Analysis of antepartum cardiotocography based on S/k proportions and probability in 20 minutes

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Abstract

Objectives: although mortality and perinatal asphyxia in newborns have been considerably reduced, there are still deficiencies in screening and diagnosis methods for intrapartum fetal well being that aim to detect its early alterations. Therefore, the purpose of this research was to apply a methodology based on probability and entropy and confirm its capacity to detect normal and abnormal fetal cardiac dynamics from 20-minute cardiotocographic tracings.

Methods: 80 cardiotocographic tracings of pregnant women in the last trimester were collected, of which the minimum and maximum fetal heart rate were evaluated every 10 seconds, as well as its repetitions along with their probability and the diagnostic S/k ratio. Finally, the statistical analysis was carried out to establish the diagnostic capacity of the method concerning the clinical evaluation and interpretation of the cardiotocographic tracing, taken as the Gold Standard.

Results: it was confirmed that S/k ratio values differentiated normal from abnormal fetal cardiac dynamics with sensitivity and specificity values of 100% and a Kappa coefficient of 1.

Conclusion: the applicability of a diagnostic mathematical method of cardiotocography was confirmed, which suggests its implementation in the clinical context to detect alterations in fetal well-being in 20 minutes.

Key words *Cardiotocography, Probability, Diagnosis*

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Introduction

Approximately 4 million babies born annually present perinatal asphyxia, of which almost 900,000 die from this cause. Several measurements are performed in the clinical context such as the biophysical profile, the modified biophysical profile, the measurement of the amniotic fluid index, and the Doppler of the umbilical artery, among others, that serve to assess fetal well-being and therefore potentially they can avoid the appearance of this outcome by detecting early alterations that can be intervened in a timely manner. However, it is cardiotocography that is used in the admission of pregnant women in the emergency services of hospitals around the world.[1]

Cardiotocographic monitoring is an accepted examination in obstetric practice that consists of continuous printed or electronic recording of the fetal heart rate and maternal uterine contractions through a monitor placed on the abdominal wall of the mother, which integrates pressure and ultrasound transmission measurements to detect uterine contractions and fetal heart rate, respectively.[2]Analysis of this exam typically involves observation of cardiotocographic tracing parameters such as baseline or the presence of accelerations and decelerations that together provide a basis for classifying the recordings as normal, suspicious, or abnormal, although the terms and criteria vary among medical institutions that establish guidelines for the interpretation of cardiotocography.[3,4]

This examination is considered to provide important information on the neurological and myocardial function of the fetus during intrapartum and antepartum surveillance, however, the implementation of this examination in its intermittent and continuous modalities in clinical practice has generated an increase in obstetric interventions that do not have necessarily led to a decrease in fetal morbidity and mortality, since there is little correlation between unfavorable outcomes and fetal heart rate, as has been evidenced in the absence of differences between neonates who die during or after a term close to delivery, when just as there are no differences regarding the rate of presentation of cerebral palsy or the presence of acidosis detected by umbilical cord blood.[5]

In addition, it has been observed that there are poor sensitivity and specificity values associated with this test, that there is no benefit from the use of cardiotocography in low-risk women, and an increase of at least 20% in the performance of caesarean sections among pregnant women. Thus, this has led to questioning the real usefulness of cardiotocographic monitoring in women who are in labor.[6-10]

Further, a factor that must be considered is the lack of reproducibility in the traditional diagnosis of fetal cardiotocography, since it depends on the visual inspection of clinicians and their experience, as well as the analysis of the factors that clinically translate into changes in fetal cardiac physiology. This limitation comprises one of the most outstanding difficulties in the field of obstetrics, because of which other approaches are required that allow for a more accurate diagnosis of fetal well-being. [11-13]

The traditional evaluation of cardiac behavior in cardiotocography focuses on the homeostatic conception, in which the functioning of healthy hearts is associated with a periodic behavior of the heart rate over time.[14] However, research in recent decades has found that both excessive periodicity and randomness are associated with disease, while an intermediate behavior corresponds to health. This conclusion is also applicable to obstetrics since sinusoidal patterns in cardiotocography have been shown to be associated with fetal disease, albeit controversially.[15,16]

Based on probability theory, which has been formalized by means of three axioms established by Kolmogorov, dimensionless mathematical measures that allow the quantification of the possible future occurrence of an event can be established. On the other hand, entropy,[17-19] which has been reinterpreted over time in the contexts of the kinetic theory of gases, statistical mechanics, and information theory,[20-22] has allowed evaluating complex systems and establishing quantifications of the changes that the systems may present over time, among others.

