Sarajevo School of Science and Technology
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# Correlation between the Apgar score and perinatal asphyxia

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**Abstract**

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Correlation between the Apgar score and perinatal asphyxia

**Introduction**

Perinatal asphyxia is defined as a decrease in blood flow or gas exchange to or from the fetus in the peripartum period. It can cause serious fetal systemic and neurologic sequelae. The incidence of perinatal asphyxia is two per 1000 births worldwide in developed countries, while the rate is up to ten times higher in developing countries, where access to maternal and neonatal care may be limited.

The Apgar score is a vitality index ranging from 0 to 10 that is assigned to each newborn at one, five, and 10 minutes after birth. The score is based on measurements of the heart rate, respiratory effort, skin color, muscle tone, and reflex irritability. A total score of 7-10 is considered “normal,” and lower Apgar scores indicate decreased vitality. However, there are many causes of low Apgar score, such as perinatal asphyxia, congenital infections, maternal fever in labor, diagnosed chorioamnionitis, malformations, and preterm birth.

Objectives

We aimed to analyze deliveries with and without perinatal asphyxia diagnosis that took place in the Gynecology and Obstetrics Department of “Cantonal Hospital Zenica”, Bosnia, between March and May 2021.

**Methods and Results**

This is a retrospective cohort study which includes 50 patients in each arm: a study group with a diagnosis of imminent perinatal asphyxia and a control group of patients without antepartum signals of fetal asphyxia. We analyzed the delivery mode, neonatal weight and length, delivery duration and Apgar score, as possible predictors of perinatal asphyxia.

**Discussion and Conclusions**

This study has shown that abnormal CTG findings during labor are associated with perinatal asphyxia. Hence, continuous CTG monitoring during the first and second stages of labor helped to timely register the threat of perinatal asphyxia, which can be confirmed by the Apgar scores at the first and fifth minutes.

**Keywords:** Perinatal asphyxia, Apgar score, cardiotocography, perinatal outcomes.

**Apstrakt**

Clara Patrícia Teixeira Pinheiro

Korelacija između rezultata Apgar i perinatalne asfiksije

**Uvod**

Perinatalna asfiksija definirana je kao smanjenje protoka krvi ili razmjena plinova od i prema fetusu za vrijeme poroda. Može izazvati ozbiljne fetalne sistemske i neurološke posljedice. Učestalost perinatalne asfiksije je dva na 1000 rođenih širom svijeta u razvijenim zemljama, dok je stopa do deset puta veća u zemljama u razvoju, ako je pristup majčinoj i neonatalnoj njezi ograničen.

Ocjena Apgar je indeks vitalnosti u rasponu od 0 do 10 koji je dodijeljena svakom novorođenčetu u prvoj, petoj i destoj minuti nakon poroda majčine groznice u porodu. Rezultat se temelji na mjerenjima brzine srca, respiratornog napora, boje kože, mišićnog tona i refleksne razdražljivosti. Ukupni rezultat 7 -10 smatra se “normalnim”,a niži Apgar rezultati pokazuju smanjenu vitalnost. Medjutim, postoji mnogo uzroka niskog rezultata Apgar-a, poput perinatalne asfiksije, urođenih infekcija, majčinske groznice u radu, dijagnosticiranog horioamnionitisa, malformacija i prijevremenog rodjenja.

Ciljevi

Cilj ovog rada bio je analizirati porode sa i bez dijagnoze perinatalne asfiksije u porodima koji su se odvijali na odjelu ginekologije i porodiljstva “Kantonalne bolnice Zenica”, u periodu mart - maj 2021. godine.

**Metode i rezultati**

Ovo je retrospektivna kohortna studija koja je uključivala 50 pacijentica u svakoj skupini - ispitivanoj studijskoj grupi sa dijagnozom neposredne perinatalne asfiksije i kontrolnoj skupini bez pomenute dijagnoze. Analiziralan je način poroda, neonatalna dužina i težina, trajanje poroda i ocjena Apgar sto je mogući prediktor perinatalne asfiksije.

**Diskusija i zaključci**

Ova studija pokazala je da su nenormalni nalazi CTG-a tokom rada povezani sa perinatalnom asfiksijom. Stoga je kontinuirano praćenje CTG-a tijekom prve i druge faze rada pomoglo da se pravovremeno registrira prijetnja perinatalnom asfiksijom, što mogu potvrditi rezultati Apgar-a u prvih i petih minuta.

**Ključne riječi:** Perinatalna asfiksija, rezultat apgar, kardiotokografija, perinatalni ishodi.

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To my colleagues and friends, thank you for this whole journey.

**Abbreviations**

| | |
|---|---|
| ApS | Apgar score |
| Bpm | Beats per minute |
| BP | Blood pressure |
| CTG | Cardiotocography |
| CS | Cesarian section |
| CST | Contraction stress test |
| ECG | Electrocardiogram |
| FHR | Fetal heart rate |
| FIGO | International Federation of Gynecology and Obstetrics |
| HIE | Hypoxic-ischemic encephalopathy |
| HR | Heart rate |
| NST | Nonstress test |
| UC | Uterine contractions |
| IUP | Intrauterine pressure |
| NICE | National Institute for Health and Care Excellence |
| PA | Perinatal asphyxia |
| $SaO_2$ | Oxygen saturation |

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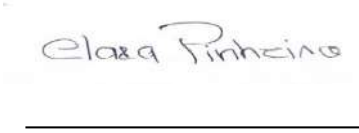
**Declaration of originality**

I hereby declare that I have written this thesis by myself and without support from any other person. In addition, I declare that I have only used the materials and the sources indicated in the in-text citation and in the bibliography. Furthermore, I declare that I have used all the materials listed therein and that I have cited all sources from which I have drawn intellectual input. No other person has submitted this thesis beforehand nor is a similar version of it been submitted towards a degree at any other institution towards an award of a degree or for a publication.



Sarajevo, July 2022

## 1. Introduction

Perinatal asphyxia (PA) is defined as an absence of blood flow or gas exchange to or from the fetus immediately before, during, or after birth.[1] Some studies have shown that it can cause serious systemic and neurologic sequelae due to decreased blood flow and/or oxygen delivery to a fetus during the peripartum period.[1, 2] The incidence of PA varies worldwide, with two per 1000 births in developed countries, whereas the rate is up to ten times higher in developing countries where access to maternal and neonatal care may be limited.[1]

The Apgar score (ApS) is a vitality index from 0 to 10 assigned to each newborn one, five, and ten minutes after birth.[3] The score is based on measurements of heart rate (HR), skin color, respiratory effort, muscle tone and reflex irritability.[4] An overall score of 7-10 is considered "normal," and a lower ApS indicates decreased vitality.[3] However, there are several possible causes of low ApS, including PA, congenital infections, maternal fever during labor, diagnosed chorioamnionitis, malformations, and prematurity.[3, 4]

### 1.1. Fetal physiology

Fetal development lasts about 40 weeks. The physiology of the fetus is different from that of the newborn, exhibiting both structural and functional differences.[5] Hence, the transition from the uterus to extrauterine life requires rapid, challenging, and coordinated steps to ensure the survival of the newborn.[5]

The fetal heart begins to beat 65 beats per minute (bpm) around the fourth week of gestation. This rate increases throughout pregnancy to 160 bpm before birth.[6] The primary function of the fetal heart is to pump oxygenated blood from the placenta to the fetal organs and, in turn, transport carbon dioxide back to the placenta, where an exchange is maintained between mother and fetus.[6] The exchange is not limited to gases, but occurs for some other substances such as food and waste products of the fetus.[6]

### 1.1.1. Basic physiology of fetal circulation

During pregnancy and delivery, the fetus's tissues must receive an adequate oxygen supply through the placenta.[6] The placenta is responsible for the various exchanges occurring between the fetus and the mother, and it has functions similar to the lungs, kidneys and liver in postnatal life.[7] The placenta includes a fetal and a maternal compartment.[7] Its primary function is transporting oxygen and nutrients to the fetus and transferring carbon dioxide, urea, and other breakdown products from the fetal to the maternal component.[7]

During delivery, complications resulting from oxygen deprivation include metabolic acidosis, asphyxia, and cerebral palsy.[2] To avoid those complications, the fetus has several defense mechanisms that allow adaptation to increased oxygen deficiencies.[7]

The fetal compartment of the placenta consists of the umbilical artery, which splits into thin arteries that penetrate the chorionic villi and end in a capillary network that extends into the intervillous space, the maternal reservoir of placental blood.[8] Maternal blood exits the aorta and passes through the internal iliac arteries to the uterine arteries. From there, the blood is transported to the intervillous space. Fetal circulation has rapid blood flow due to low fetal blood pressure.[8]

