9).

The development of KANET represents a significant step towards standardizing the assessment of fetal neurodevelopment (9). Before KANET, assessment of fetal behavior by two-dimensional ultrasound (2D US) was less standardized and more subjective. The test provides a structured and objective method to evaluate fetal neurological function, making it possible to compare results across different clinical settings and studies (1, 4, 5).

The results from KANET can inform clinical decisions and management strategies (1-9). For instance, identifying a fetus at high risk for neurological issues allows healthcare providers to plan for appropriate monitoring and interventions postnatally, potentially improving long-term outcomes for the child (9).

KANET has spurred further research into prenatal neurodevelopment and the factors that influence it (1). It has opened up new avenues for exploring how prenatal interventions might mitigate or prevent neurodevelopmental disorders (1-9).

Ten Years of Wide Clinical Use of KANET

Based on the detailed review of the investigation which has been conducted for almost

ten years, here are the most important points regarding the use of KANET over the mentioned period (1-9):

- development and purpose of KANET,
- clinical findings and reliability,
- postnatal outcomes.

KANET was developed to provide a standardized method to evaluate fetal neurodevelopment using four-dimensional ultrasonography (4D US) (9). This test assesses fetal behavior and general movements to identify potential neurodevelopmental disorders early, even before birth.

The test has been widely used across multiple centers, with numerous published papers reporting over 3,709 fetuses assessed (1). The findings revealed that abnormal or borderline KANET scores are more prevalent in high-risk pregnancies (1-11).

KANET demonstrated high specificity and a low false-negative rate, indicating that a normal KANET score strongly correlates with normal postnatal development (1). However, its sensitivity, particularly in detecting conditions like cerebral palsy (CP), remains limited (1).

Of the infants assessed postnatally, a vast majority (98.3%) had normal development. Abnormal KANET scores were associated with a higher incidence of severe developmental delays and conditions like CP (1). However, even among those with abnormal KANET scores, a significant number still developed normally postnatally (1).

Challenges and Limitations of KANET

While KANET has significant benefits, it also has limitations, such as its sensitivity in detecting specific conditions like CP (1). Despite these limitations, its high specificity and positive predictive value make it a valuable tool in prenatal screening and diagnosis (1).

In summary, the introduction of KANET into clinical practice has been a groundbreaking development in prenatal medicine. It has enhanced the ability of clinicians to detect and understand neurodevelopmental issues

early in life, offering significant potential for early intervention and better outcomes for affected individuals (1-9).

The accuracy of KANET in predicting neurodevelopmental outcomes, particularly for conditions like CP, is constrained by the test's limited sensitivity (1). Additionally, the diverse intrauterine environment complicates the interpretation of fetal neurobehavioral data.

Promising Long-Term Investigations Post-KANET Scoring

Recent studies have explored the correlation between KANET scores and long-term neurodevelopmental outcomes, especially in cases involving pregnancies complicated by gestational or pregestational diabetes (10,11). Research, including a PhD thesis focused on assessing fetal behavior via 4D US in pregnant women with gestational diabetes, has shown significant differences in fetal movements between complicated and uncomplicated pregnancies (10-12). Higher HbA1c levels were associated with altered fetal behavior (12). Preliminary findings indicate that children with lower KANET scores as fetuses tend to perform worse on neurodevelopmental tests at ten years of age. These promising results warrant further investigation.

Recommendations for Future Use of KANET

It could be suggested that while KANET is a valuable tool for early detection of poten-

tial neurodevelopmental issues, it should not replace comprehensive postnatal assessments.

KANET is the first neurological test that very successfully separates healthy children from those with suspected cerebral palsy, and soon for some other neurodevelopmental diseases. After attending a week-long education (we have centers in Zagreb, Sarajevo and Athens) attendees are awarded a KANET diploma.