Based on these two theories, a methodology has been developed that manages to differentiate between normal cardiotocographic tracings of patients, as well as those in evolution between both states, by considering fetal cardiac dynamics as a probabilistic system, where the entropy S/k ratio allows evaluating the self-organization of the probability distribution of said systems.[23,24] However, this method must be validated with a greater population extension to confirm that the diagnostic parameters of this method are preserved and are clinically applicable.

The purpose of this research is to apply a diagnostic mathematical methodology based on probability and the S/k ratio to confirm its clinical applicability, for which 80 cardiotocography records of pregnant women in the last trimester were analyzed and the diagnosed fetal well-being was evaluated with this method with respect to the traditional clinical interpretation through a blind study to quantify its accuracy and diagnostic agreement.

Methods

Eighty cardiotocography records were analyzed in this research, which were taken from Insight Group and San Luis Clinic's databases in Bogotá and Bucaramanga, Colombia, respectively. The records were collected between 2019 and 2020. These records came from previously healthy pregnant women over 21 years of age who underwent cardiotocography in the last trimester and consisted of the printed cardiotocography tracing performed by medical indication along with data related to the medical diagnosis. The clinical interpretation of the tracings was established as reactive and non-reactive, coinciding with the diagnosis of normality and abnormality based on the clinical and paraclinical examination of an obstetrics specialist.

The treatment of the data consisted, initially, in blinding the clinical diagnoses of the cardiotocography records to develop a blind study. Those tracings considered non-reactive and that after the clinical evaluation was diagnosed as fetal normal, were discarded. Additionally, the tracings that did not meet the minimum quality necessary to be interpreted by the clinical expert in obstetrics were not taken into account. After this, 80 cardiotocographic records were analyzed, which were taken individually, and the values of the minimum and maximum fetal heart rate were discriminated every 10 seconds during the 20 minutes of tracing the records by visual inspection of the records according to the visualization of the clinical expert. Then, all heart rate values were compiled and the probability of the number of times a certain heart rate was repeated in 10-second intervals was calculated by applying Equation 1 manually, as follows:

$$P_n = \frac{\text{Frequency of occurence of heart rates}}{\text{Totality of heart rate frequencies}} \quad \text{Equation 1}$$

Subsequently, all the frequencies of each tracing were added, and their probability and the maximum probability of the complete cardiotocography tracing were obtained. Then, the entropy of the cardiotocographic tracing was calculated using Equation 2:

$$S = -k \sum_{n=0}^{N} P_n \, Ln(P_n) \qquad \text{Equation 2}$$

Where S corresponds to the entropy of the tracing and k the Boltzmann constant or $1.38x10^{-23}$ Joules/Kelvin.

Equation 2 was cleared in terms of the S/k ratio, thus obtaining Equation 3 in order to issue a mathematical diagnosis:

$$\frac{S}{k} = -\sum_{n=0}^{N} P_n \, ln(P_n) \qquad \text{Equation 3}$$

Regarding the statistical analysis, the clinical diagnoses of reactivity and non-reactivity of each cardiotocography tracing were established based on clinical parameters (considered as the gold standard), were unblinded, and compared with respect to the mathematical diagnosis, which encompasses: normality, evolution to disease, and abnormality. Based on this, the sensitivity, specificity, and diagnostic agreement of the mathematical method to diagnose normality and abnormality were calculated in relation to the clinical diagnosis of reactivity and non-reactivity, respectively, excluding the mathematical cases of evolution.

According to article 11 of resolution 008430 of 1993 of the Ministry of Health,[25] this investigation is considered risk-free, since mathematical calculations were carried out on non-invasive diagnostic tests previously requested and compiled in databases, thus maintaining anonymity and integrity of the research subjects.

Results

The probability values obtained through Equation 1 of the fetal cardiac dynamics of all the tracings ranged between 0 to 0.883, where the values of the reactive records were found between 0 to 0.383 while the non-reactive records were found between 0 to 0.383. 0.683 (Table 1).

On the other hand, the values of the S/k ratio of the fetal cardiac dynamics of all the tracings obtained through Equation 3 ranged between -2.35 to -0.98, whereas the values of the normal tracings were between - 1.99 to -1.71, while abnormal records ranged between -2.35 to -0.98. The values of the cases mathematically diagnosed as "evolving to disease" ranged from -2.01 to -1.68 (Table 2). As can be seen in Figure 1, the values that correspond to normality are found between the extremes of the evolution of the disease and abnormality, with no overlapping between these values, which allows visualizing that the quantifications of the methodology manage to establish these differences.