The amniotic fluid and membranes enclose the fetus in the uterus. The later is formed by two layers: the amnion and the chorion.[7] The membranes are an envelope for the amniotic fluid and the fetus, protecting them from harmful microorganisms and trauma.[8] Amniotic fluid is produced throughout pregnancy initially by the fetus's lungs and by the fetal kidneys after the second trimester of pregnancy, and it´s volume varies from 500 to 2000 ml.[8] It is ingested through and absorbed by the fetal gastrointestinal tract.[8] Amniotic fluid allows fetal movement, protects it from external mechanical forces, and prevents the umbilical cord from being compressed during labor.[8]

The umbilical cord is the structure that connects the fetus to the placenta. It consists of two umbilical arteries (carrying deoxygenated blood from the fetus to the placenta) and an umbilical vein (carrying oxygenated blood from the placenta to the fetus) surrounded by a gelatinous layer called Wharton's jelly.[8] These vessels are lined by the fetal membranes and a layer of connective tissue that ensures that the external pressure exerted on the umbilical cord is balanced and that the umbilical vein can maintain blood flow during labor.[8]

The placental barrier is highly permeable to gases involved in cellular respiration.[7] Their diffusion is regulated by the difference in partial pressures of the gases between the fetus and the mother.[7] In the intervillous space, the slow passage of maternal blood through the villi allows easy oxygen and carbon dioxide exchange by simple diffusion.[8]

Oxygenated blood with a saturation ($SaO_2$) of 75% is transported from the placenta through the umbilical vein to the fetus.[8] The fetus's deoxygenated blood $SaO_2$ of 25% is transported to the placenta through the umbilical arteries. Blood flow between the placenta and fetus is regulated by blood pressure.[8] In response to oxygen deprivation, the fetus increases its blood pressure (BP) to maximize blood flow in the placenta and diffusion of gases and nutrients.[8]

Normal cellular metabolism is aerobic and uses mainly oxygen and glucose as energy sources.[8] Carbon dioxide and water are the waste products excreted through the bloodstream. In addition, glucose accumulates in glycogen stores at the last trimester of pregnancy, which is necessary to compensate for possible oxygen deficits through glycogenolysis.[8]

### 1.1.2. Fetal response to hypoxia

Before describing mechanisms of fetal response to oxygen deprivation, it is important to define three main concepts:

**Hypoxemia** is a decrease in blood oxygen partial pressure. Peripheral blood flow is reduced.[7] However, central organs and peripheral tissues are intact and sufficient oxygen is provided to maintain aerobic metabolism.[8] The fetus can endure hypoxemia for days and weeks.[7] Nevertheless, a fetus submitted to chronic hypoxemia will cope deficiently with labor contractions due to limited energy reserves.[7, 8]

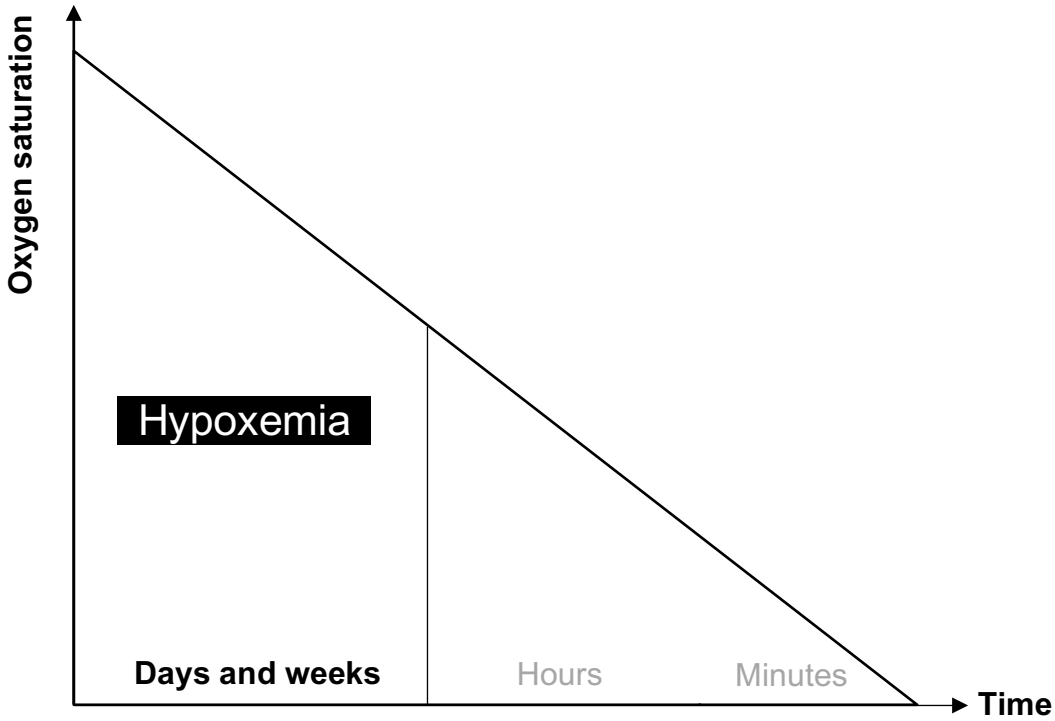



**Figure 1.** Fetal response to hypoxemia.

Early fetal defense mechanisms against hypoxemia consist of more efficient oxygen uptake, reduction in fetal and respiratory movements.

**Hypoxia** represents the second stage of oxygen deficiency when peripheral tissues are affected. Hypoxia can last for several hours without harming the fetus.[9] Fetal well-being depends on maternal oxygenation and placental blood flow. The disturbances in maternal oxygenation, uterine blood flow, and fetal gas transportation across the placenta can result in fetal hypoxia and non-reassuring fetal status.[10] Fetal distress results from transient or permanent fetal hypoxemia and can lead to metabolic acidosis.[10] There are three stages of decay when oxygen levels are expended: Transient hypoxia with no metabolic acidosis, tissue hypoxia with increased risk of developing metabolic acidosis and hypoxia with metabolic acidosis.[8, 10]

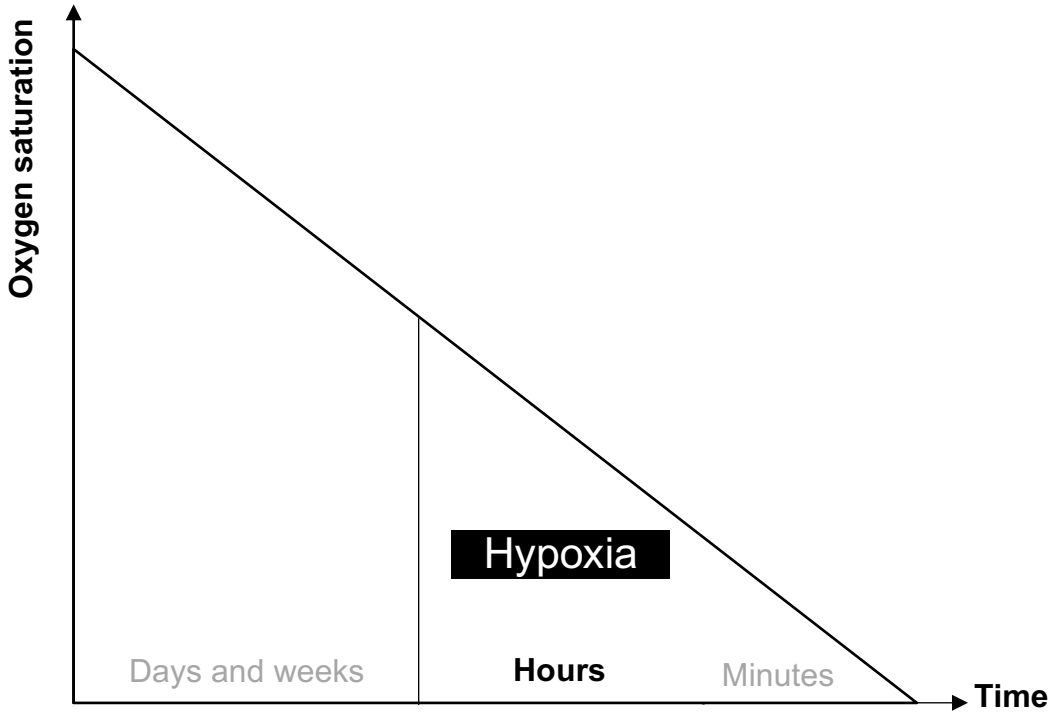



**Figure 2.** Fetal response to Hypoxia.

The main fetal reaction to hypoxia consists of an increase in stress hormones and a decrease in peripheral blood flow, resulting in a blood flow redistribution to the heart and brain. Anaerobic metabolism occurs in the peripheral tissues. This situation can be endured for several hours.

