"SERUM AND URINARY URIC ACID AND CREATININE RATIO AS BIOMARKER IN PERINATAL ASPHYXIA"

BY

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Dissertation submitted to

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In partial fulfillment of the requirements for the degree of

DOCTOR IN MEDICINE IN PEDIATRICS

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I hereby declare that this dissertation/thesis entitled "**SERUM AND URINARY URIC ACID AND CREATININE RATIO AS BIOMARKER IN PERINATAL ASPHYXIA**" has been prepared by me under the supervision and guidance of **Dr R.H GOBBUR,** M.D, Professor, Department of Pediatrics. This is being submitted to BLDE (Deemed to be University) Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, in partial fulfillment of the requirement for the award of a master's degree in Pediatrics. This work has not been submitted to any University by me for award of any degree.

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ABSTRACT

Background

According to the WHO, the main cause of early neonatal mortality is perinatal asphyxia, which is defined as the inability to establish breathing at birth and is thought to be responsible for 900,000 fatalities annually.[1] An estimated 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths that occur each year worldwide are thought to be caused by hypoxia that affects newborns (birth asphyxia) or foetus (fresh stillbirth). Newborns delivered intramurally can be considered asphyxiated if the APGAR score is less than 7 at birth. At 1 minute after birth, **moderate** birth asphyxia is defined as an **APGAR score of four to six**, while **severe** birth asphyxia is defined as an **APGAR score of three or lower**.

Acute kidney injury occurs during moderate to severe Birth Asphyxia. Chronic renal insult may result from hypoxia, hypotension, and the use of nephrotoxic drugs both during pregnancy and after delivery. The most prevalent of the recognized consequences is Acute Renal Failure (ARF), which has a poor prognosis and can cause irreversible renal impairment in as many as 40% of survivors[10]. Most of the studies on acute kidney injury following perinatal asphyxia focus only on Urinary uric acid and creatinine ratio. The ratio of serum Uric acid to creatinine as a biomarker for prenatal hypoxia has not been the subject of any published research. Ours is the first research of its type. To determine the severity of hypoxia and its result, the study must correlate maternal variables with neonatal resuscitation level, serum creatinine, and uric acid level in resuscitated neonates.

Aims & Objectives:

1. To determine serum uric acid and creatinine levels and urinary uric acid and creatinine levels in neonates with perinatal asphyxia and try to correlate them.
2. To compare the extent of Renal injury with the severity of asphyxia and the level of resuscitation done at birth.

Results:

A total of 68 cases and 61 controls were analyzed. Most of the infants in the case groups were male, comprising 64.7% (n=44). Among the cases, 36.8% (n=25) underwent lower-segment cesarean section (LSCS), while 63.2% (n=43) had a vaginal delivery, out of which 58.1%(n=25) were primigravida and 41.8%(n=18). At an APGAR score of 5 min, 10.2% (n=7) had an APGAR score of 0-3, while 41.1% (n=28) had an APGAR score between 4-6, and later, 48.5% (n=33) had an APGAR score greater than 7. There is an association between renal parameters and APGAR score at 5 min and found that there is a statistical significance between all these after applying the chi-square test (p-value <0.01).

Conclusion:

This study shows that **serum and urinary uric acid and creatinine ratios** have potential as **biomarkers for perinatal asphyxia**. There's an important link between these biochemical markers and **low APGAR scores**, which supports their role in early diagnosis.

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LIST OF ABBREVIATIONS

ATP	Adenosine Triphosphate
ARF	Acute Renal Failure
AKI	Acute Kidney Injury
IVC	Inferior Vena Cava
SVC	Superior Vena Cava
UA	Uric Acid
Cr	Creatinine
SVC	Superior Vena Cava
UOP	Urine Output
WHO	World Health Organization
HIE	Hypoxic Ischemic Encephalopathy
LDH	Lactate Dehydrogenase
CK-MB	Creatine Kinase Muscle-Brain Fraction
AST	Aspartate Aminotransaminase
ALT	Alanine Aminotransaminase

Introduction

According to the WHO, "one of the main causes of early neonatal mortality is perinatal asphyxia, which is defined as the inability to establish breathing at birth and is thought to be responsible for 900,000 fatalities annually".[1] Worldwide, birth asphyxia is a prevalent and dangerous neonatal issue that greatly increases infant morbidity. Lack of oxygen or blood flow to the foetus or newborn causes perinatal asphyxia, a disorder of varying severity and duration that causes multiple organ failure.[2]

Neonatal asphyxia is the most common problem that has a substantial effect on morbidity and mortality of infants. An estimated 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths that occur every year worldwide are thought to be caused by hypoxia that affects newborns (birth asphyxia) or foetuses (fresh stillbirth). There is a significant worldwide burden of prenatal asphyxia. According to a global estimate, 104 neonates die from this illness per hour. The situation is terrible in India, where statistics show that perinatal hypoxia is the cause of between 2,50,000 and 3,50,000 neonatal deaths each year, most of which happen in the initial three days of life. [3]

Newborns delivered extramurally can be assessed by (a)cried immediately at birth or (b) did not cried at birth and gasping. Newborns delivered intramurally can be considered asphyxiated if the APGAR score is less than 7 at birth. At 1 minute after birth, **moderate** birth asphyxia is defined as an **APGAR score of four to six**, while **severe** birth asphyxia is defined as an **APGAR score of three or lower**[4].