The previous results indicate that mathematically (Table 2), there was a correspondence of the mathematical diagnosis of normality with respect to the clinical diagnostic parameter; such an observation is also consistent with the mathematical diagnosis of abnormality with respect to clinical nonreactivity. In addition, the cases mathematically diagnosed as "evolving to disease" included reactivity and non-reactivity, which suggests that the method detects, for the first scenario, underdiagnosed alterations and the second, the improvement of the clinical condition from disease, respectively.

The sensitivity and specificity values of the mathematical methodology with respect to the clinical diagnosis to differentiate normality and abnormality were 100% and 100%, respectively. The *Kappa* coefficient obtained was 1. In the statistical analysis, those cases compatible with the evolution towards normality or abnormality were not included since it was sought to verify the capacity of the method to diagnose only these two states and not the intermediate variations. Figure 2 shows the results of the ROC curve of this diagnostic methodology.

Discussion

This is the first research in which a methodology based on the entropy S/k proportion and probability theory is applied to confirm its diagnostic applicability to differentiate normality from abnormality based on fetal heart rate values when evaluating 80 cardiotocographic tracings over 20 minutes. Likewise, due to the objective and reproducible nature of the methodology, since it is

Table 1

Probability values of heart rates.

Heart rate range	Case number 1	2	3	4	5	6	7	8	9	10	11	12
70	0	0	0	0	0	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0	0	0	0	0	0
80	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0	0	0	0	0
100	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
110	0	0	0	0	0	0	0	0	0	0	0	0
115	0	0.008	0	0	0	0	0	0	0	0	0	0
120	0.008	0.017	0.017	0.050	0.017	0	0	0.008	0.067	0.042	0	0
125	0.058	0.050	0.033	0.033	0.033	0.017	0	0.142	0.683	0.558	0.008	0.033
130	0.092	0.058	0.042	0.125	0.125	0.017	0.092	0.150	0.042	0.100	0.033	0.050
135	0.150	0.250	0.108	0.358	0.208	0.133	0.025	0.417	0.108	0.117	0.050	0.050
140	0.200	0.192	0.158	0.108	0.225	0.292	0.050	0.125	0.033	0.133	0.425	0.333
145	0.133	0.283	0.350	0.158	0.175	0.167	0.192	0.067	0.042	0.017	0.100	0.125
150	0.158	0.033	0.083	0.058	0.067	0.008	0.083	0.042	0.017	0.017	0.083	0.058
155	0.167	0.058	0.192	0.100	0.133	0.325	0.067	0.050	0.008	0.008	0.133	0.025
160	0.017	0.033	0.017	0.008	0.008	0.042	0.025	0	0	0.008	0.150	0.092
165	0.008	0.017	0	0	0.008	0	0.083	0	0	0	0.017	0.058
170	0	0	0	0	0	0	0.133	0	0	0	0	0.142
175	0.008	0	0	0	0	0	0.125	0	0	0	0	0.025
180	0	0	0	0	0	0	0.033	0	0	0	0	0.008
185	0	0	0	0	0	0	0.083	0	0	0	0	0
190	0	0	0	0	0	0	0.008	0	0	0	0	0
195	0	0	0	0	0	0	0	0	0	0	0	0
200	0	0	0	0	0	0	0	0	0	0	0	0

The table indicates the probability values that were obtained for each heart rate range of 5 barks.