**Asphyxia** is the most critical stage, with generalized oxygen deficiency affecting central organs, associated with metabolic acidosis.(2) The final stage of asphyxia is the system's collapse with brain and heart failure. Asphyxia lasting only a few minutes can cause irreparable damage.(2)

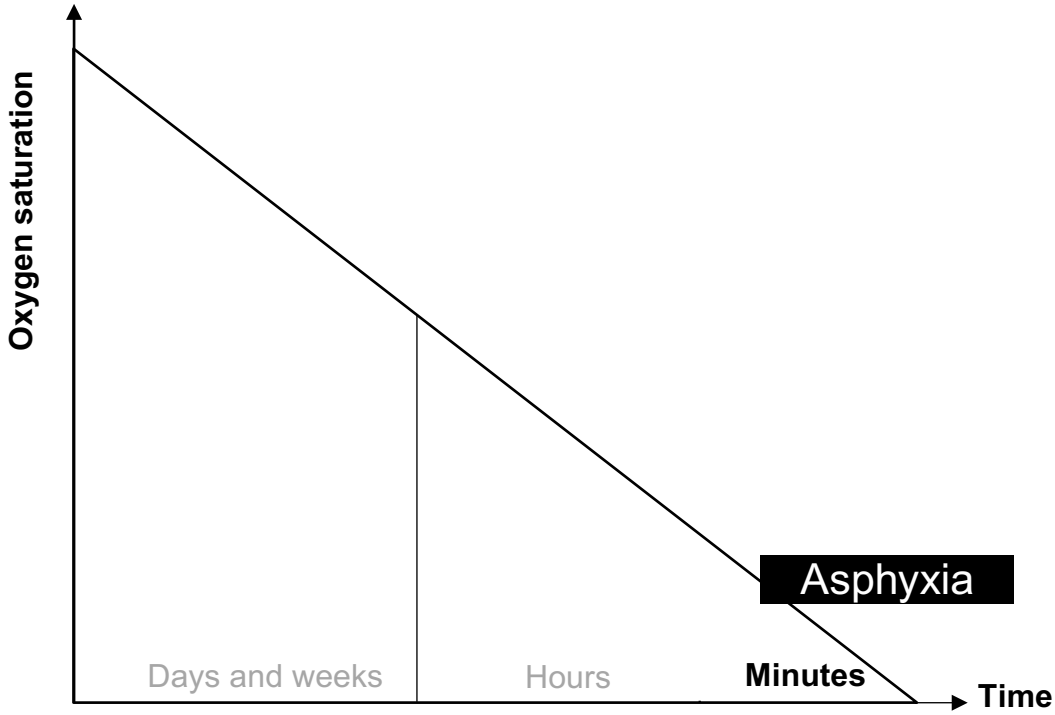



**Figure 3.** Fetal response to Asphyxia.

During the asphyxia stage, oxygen saturation is very low and there is a risk of central organ function failure. When fetal defenses reach their final state, the entire system collapses with brain and heart failure.

Hypoxemia has been described as the initial phase of oxygen deprivation. The fetal response depends on the activation of chemoreceptors in the large blood vessels, which are activated by the decrease in arterial blood $SaO_2$.[11] Initially, the response is limited to an increase in the efficiency of oxygen uptake and a decrease in fetal activity. In the long term, the response includes a growth rate decrease. These responses reduce the energy and oxygen requirements of the fetus, allowing for a sustained energy balance.[11] The fetus can resist a situation of controlled hypoxemia for up to several weeks, but prolonged stress of this type can decrease fetal growth rate and reduce its ability to control future episodes of acute hypoxia during delivery.[11]

If $SaO_2$ continues to decline, the above responses may not be sufficient to maintain energy balance, and the fetus can enter a hypoxic state.[7] The autonomic nervous system is responsible for controlling fetal response to the lack of oxygen. The primary response is an alarm response resulting from activation of the sympathetic-adrenergic system, which releases stress hormones or catecholamines, such as epinephrine and

norepinephrine. As a result, there is a decrease in peripheral blood flow, and blood is redirected to the heart, the brain and the adrenal glands.[12] Blood flow may also increase to ensure adequate oxygenation. Epinephrine activates beta receptors that activate the enzyme phosphorylase, which is responsible for converting stored glycogen into glucose, and peripheral tissues begin anaerobic metabolism.[8] The fetus can sustain this state for several hours, keeping the central organs unaffected and maintaining aerobic metabolism by blood redistribution.[8]

Finally, when $SaO_2$ becomes too low, energy production is insufficient. As a result, the fetus enters a state of asphyxia, associated with an increased risk of organ failure. The fetus responds with maximal activation of the sympathetic nervous system and release of catecholamines.[8] Anaerobic metabolism is initiated in the central organs, and glycogen reserves are drawn from the liver and myocardium for glycogenolysis, increasing redistribution of blood to central organs.[12] In the final stage of asphyxia, the fetus enters metabolic acidosis. Neonatal metabolic acidosis has been associated with long-term developmental complications such as cerebral palsy.[12] The fetus has compensatory mechanisms for transient hypoxia during labor, such as decreasing heart rate, decreased oxygen consumption, redistribution of cardiac output to perfuse central organs and a change to anaerobic metabolism.[12] However, prolonged and uninterrupted fetal hypoxia can gradually lead to acidosis with cell death, tissue damage, organ failure and death.[7]

During labor, uterine contractions cause multiple physiologic acute episodes of fetal hypoxia. Therefore, regular monitoring and immediate intervention are crucial.[12]

### 1.2. Fetal surveillance methods

Fetal monitoring during delivery has been essential in Obstetrical clinical practice. Its main goal is to prevent complications and harm related to hypoxia and metabolic acidosis during labor and avoid unnecessary interventions that may lead to fetal and/or maternal morbidity.[13, 14]

#### Antepartum fetal surveillance methods

**Maternal awareness of fetal movement** is the least expensive test, but its sensitivity is very low, and it has a high rate of false positives. Some studies have shown that it has not been helpful in reducing fetal mortality. It may be associated with increased harm due to unnecessary interventions.[13, 15]

**Nonstress test (NST)** is a non-invasive method of monitoring high-risk pregnancies performed in the third trimester, to test whether the fetus is at risk for intrauterine death or neonatal complications.[16] The NST is used from 32 weeks of gestation until the end of pregnancy. The presence of fetal movements and acceleration of FHR are the essential features of the NST.[16]

A CTG is used for the prenatal NST to record the FHR pattern, fetal movements, and uterine contractions.[15] Maternal blood pressure is also monitored. The NST involves 20 minutes of continuous FHR monitoring, assessing the number, amplitude, and duration of accelerations that usually correlate with fetal movements.[15] The interpretation of the NST is as reactive or nonreactive.[16]

A reactive or normal NST is present if two or more FHR accelerations occur within 20 minutes.[16]

If insufficient accelerations are present, the FHR should be monitored for at least 40 minutes to account for the fetal sleep cycle before it is considered a nonreactive NST.[15] In addition, vibroacoustic stimulation may be used to stimulate fetal movement.[16] Continuous nonreactive NST may indicate central nervous system depression, but further investigation is needed, usually in the form of a biophysical profile or contraction stress test.[16]

The **contraction stress test (CST)** registers the response of the fetal heart to hypoxia induced by uterine contractions from intravenous infusion of oxytocin.[15] The CST is interpreted based on the presence or absence of late decelerations. Contraction stress tests are classified as:

1. *Negative:* if FHR is regular, has good variability, and has less than 20% late decelerations in 10 contractions.
2. *Positive:* if more than 50% late decelerations occur. If the fetus is mature, this is an indication for delivery. Otherwise, obstetricians should perform other tests to assess fetal well-being.
3. *Equivocal-suspicious:* Significant variable decelerations or intermittent late decelerations.

4. *Unsatisfactory:* An uninterpretable curve or fewer than three contractions in 10 minutes.