At the moment, our groups are ready to submit a research project related to Screening for cerebral palsy with KANET test and artificial intelligence. We believe that KANET is an ideal test for screening procedures. In the meantime, all groups in collaborative studies are trying to assess scientifically reliable sensitivity, specificity and accuracy of the new test. Until now, 14 PhD thesis were defended in Croatia, Greece, Romania, Bosnia and Herzegovina, Saudi Arabia, Indonesia, Qatar, Egypt, Libya, and India.

Acknowledgment: Thank you to all the colleagues who have worked for years on the development and use of KANET in clinical practice.

Author Contribution: Conceptualization, Formal Analysis, Methodology, Writing – Original Draft, and Writing – Review & Editing were carried out by Asim Kurjak.

Financial support and sponsorship: There was no funding.

Conflict of interest: The authors have nothing to disclose.

REFERENCES

1. Kurjak A, Stanojevic M, Antsaklis P, Panchal S, Porovic S, Salihagic Kadic A, et al. A Critical Appraisal of Kurjak Antenatal Neurodevelopmental Test: Five Years of Wide Clinical Use. *Donald School J Ultrasound Obstet Gynecol.* 2020; 14 (4):304-10. doi: 10.5005/jp-journals-10009-1669.
2. Kurjak A, Miskovic B, Stanojevic M, Amiel-Tison C, Ahmed B, Azumendi G, et al. New scoring system for fetal neurobehavior assessed by three- and four-dimensional sonography. *J Perinat Med.* 2008;36(1):73-81. doi: 10.1515/JPM.2008.007.
3. Kurjak A, Stanojević M, Predojević M, Laušin I, Salihagić-Kadić A. Neurobehavior in fetal life. *Semin Fetal Neonatal Med.* 2012;17(6):319-23. doi: 10.1016/j.siny.2012.06.005.
4. Kurjak A, Antsaklis P, Stanojevic M, Vladareanu R, Vladareanu S, Neto RM, et al. Multicentric studies of the fetal neurobehavior by KANET test. *J Perinat Med.* 2017;45(6):717-27. doi: 10.1515/jpm-2016-0409.
5. Kurjak A, Spalldi Barišić L, Stanojević M, Antsaklis P, Panchal S, Honemeyer U, et al. Multi-center results on the clinical use of KANET. *J Perinat Med.* 2019;47(9):897-909. doi: 10.1515/jpm-2019-0281.

6. Kurjak A, Spalldi Barišić L, Antsaklis P, Stanojevic M, Medjedovic E. What did We Learn from the Structural and Functional Development of Fetal Brain Using Four-dimensional Sonography? *Donald School J Ultrasound Obstet Gynecol* 2020;14(3):245–61. doi: 10.5005/jp-journals-10009-1659.
7. Kurjak A, Stanojevic M, Antsaklis P. Recent Results and Future Challenges in the Assessment of Fetal Brain Function. *Donald School J Ultrasound Obstet Gynecol* 2021;15(1): 10–37. doi: 10.5005/jp-journals-10009-1682.
8. Antsaklis P, Kurjak A. KANET Test in Clinical Practice: Lessons Learned and Future Challenges. *Donald School Journal of Ultrasound in Obstetrics & Gynecology* 2023;17(2):165-80. doi: 10.5005/jp-journals-10009-1970.
9. Stanojevic M, Talic A, Miskovic B, Predojevic M, Vladareanu R, Vladareanu S, et al. An attempt to standardize Kurjak's Antenatal Neurodevelopmental Test: Osaka Consensus Statement. *Donald School J Ultrasound Obstet Gynecol*. 2011; 5: (4): 317-29. doi: 10.5005/jp-journals-10009-1209. doi: 10.1515/JPM.2008.007.
10. Athanasiadis AP, Mikos T, Tambakoudis GP, Theodoridis TD, Papastergiou M, Assimakopoulos E, et al. Neurodevelopmental fetal assessment using KANET scoring system in low and high risk pregnancies. *J Matern Fetal Neonatal Med*. 2013;26(4):363-8. doi: 10.3109/14767058.2012.695824.