Table 2

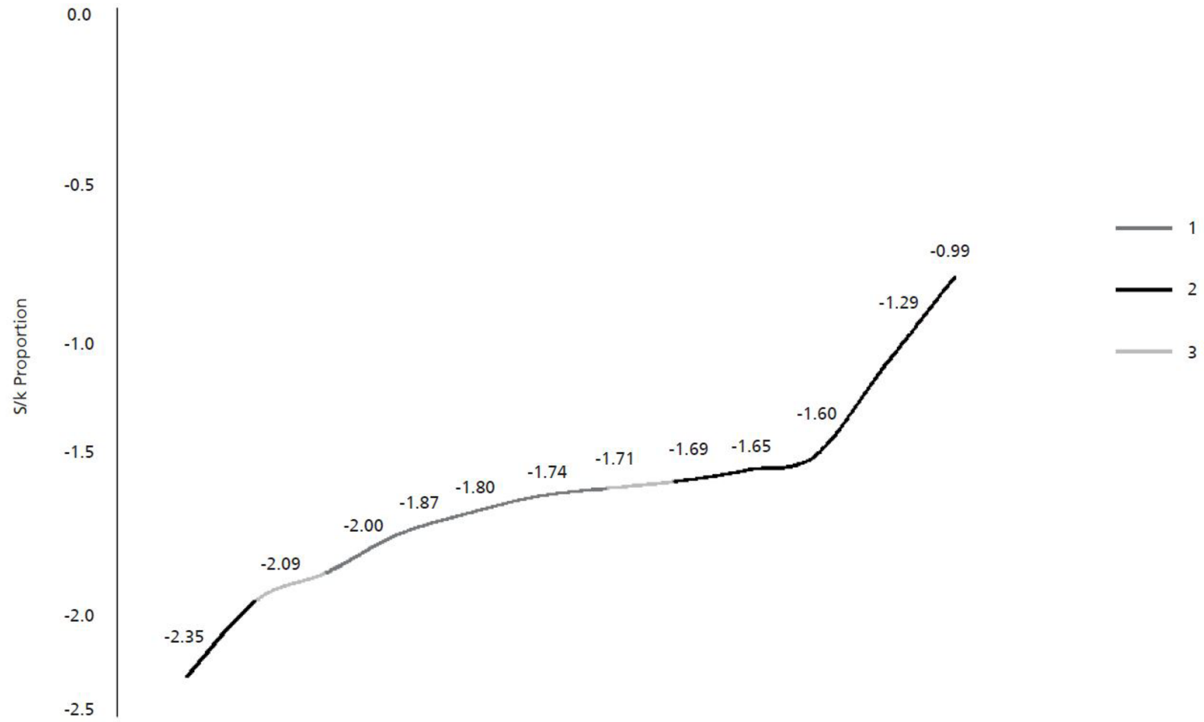
Values of proportion S/k and its interpretation.

No	S/k	Max P	Math	Dx Conventional Dx	Interpretation
1	-1.9984	0.200	Normal	Normal	R
2	-1.7968	0.283	Normal	Normal	R
3	-1.7378	0.350	Normal	Normal	R
4	-1.7096	0.358	Normal	Normal	R
5	-1.8697	0.225	Normal	Normal	R
6	-1.6007	0.325	Abnormal	Premature rupture of membranes	NR
7	-2.3535	0.192	Abnormal	Maternal arterial hypertension	NR
8	-1.6489	0.417	Abnormal	Intent to abort	NR
9	-0.9873	0.683	Abnormal	Childbirth premature	NR
10	-1.2912	0.558	Abnormal	Risk of loss of fetal well-being	NR
11	-1.6856	0.425	Evolution	Normal	R
12	-2.0908	0.333	Evolution	Irregular uterine activity	R

S/k = S/k ratio; P = Probability; Dx = Diagnosis; NR = Non-reactive; R = Reactive.

Figure 1

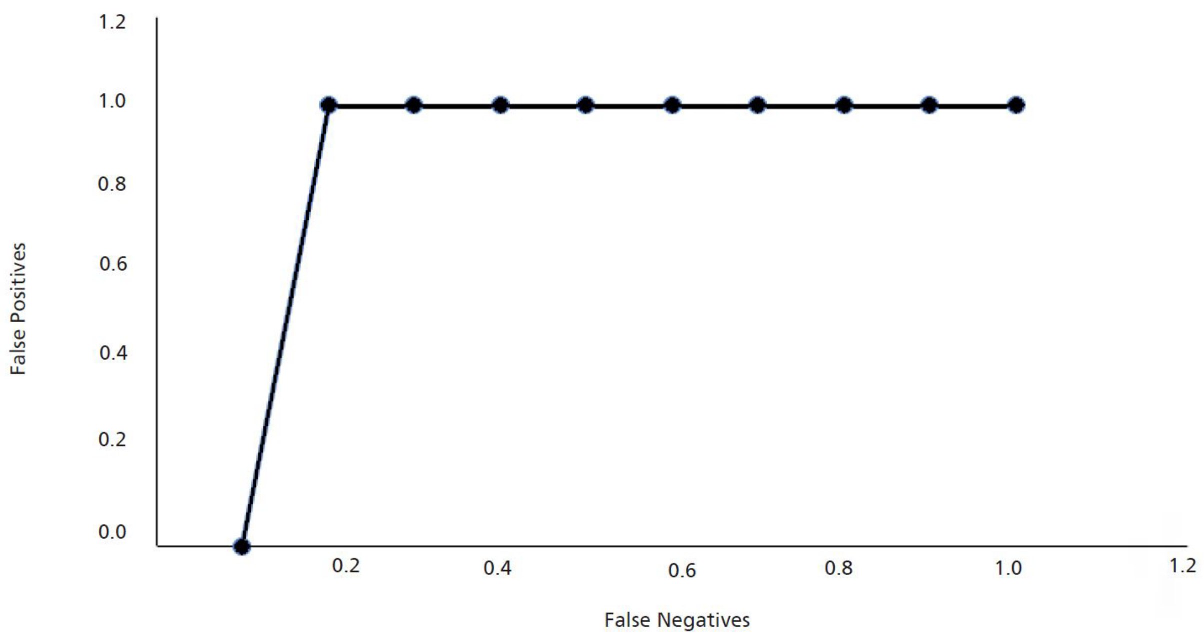
Representation of the spectrum of the values of the S/k proportion.