The **biophysical profile** is an ultrasonographic method of antenatal evaluation of fetal wellbeing, usually performed in the third trimester of pregnancy.[17] It`s evaluation may also take into consideration CTG tracing.[17] Ultrasound evaluates four variables: fetal movement (three or more discrete movements of the body within 30 minutes); fetal tone (one or more times of extension of a fetal limb with return to flexion, opening or closing of a hand); fetal respiratory movements (one or more episodes of 30 seconds within 30 minutes); and amniotic fluid volume (a single pocket of amniotic fluid of more than 2 cm is considered normal).[17]

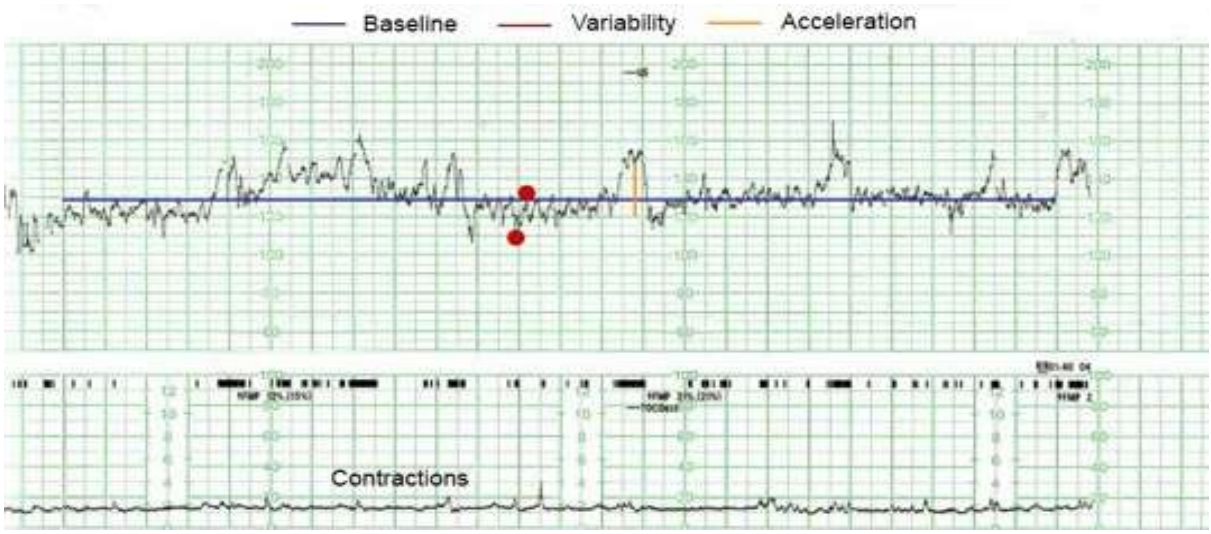
Each parameter is scored 0 (abnormal, inadequate, or absent) or 2 (present or normal). A total score of 8 (or 10 if CTG is taken into consideration) means there is no evidence of asphyxia, a score of 6 is equivocal, and a score of 4 or less is abnormal and it requires obstetrical intervention.[17]

### 1.2.1. Cardiotocography

Intermittent auscultation was the predominant method of monitoring during labor until CTGs became widely used in the latter part of the twentieth century.[15]

FIGO states that intermittent auscultation is equivalent to continuous electronic fetal monitoring in diagnosing intrapartum fetal compromise.[18] Therefore, studies have shown that intermittent auscultation use is preferred in low and middle-income countries, in low-risk patients, because fewer interventions are required, the false-positive rate is lower, and health personnel have more contact with the mother.[18]

Cardiotocography is a monitoring technology introduced in the 1960s and has been used daily in clinical obstetric practice in most hospitals in industrialized countries to assess fetal oxygenation in late pregnancy and at birth.[19]




(Image used with the author`s consent)

**Figure 4.** Normal CTG recording.

A CTG recording is interpreted by assessing it´s baseline (mean value of the FHR), variability (fluctuations in baseline FHR), accelerations (temporary increase in FHR), decelerations (temporary decrease of FHR), and contractions.

The CTG continuously records FHR and uterine contractility (UC). It was introduced with the goal of early detection of fetal intrapartum hypoxia, in order to decrease the occurrence of associated cerebral palsy.[20]

Normal FHR patterns are a reliable indicator of fetal well-being. However, up to 50% of the findings classified as pathological reflect physiological changes and are classified as false positives.[21] Literature has shown that this false pathological findings can lead to an increase in the number of cesarean sections (CS) and instrumental vaginal deliveries.[21]

### 1.2.1.1. Physiology and interpretation

CTG has been used in intrapartum fetal monitoring for more than 50 years. It records continuously and simultaneously FHR and UC.[22] Fetal monitoring can be performed externally prior to rupturing the membranes or internally after rupturing of the membranes.[23] External monitoring uses two devices placed on the maternal abdomen: an ultrasound sensor that records FHR and an external transducer that records the presence of uterine contractions.[23] Internal fetal monitoring uses a scalp electrode, which allows accurate recording of each fetal heartbeat, and an intrauterine

pressure (IUP) transducer, which detects pressure fluctuations of uterine contractions.[23] A minimum of 20 minutes is required for proper interpretation of the CTG recording, as changes in uterine activity and fetal activity status may temporarily affect the recording.[23]

The recording rate is 1 centimeter per minute, time is displayed every 10 minutes, and the recording is printed every 30 minutes. Uterine activity is displayed between 0 and 100 relative units if a tachometer is used and between 0 and 100 mmHg if an IUP sensor is used. In addition, FHR between 50 and 210 bpm can be recorded.[23]

Basal fetal heart rate during the second half of pregnancy results from the effects of the influences of the sympathetic (FHR increases) and parasympathetic (FHR decreases) nervous systems.[23]

According to the 2015 guidelines from FIGO, **basal FHR** should be measured in 10-minute periods, and normal values are between 110 and 160 bpm. It is referred to as *tachycardia* when the FHR is above 160 bpm and *bradycardia* below 110 bpm.[23] Basal FHR can be altered by the effects of autonomic nervous system and changes in the myocardium due to hypoxia or hyper- and hypothermia.[23]

**FHR variability** is defined as fluctuations in the baseline FHR that are irregular in frequency and amplitude.[7] The degree of fluctuation is based on peak-to-trough amplitude in bpm. It can be classified as *absent* when the amplitude range is undetectable, *minimal* when the amplitude range is detected < 5 beats per minute, *normal* when the amplitude range is ≥ 5-25 bpm and *marked* when the amplitude range is > 25 bpm.[7] FHR variability has been pointed as an important indicator of fetal status because it shows whether the fetal central nervous system can adjust to the cardiovascular system in response to changes in oxygenation. [7] Therefore, variability reduction is one of the most important pieces of information CTG obtains, as it can facilitate the detection of an approaching hypoxic episode.[7] FHR variability alone cannot serve as the sole indicator of fetal well-being. The presence of low variability should alert the physician. However, good FHR variability should not be taken as reassuring.[23]

As mentioned earlier, it is normal to have FHR fluctuations called accelerations or decelerations.

**Accelerations** have been described as a FHR increase of more than 15 beats for more than 15 seconds above the baseline. This is a sign of normal fetal

oxygenation and records a physiologic fetal response to changes in the fetal environment or fetal movement. A CTG is considered reactive when it has at least two accelerations within 20 minutes.[7, 23] *Periodic accelerations* occur associated with contractions and indicate blood transfer from the placenta to the fetus.[23]

In contrast, **decelerations** are defined as a FHR decrease under the baseline of more than 15 beats for more than 15 seconds. Some decelerations are caused by physiologic changes in the fetal environment, such as labor-related ones. Nevertheless, they may indicate the development of a hypoxic episode, so its important to recognize them.[7, 23]

Depending on how they relate to contractions, some authors had it classified as follows:

*Early decelerations* occur when FHR decrease coincides with the peak of the contraction. Those are physiologic and happen due to an autonomic fetal response to fetal head compression during contractions.[23]

*Variable decelerations* are the most common type of decelerations during labor. They are rapid V-shaped decelerations seldom associated with uterine contractions. They are a baroreceptor-mediated fetal response to increased arterial pressure, which usually occurs with umbilical cord compression. They can translate hypoxia when they become U-shaped and lose their variability, and/or if they exceed 3 minutes of duration. In these situations, a decreased scalp pH and an accumulation of $CO_2$ in fetal blood are often observed.[23]

*Late decelerations* happen when there is a time delay between the peak of contraction and the nadir of the deceleration. They are usually U-shaped and present with low variability. They relate to chemoreceptor-mediated response to fetal hypoxemia and can be associated with cases of fetal growth restriction, abnormal uterine activity with increased contraction frequency, and placental insufficiency.[7, 23]

**Uterine activity** is measured on a CTG by the frequency of contractions. The standard frequency is two to three contractions every 10 minutes on the latent phase of the first stage of labor, increasing to four to five contractions in the active phase of labor. Intensity is measured with the IUP sensor. During contractions in which the IUP exceeds 30 mmHg, there is a decrease in placental blood flow and gas exchange between the fetus and the mother.[7, 23]

*Tachysystole* (more than five contractions every ten minutes in two successive 10 minutes) is responsible for decreasing fetal reoxygenation capacity.[7] The fetus requires 60 to 90 seconds between contractions to normalize its blood gas levels.[7]

*Infrequent contractions*, which prolong the time of expulsion and thus birth, are also responsible for potential periods of hypoxia.[7] Therefore, it is vital to record the duration of the second stage of labor to assess the risk of intrapartum hypoxia.[7]

#### 1.2.1.2. Advantages and disadvantages

Cardiotocography is considered mainly as a screening tool. It is undeniable that there are two scenarios in which CTG provides essential information about the fetal status.[20] A normal and responsive CTG indicates a fetus with no problems coping with labor. In contrast, a CTG with a complete loss of reactivity and variability identifies a fetus unable to respond to the environmental changes that occur during labor.[20] CTG is the most used intrapartum monitoring in developed countries. It has shown high sensitivity but lacks specificity for predicting true fetal hypoxia.[20] However, CTGs classified as abnormal, only reflect 40-60% of fetuses with hypoxia. Also, CTG has several limiting factors. First, it´s interpretation depends on the correct identification and analysis of risk patterns. Misinterpretation of CTG has been reported to account for about 34% of unnecessary intrapartum interventions.[20] In addition, FIGO does not recommend the universal use of CTG intra-partum monitoring in low-risk pregnancies, as it can increase CS deliveries without an associated increase in benefits.[20]

Finally, studies have shown that CTG needs to be supplemented with other tests because of its low predictive value for hypoxia when used alone.[20]

### 1.3. Assessment of labor and neonate outcomes

As previously mentioned, fetal monitoring has been described as a method of detecting fetal distress and oxygen deprivation. Once the fetus is born, we need to assess its condition to obtain additional information about oxygenation status. Standard assessment methods are the Apgar score and the occurrence of neonatal complications.[24]

### 1.3.1. Mode of delivery and its indications

Mode of delivery refers to the route and medical aid needed during birth. It can be divided into vaginal delivery and cesarean delivery.[25] The first is further subdivided between a natural vaginal delivery, often called eutocic delivery, or a vaginal assisted delivery, using a vacuum extractor or forceps. Cesarean section (CS) is an obstetric procedure in which the newborn is delivered through a vertical or horizontal incision in the lower abdomen.[25] Delivery by CS may be recommended to mitigate fetal or maternal morbidity and mortality.[25] There are a myriad of cesarean-section indications, depending on maternal and/or fetal indications.

**Cesarean-section indications according to Robson Classification[26, 27]**

**1) Classification regarding the urgency of the CS**

1. Planned CS
    a. a. When the reason for surgery does not require the CS to be performed on the same day that is scheduled.
2. Urgent CS
    b. When there is a clinical situation that needs to be resolved quickly, but there is no imminent danger to the fetus and/or the mother.
    c. The time between the indication for surgery and the start of CS should not exceed 180 minutes.
2. Emergent CS
    a. When there is imminent danger to the health of the fetus and/or mother, which can be reduced if the surgery is carried out as quickly as possible.
    b. The time between the indication for surgery and the beginning of the CS should not exceed 15 minutes.

**2) Classification concerning absence of labor or different labor stages**

1. CS in the *absence of labor* is defined as a CS performed before the occurrence of rhythmic uterine contractions that have an impact on the uterine cervix.
2. CS in the *first phase of labor* is when it is performed after the occurrence of rhythmic contractions which affect the cervix, but before complete cervical dilation.
3. CS during the *second stage of labor* is performed after complete cervical dilation.

**3) Classification according to the main reasons for CS**

1. *Maternal pathology* that contraindicates vaginal delivery (HIV positive, severe cardiovascular or pulmonary disease or invasive cervical carcinoma).
2. *Fetal anomaly* that contraindicates vaginal delivery (hydrocephalus with macrocephaly, abdominal wall defects, myelomeningocele).
3. *Pregnancy-related pathology* (placenta previa, placenta accreta, suspected placental abruption, eclampsia, intrauterine growth restriction, pathological antepartum cardiotocography).
4. *Prior uterine surgery* (history of two previous CS, a previous CS with corporal hysterotomy, myomectomy, or previous uterine rupture).
5. *Abnormal fetal presentation* (transverse lie, breech presentation, posterior chin face presentation).
6. *Multiple pregnancies* (triple pregnancy, twin pregnancy with the first fetus in breech presentation).
7. *Suspected cephalopelvic incompatibility*.
8. *Unsuccessful attempt to induce labor* (use of pharmacological and or mechanical means to induce labor without reaching the active phase of the labor, i.e., 4 cm dilatation).
9. *Stationary labor* (dynamic and mechanical dystocia, unsuccessful attempt of ventouse or forceps assisted delivery).
10. *Intrapartum non-reassuring fetal state* (pathological or suspicious CTG).

**4) Classification based on the main characteristics of pregnancy**

(All CS must be classified in one of the following groups, and no CS can be in more than one group)

Group 1. Nullipara, unifetal pregnancy, cephalic presentation, ≥ 37 weeks, in spontaneous labor.

Group 2. Nullipara, unifetal pregnancy, cephalic presentation, ≥ 37 weeks, induced labor or CS before the onset of labor.

Group 3. Multipara (excluding previous CS), unifetal pregnancy, cephalic presentation, ≥ 37 weeks + 0 days, in spontaneous labor.

Group 4. Multipara (excluding previous CS), unifetal pregnancy, cephalic presentation, ≥ 37 weeks + 0 days, induced labor or CS before the onset of labor.

Group 5. Prior CS, unifetal pregnancy, cephalic presentation, ≥ 37 weeks + 0 days.

Group 6. Nullipara, pelvic presentation.

Group 7. Multipara pelvic presentation (including prior CS).

Group 8. Multiple pregnancies (including prior CS).

Group 9. Transverse/oblique situation (including previous CS).

Group 10 Preterm (<37 weeks + 0 days), single gestation, cephalic presentation (including previous CS).

In this work we focused on intrapartum non-reassuring fetal state classified as one of the main reasons for CS delivery.

Non-reassuring fetal status has been used to describe suspected fetal hypoxia. The progressive fetal hypoxia and/or acidemia resulting from inadequate fetal oxygenation is defined as fetal distress.[10] It manifests as reduced fetal movements, changes in fetal cardiac pattern, fetal growth restriction, and the presence of meconium-stained fluid.[10] Persistent fetal hypoxia is associated with perinatal morbidity and mortality. It can lead to complications such as encephalopathy, seizures, cerebral palsy, and neurodevelopmental delays.[10] In addition, FHR changes significantly in response to prolonged oxygen deprivation, making FHR monitoring a valuable and frequently used means for real-time assessing fetal oxygenation status.[10]

### 1.3.2. Apgar Score

This method was developed in 1953 by Virginia Apgar. The technique has become broadly used in clinical practice with the passing years. The ApS considers the status of a newborn infant at 1, 5, and 10 minutes after birth.[4] The assessed parameters are appearance (skin color), pulse (heart rate), grimace (reflex irritability after stimulation), activity (muscle tone and movement), and respiration.[3]

An ApS of 7 or more means that the newborn is healthy. Conversely, a low ApS may indicate a risk of neonatal compromise.[4] For example, an ApS at 1 minute between 0 and 6 is associated with the risk of cerebral palsy.[4] Also, an ApS of < 7 at 5 minutes increases the risk of neonatal respiratory distress and hypoxic-ischemic encephalopathy (HIE). A very low ApS at 5 minutes between 0 and 3 correlates with neonatal mortality and risk of neonatal death in term infants. The ApS is a reasonable predictor of neonatal mortality.[4]

Each variable is assigned a score between 0 and 2 points. The points are summed up, with 10 points being the maximum score that can be obtained during minute 1 and minute 5.[4]

There is a high correlation between a low ApS at 5 minutes and neonates who have experienced asphyxia during birth.[28] However, there are many other reasons for a low ApS unrelated to asphyxia, immaturity, upper airway manipulation, meconium aspiration, or carbon dioxide anesthesia. An ApS ≤ 7 at 5 minutes is associated with metabolic acidosis and cerebral palsy and may require further intervention.[28]