Number 1 represents the normal cases, while number 3 indicates the compatible cases with the evolution towards disease, and number 2 is the cases diagnosed as abnormal.

Figure 2

ROC curve of the diagnostic methodology.



ROC curve of the diagnostic methodology. For the construction of this curve, only the results of normal or abnormal cases were considered, excluding cases in evolution to normality or illness.

quantitative and does not depend on medical interpretation to diagnose normality or detect alterations in cardiac dynamics, the results of this study suggest that this method can be automated and incorporated into cardiotocographs, allowing to facilitate the diagnosis of fetal well-being with greater security.

Acute fetal distress refers to severe hypoxia with a high probability of fetal asphyxia and is diagnosed by analyzing changes in cardiac dynamics and acid-base balance.[26] However, the accuracy of this intrapartum diagnosis may be hampered by the difficulty obtaining or interpreting cardiotocography, fetal scalp pH assessment, pulse oximetry, and intrapartum ST-segment monitoring.[5,11]

The accuracy of these methods may be low when evaluated independently, in addition to the fact that these indicate the fetal status only for a cut-off time and do not indicate its evolution prospectively, for which reason the use of various diagnostic methods should be considered to increase the security of the clinical diagnosis.[26] In addition, the lack of precise diagnostic criteria hinders even more the correlation of the results of the complementary tests among the clinical scenarios, thus depending on the experience of the clinician to determine the diagnosis.[27] These considerations raise the question of developing new current diagnostic tools based on another perspective.

It is important to highlight that the cases of evolution towards disease were excluded from the statistical analysis, because this study sought to verify the ability of the method to diagnose normality and abnormality, not intermediate states. However, it is important to emphasize that obtaining a compatible mathematical diagnosis as evolution towards disease but with a clinical interpretation of reactivity suggests an underdiagnosed alteration that requires more attention. In the opposite case, that is, cases clinically diagnosed as abnormal but mathematically as evolving towards disease, suggests that there may be an improvement in the clinical state. These considerations will be analyzed in future studies that will confirm these observations.

Thus, in previous investigations based on the theoretical perspective of physics and mathematics,[28] together with the new conceptions of the processes of normality and abnormality in health, other methods have been developed, such as one based on the law of Zipf/Mandelbrot in obstetrics which has proved its usefulness to detect changes in fetal cardiac dynamics from cardiotocographic records.[29] These methods are also independent of the qualitative criteria and the experience of the evaluator, demonstrating their possible application in real clinical scenarios.

Also, following this same theoretical thinking of contemporary physics,[22] new diagnostic methods in cardiology and oncology have been generated as well as other predictive methods[30,31] that suggest that this approach is adequate to reevaluate the usefulness of physics and mathematics in biomedical phenomena.

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Authors' contribution

Conception and design of the studio: Rodríguez JO; Data collection: Correa SC, Villamizar ML; Data analysis: Páez JA, Correa SC, Cortés JA; Mathematical calculations and statistical measures: Correa SC, Prieto SE; Results analysis: Rodríguez JO, Villamizar ML, Simanca FA; Manuscript writing: Prieto SE, Cortés JA, Simanca FA; Critical review of the intellectual content of the manuscript: Rodríguez JO, Correa SC, Páez JA, Simanca FA. The authors approved the final version of the article and declare no conflicts of interest.

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