## 1.4. Correlation between fetal surveillance methods and neonate outcomes

Antepartum fetal surveillance is used to assess fetal status before the onset of labor.[13] Fetal surveillance methods help to find abnormal physiological conditions of the fetus, detect and determine the severity of acute or chronic fetal hypoxia and the risk of fetal death in low and high-risk pregnancies, such as the ones complicated by preexisting maternal conditions (i.e. hypertension, diabetes mellitus, acute febrile illness, sickle cell anemia), and fetal conditions (i.e. fetal growth restriction, fetal infections, fetal cardiac arrhythmias), and also pregnancy-related conditions such as preeclampsia.[13, 29]

Prenatal fetal well-being screening aims to identify fetuses at risk of fetal distress through a series of tests and, when necessary, intervene to prevent irreversible harm.[13] Therefore, their indications are relative and recommended in pregnancies with an increased risk of premature fetal loss, starting no earlier than 39 weeks in low-risk pregnancies. In high-risk pregnancies, the disease itself determines the onset and frequency.[13]

### 1.4.1. Association between CTG and Apgar Score

Predicting perinatal outcomes based on CTG findings remains a challenge.[30] Intrapartum monitoring of FHR patterns aim to identify fetuses at risk of hypoxia and acidemia, intervene to avoid fetal compromise, and achieve timely delivery to prevent neurologic complications.[30] Respiratory distress, hypoxic-ischemic encephalopathy (HIE), and neonatal death are some of the risks fetuses face at birth.[30] However, they can be avoided if the medical team is informed of the fetus's condition in the womb. Despite the well-known limitations of CTG, namely its considerable intra-and interobserver disagreement of CTG analysis, it is known that there is an association between a low Apgar score and pathological CTG, and nearly one-fifth of pathological CTGs may result in a low Apgar score at 5 min.[31]

Also, intrapartum fetal heart rate variability is physiologically relevant and can be used to predict acidemia and ApS at birth in neonates without severe cases of morbidity.[30]

There is a significant correlation between pathologic CTG and neonatal status. Abnormal CTG has shown that it affects fetal outcomes, such as poor ApS at 1 minute and 5 minutes, increased rate of cesarean delivery and neonatal resuscitation.[31]

In this study, we aimed to analyze the method of delivery, indication for assisted vaginal delivery and CS, weight and length of the neonate and the duration of delivery itself in terms of Apgar score, as a predictor of perinatal asphyxia.

## 2. Methods and materials

This is a retrospective cohort study analyzing deliveries that took place in the Department of Gynecology and Obstetrics Department of “Cantonal Hospital Zenica", Bosnia, between March and May 2021.

### 2.1. Patients

This retrospective research included a total of 100 selected deliveries, of which 50 were included in the study group with a diagnosis of imminent perinatal asphyxia. Fifty patients without antepartum signals of fetal hypoxia were included in the control group.

All the patient data was collected from the book of medical documentation of the “Zenica Cantonal Hospital”. In this research, maternal and fetal/neonatal variables were considered, including: maternal age; number and mode of previous deliveries; delivery method; intrapartum CTG findings; time between hospital admission and delivery; operative (CS or instrumental vaginal) delivery indications; neonatal weight, length and sex, and Apgar score. The above variables were analyzed to understand their correlation with perinatal asphyxia.

### 2.2. Inclusion and exclusion criteria

Women with a suspected diagnosis of fetal asphyxia and/or low Apgar scores were included in the study group. Women with obstetric diagnosis suggestive of fetal compromise, such as placental abruption and umbilical cord prolapse were also included.

Exclusion criteria comprised women with <18 years, multiple pregnancy and all elective CS, that did not have to undergo the process of labor.

### 2.3. Statistical analysis

Data obtained from medical records were entered into SPSS vs. 28.0, which was used for statistical analysis. We presented continuous variables as mean ± standard deviation, while categorical variables were presented as frequencies and

percentages. T-Student test and Qui-square tests were used to analyse the independent samples of quantitative and nominal variables. A p-value of ≤0.05 was considered statistically significant. The results were presented in figures and tables.

## 3. Results

In this retrospective cohort study, the maternal age, number of previous maternal deliveries, delivery method and its indications, CTG findings, neonatal weight, length, and sex, and Apgar score variables were analyzed and compared as predictors of perinatal asphyxia.

### Maternal age

In the *study group* the mean maternal age was 28.6 years ± 5.8, with a minimum age of 19 years and a maximum age of 42 years, while in the *control group* it was 26.5 years ± 4.9, with a minimum age of 18 years and a maximum age of 37 years (**Figure 5).**

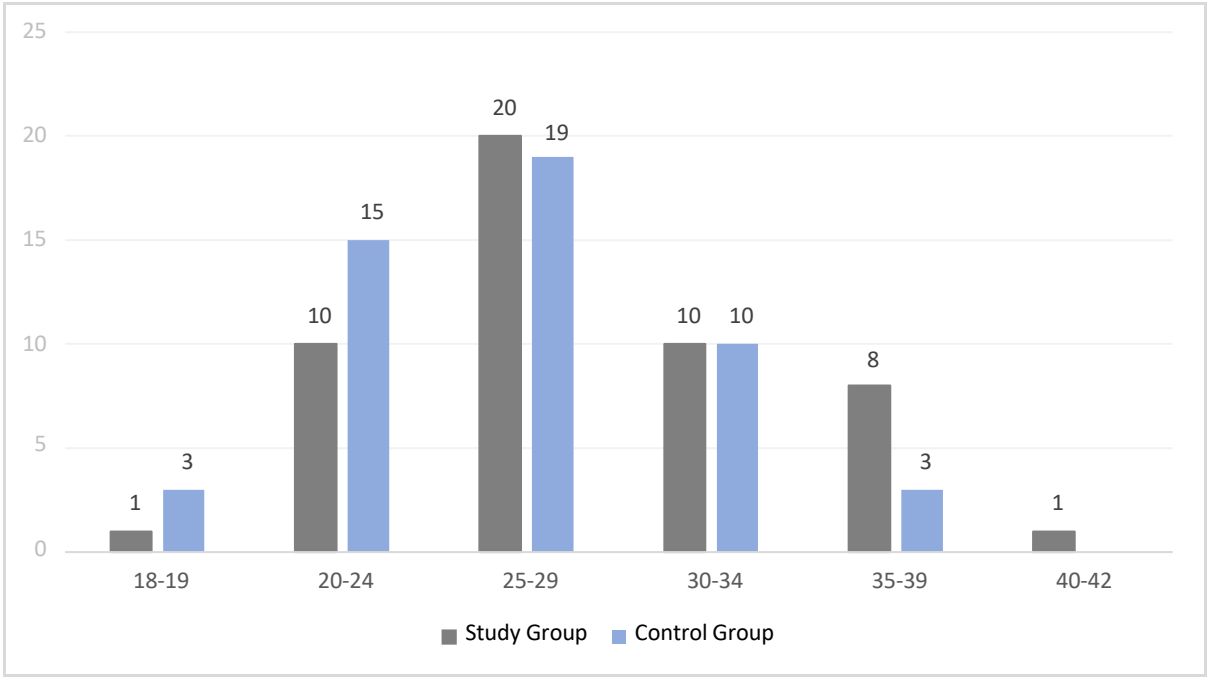



**Figure 5**. Maternal age distributions.

The maternal age range varied between 18 and 42 years. This were the minimum and maximum ages in the study group, respectively; while the minimum and maximum ages in the control group were 18 years and 37 years, respectively.

**Previous deliveries**

The mean number of deliveries in the *study group* was 1.6 ± 0.9 [1- 4]. Sixty-two percent (62%) had 1 previous delivery, 18% had 2, 16% had 3 and only 4% had 4 previous deliveries. The mean number of previous deliveries in the *control group* was 1.7 ± 1.09 [1-6]. Fifty-eight percent (58%) had 1 previous delivery; 26% had 2; 10% had 3; 2% had 4; 2% had 5 and 2% had 6 previous deliveries **(Figure 6)**.

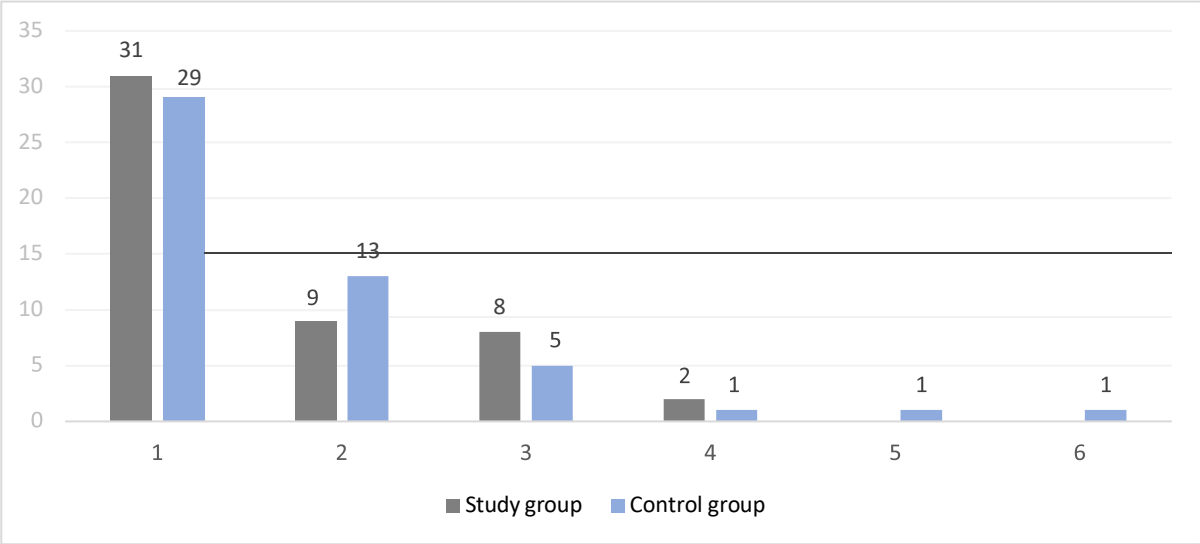



**Figure 6**. Previous deliveries distribution

The graph shows the distribution of previous deliveries. Most mothers had one previous delivery. The maximum number of deliveries was registered in control group (6 deliveries).

**Newborn gender**

Regarding the newborn gender in the study group, 54% were male and 46% female. Similar percentages were observed in the control group where 52% were male and 48% female.

**Newborn weight and height**

The mean newborn weight in the *study group* was 3423g ± 0.7**,** with the lowest weight being 1800g and the highest weight being 4730g**.** Of the newborns in this group, 12% were small for gestational age (< 2500g) and 20% were macrosomic (>4000g). In the *control group* the mean newborn weight was 3428g ± 0.5, with the lowest weight being 2320g and the highest weight being 4460g. Of the newborns in

this group, 6% were small for gestational age (< 2500g) and 16% were macrosomic (>4000g) **(Figure 7).**

The mean of the newborn length in the *study group* was 49.4 cm ± 3.7 cm with the smallest baby being 31cm and the largest 55cm, while in the *control group* was 49.1 cm ± 2.5 cm with the smallest baby being 40cm and the largest 53cm **(Table 1).**

The difference in newborn weight between the two groups was 0.05g ± 0.1 (p=0.481). The mean difference between neonatal length in both groups was of 0.2 ± 0.64cm, p=0.78 **(Table 1).**

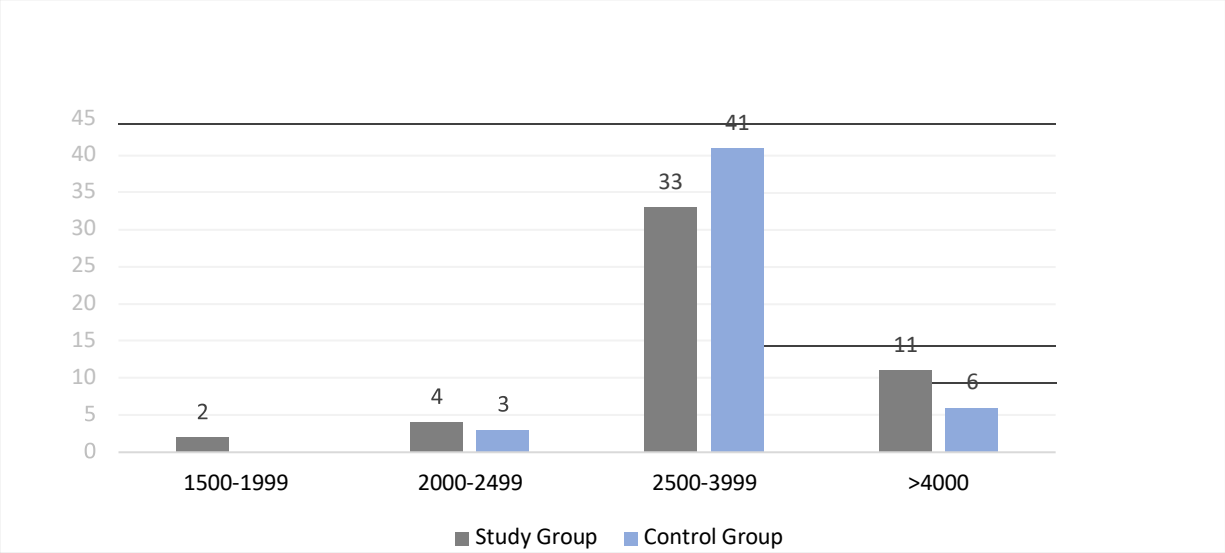



**Figure 7**. Average birth weight (grams).

Most newborns were born within adequate birth weight (between 2500g and 4000g). In the study group, the lowest registered weight was 1800g and the highest was 4730g; while in the control group the registered lowest and highest weights registered were 2320g and 4460g, respectively.

**Table 1.** Mean newborn weight and length comparison.
There were no statistically significant differences between mean newborn weight and length of both groups.

| | Total | p-value |
|---|---|---|
| **Mean weight (grams)** | | |
| Study Group | 3423 | 0.48 |
| Control Group | 3428 | |
| **Mean length (cm)** | | |
| Study Group | 49.3 | 0.78 |
| Control Group | 49.1 | |

## Fetal growth restriction and macrosomia

In the *study group* there was a total of 12% (n=6) of newborns with FGR, and 6% (n=3) in the *control group*. A chi-square test was performed to compare the FGR in both groups. There was no statistically significant association between them ($\chi^2$= 0.435, p = 0.509).

There was a total of 22% (n=11) macrosomic neonates in the *study group*, and 16% (n=8) in the *control group*. A chi-square test was performed to relate the macrosomia findings in both groups. There was no statistically significant association between them ($\chi^2$= 0.05, p = 0.823) **(Table 2).**

**Table 2.** Fetal growth restriction versus macrosomia.
There were no statistically significant differences between both groups regarding the occurrence of fetal growth restriction and macrosomia.

| | Total | p-value |
|---|---|---|
| **FGR rate** | | |
| Study Group | 6 (12%) | 0.509 |
| Control Group | 3 (6%) | |
| **Macrosomia rate** | | |
| Study Group | 11 (22%) | 0.823 |
| Control Group | 8 (16%) | |

**Peripartum diagnosis**

The main peripartum diagnosis on the *study group* was imminent asphyxia (78%); 10% uterine disruption; 8% placental abruption; 2% preeclampsia and 2% post-partum hemorrhage **(Figure 8).**

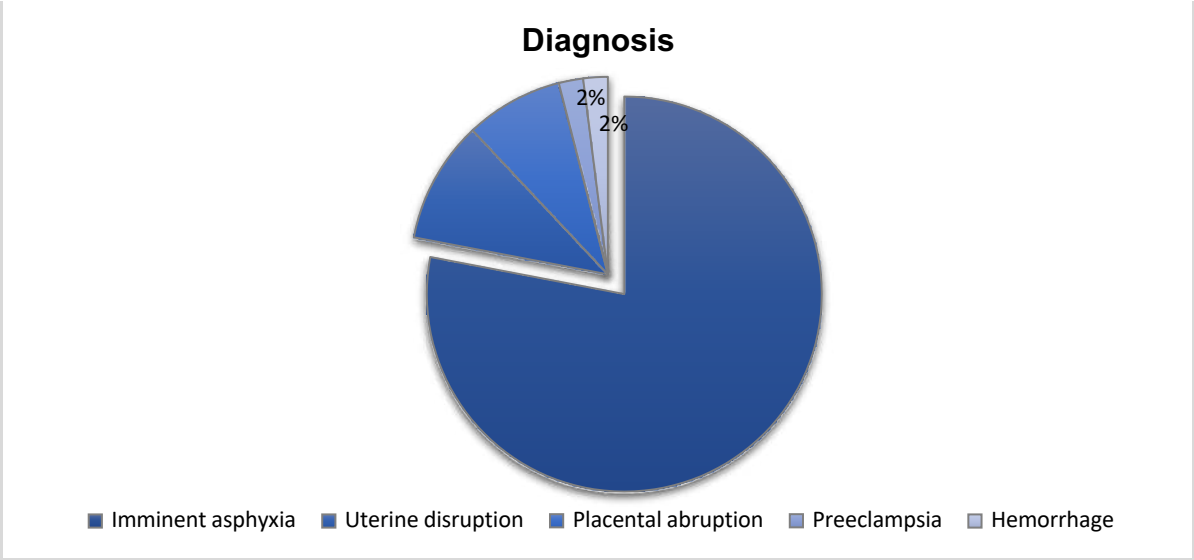



**Figure 8**. Diagnosis of the study group patients.
Seventy-eight percent of the peripartum diagnosis observed in the study group were imminent asphyxia, followed by uterine disruption, placental abruption, preeclampsia, and hemorrhage.

**Mode of delivery**

Concerning mode of delivery, all neonates in the *study group* (100%) were delivered by CS. However, in the *control group* 72% of the neonates were delivered vaginally and only 28% by CS **(Figure 9).**

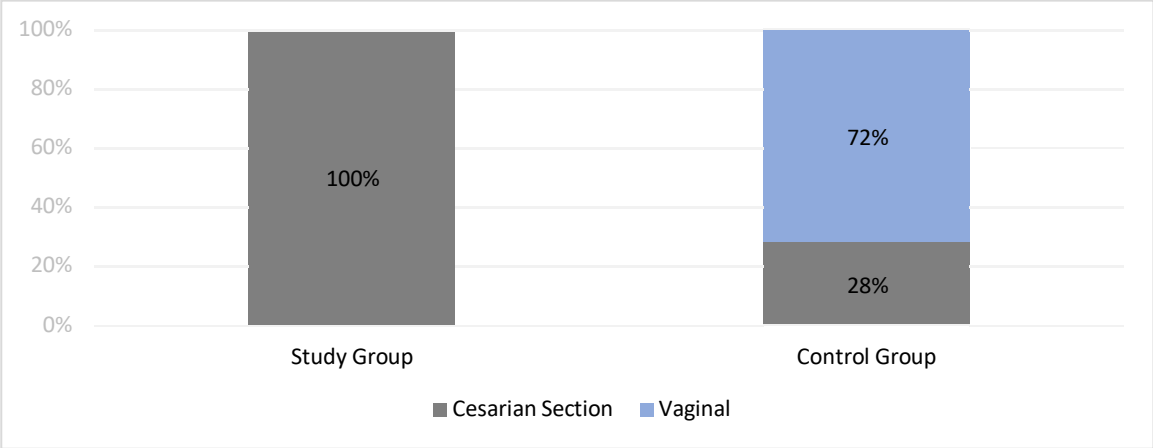



**Figure 9**. Mode of delivery.

The mode of delivery in the study group was CS (100%) whereas in the control group the majority of deliveries were vaginal (72%).

**Time between gravida admission and delivery**

The mean time between maternal hospital admission and delivery was 32h12 in the study group and 33h21 in the control group. The mean difference in total time between the two groups was of 1h08 ± 12h29, p=0.927 **(Table 3).**

**Table 3.** Time between gravida admission and delivery.

There was no statistically significant difference between both groups regarding time between gravida admission and delivery.

| | | p-value |
|---|---|---|
| **Mean difference in total time since admission to delivery** | | |
| Study Group<br>Control Group | 1h08min | 0.927 |

**Apgar score**

In the *study group* the mean ApS at 1 minute was 7.1 ± 1.7 [1-9] and 4% of the population had less than 3 ApS in the first minute. The mean ApS at 5 minutes was 8.3 ± 1.03 [4-10] and 4% of the population had < 7 at the 5$^{th}$ min.

As for the *control group* the mean ApS at 1 minute was 8 ± 1.7 [6-9] and no newborn had less than 3 ApS in the 1st minute. The mean ApS at 5 minutes was 8.9 ± 0.5 [7-10] and there were no newborns with less than 7ApS in the at 5th minute **(Table 4).**

The difference in Apgar score at 1 minute between both groups was 0.84 ± 1.8, **p=0.002**. The difference in Apgar score at 5 minutes between both groups was 0.58 ± 1.1, **p=0.001**. There was a statistically significant difference in Apgar Scores between both groups on the 1st and 5th minutes **(Table 4).**

**Table 4.** Apgar score.

The Apgar scores at 1 and 5 minutes after delivery were significantly lower in the study group when compared with the control group.

| | **Mean Apgar** | **p-value** |
|---|---|---|
| **Apgar Score 1min** | | |
| Study Group | 7.12 | **0.002** |
| Control Group | 7.96 | |
| **Apgar Score 5min** | | |
| Study Group | 8.30 | **0.001** |
| Control Group | 8.88 | |

## 4. Discussion and conclusions

We have analyzed the association between PA and ApS. The ApS assesses the general health of the newborn, and therefore a low ApS score has been an indicator of asphyxia.[31]

The mean age of mothers in our study group was 28.6 years ± 5.8 years. Most patients comprised between the ages of 20 and 34 years old. Maternal age between both groups was similar (control group 26.5 years *vs* study group 28.6 years). A study by Aslam et al. showed that mothers aged 20-25 years have a higher risk of developing obstetric asphyxia than younger or older mothers.[29] Also, the Journal of Obstetrics and Gynecology supports that young maternal age (< 20 years) has an increased risk of PA. Immaturity of the cervix, uterine blood supply, and young gynecologic age were reported as associated factors.[32] On another hand, other study states that mothers older than 35 years were at increased risk for PA. For young mothers, it was found that there was no increased risk for PA unless additional maternal comorbidities were present.[33] Regarding parity, 62% of women in the study group already had 1 previous delivery, and the rate was similar in the control group at 58%. This difference was not statistically significant. However, Aslam et al., suggest that there was an increased risk for PA when infants are born to primiparous women. Another study also found evidence that fetal distress was more pronounced in primigravida, being the main reason for prolonged labor duration.[29, 34] Although newborn gender was not analyzed in relation to PA prediction, we observed a prevalence of male neonates in both study and control groups. Nadeem et al. also showed that this difference was not statistical significant.[35] In our study, the mean difference in newborn weight between the two groups was not statistically significant (see table 1). Nevertheless, FGR rates were higher in the study group when comparing with the control group (12% vs 6%), despite this not being statistically significant. This goes against the work of Aslam et al., in which he states that low birth weight was highly related with birth asphyxia. This was mainly related to maternal comorbidities, such as hypertension or diabetes.[29] We had a 22% rate of macrosomic newborns in the study group compared with 16% in the control group, although this difference was not statistically significant. This may lead to a potentially higher risk of asphyxia, because of the higher oxygen needs of these newborns. A study by Gu S et al. has shown that maternal age, male gender, and maternal BMI at early pregnancy were risk factors for macrosomia.[36]

Regarding mode of delivery, in our study, 100% patients in the study group experienced CS compared to 28% in the control group. The apparent reasons for this increased rate of CS are the neonatal diagnosis/CTG findings of imminent asphyxia, uterine disruption, placental abruption, preeclampsia, and hemorrhage. A study by Herrera et al. came to similar conclusions as our work, and concluded that rapid delivery could be life-saving for the fetus and could reduce the risk of PA.[33] In our study, 4% of neonates with ApS at < 3 after 1 minute and 4% of neonates with ApS at < 7 after 5 minutes were in the study group. There were no neonates with ApS less than 3 and 7 at 1 and 5 minutes in the control group, respectively. There was a statistically significant difference of ApS between both groups at 1 minute and 5 minutes (**p=0.002** and **p=0.001**, respectively). Our results have shown that the CTG abnormal findings observed during the labor monitoring were significantly associated with the presence of PA. Without adequate monitoring it would not be possible to diagnose high-risk events in a timely manner. CTG monitoring can help clinicians identify women who need early obstetric intervention.

**Strengths and limitations**

The most important strength of our work was to show the clinical workflow and obstetrical decisions regarding CTG abnormal findings during labor, and the real outcomes of those decisions made at the Gynecology and Obstetrics Department of "Cantonal Hospital Zenica".

The most important limitations of our work were the retrospective data collection, which was subject to missing data that cannot be recollected without being subject to recall bias. Also, our sample size was relatively small, and this could have had some effect in our analysis. For example, borderline p values could have been statistically significant in a more robust sample size.

In conclusion, there was a significant correlation between abnormal CTG findings and PA findings in the newborn, as assessed by the Apgar score.

The present study has shown that intensive monitoring of patients during the first and second phases of labor helped to timely register the threat of PA, which can be observed by the ApS in the first and fifth minutes. There was no statistically significant difference between the study and control groups regarding maternal parity, age, newborn weight, and length. Although some of these findings were supported by

other studies in literature, it could be possible that newborn weight could have been underestimated in our study due to small sample size. Further studies should be performed in this area to ascertain these possible differences.

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