Risk factors for Perinatal Asphyxia: Antenatally, maternal factors like hypertensive disorders, infections, or bleeding; Foetal factors like breech presentation, long-term foetal distress, or growth restriction. Intrapartum elements such as infections, placental haemorrhage, uterine rupture, complications involving the umbilical cord, and extended labour represent various risk factors for birth asphyxia, which may arise unexpectedly. Birth asphyxia is a potentially fatal condition that affects 20/1000 live births.

It can also cause psychological anguish for the parents, and mental health issues of a child can disrupt the child's growth and bonding. The history of prior antenatal complications also increases the likelihood of general psychological suffering for parents following perinatal asphyxia, and birth asphyxia causes post-traumatic syndrome.[5]

The evaluation includes a comprehensive assessment of maternal and intrapartum risk factors that may affect the child. This encompasses the mother's pre-existing health conditions, complications during pregnancy, any fetal abnormalities detected prior to birth, the presence of amniotic fluid stained with meconium, maternal signs of infection, and the delivery method employed.[4]Almost all organs in the body are impacted by perinatal asphyxia. However, the most commonly affected systems are the respiratory system (23%), the cardiovascular system (25%), the nervous system (31%), and the kidneys (40%). Multiple organ systems may malfunction as a result of prolonged hypoxia. [6]

Acute kidney injury occurs during moderate to severe Birth Asphyxia. Chronic renal insult may result from hypoxia, hypotension, and the use of nephrotoxic drugs both during pregnancy and after delivery. Convulsions, shock, and other metabolic abnormalities can result from any departure from the normal amounts of electrolytes (calcium, potassium, and sodium)[7]. The kidney is the organ most susceptible to hypoxia, aside from the central nervous system.

Birth asphyxia leads to ischemia within the proximal tubule, subsequently leading to acute renal failure. Acute tubular necrosis, a complication that can vary in severity, is often reversible. But in most severe asphyxiated newborns, there may be Cortical Necrosis(Irreversible). In both conditions, serum urea and creatinine rise. Newborns affected by perinatal asphyxia will have anaerobic metabolism, reduced adenosine triphosphate (ATP) production, ion pump impairment, and accumulation of intracellular calcium, chloride, water, sodium, and extracellular potassium, resulting in electrolyte abnormalities [8,9].

The most prevalent of the recognised consequences is Acute Renal Failure (ARF), which has a poor prognosis and can cause irreversible renal impairment in as many as 40% of survivors[10]. Most of the studies on acute kidney injury following perinatal asphyxia focus only on Urinary uric acid and creatinine ratio. A normal-term neonate may pass urine by 48 hours after delivery, whereas in asphyxiated neonates, it might be more delayed.

Hence, there is a need to study the Serum Uric acid to creatinine ratio as an early biomarker for acute kidney injury in perinatal asphyxia. The ratio of serum Uric acid to creatinine as a biomarker for prenatal hypoxia has not been the subject of any published research. Ours is the first research of its type. To determine the severity of hypoxia and its result, the study must correlate maternal variables with neonatal resuscitation level, serum creatinine, and uric acid level in resuscitated newborns.

NEED FOR THE STUDY

Perinatal asphyxia is a major cause of morbidity and mortality of neonates, necessitating early and reliable biomarkers for prompt diagnosis and intervention. Serum and urinary uric acid-to-creatinine ratios have been proposed as potential indicators of hypoxic injury, as hypoxia increases purine metabolism, leading to elevated uric acid levels. These biomarkers offer a non-invasive, cost-effective alternative to traditional methods and may help assess the severity of asphyxia. This study aims to evaluate their diagnostic and prognostic utility, improving early detection and management of affected neonates.

Aims & Objectives:

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REVIEW OF LITERATURE

Perinatal asphyxia is a major cause of morbidity and mortality of neonates, necessitating early and reliable biomarkers for prompt diagnosis and intervention. Serum and urinary uric acid-to-creatinine ratios have been proposed as potential indicators of hypoxic injury, as hypoxia increases purine metabolism, leading to elevated uric acid levels.

Aetiology

Any condition that impairs the foetus's blood or oxygen flow is considered perinatal asphyxia, and its causes can be traced back to the mother's circulation, placental factors, or foetal problems. Maternal hemodynamic impairment (such as amniotic fluid embolism, sepsis, or shock), uterine difficulties (such as rupture), anomalies of the cord and placenta (such as placental abruption, cord compression/knots), and infections are among the common causes.

In 80% of newborns in need of resuscitation, asphyxia may happen in the final seconds before delivery or right after. About 20% of cases of perinatal asphyxia occur antepartum. To find the root cause, a comprehensive obstetric and peripartum history/records is essential. However, only a small percentage of newborns with a significant antenatal complication have a documented sentinel episode.[13]

Epidemiology of Perinatal Asphyxia

The incidence of term perinatal asphyxia varies significantly depending on the availability of maternal and neonatal healthcare. In developed countries it is two per 1000 live births, indicating benefits such as advanced antenatal care, prompt neonatal resuscitation and skilled birth attendance. In contrast, in developing countries, where essential maternal and neonatal care access or utilisation is limited, the incidence can be >10 times higher, exceeding 20 per 1,000 live births.[14,15]

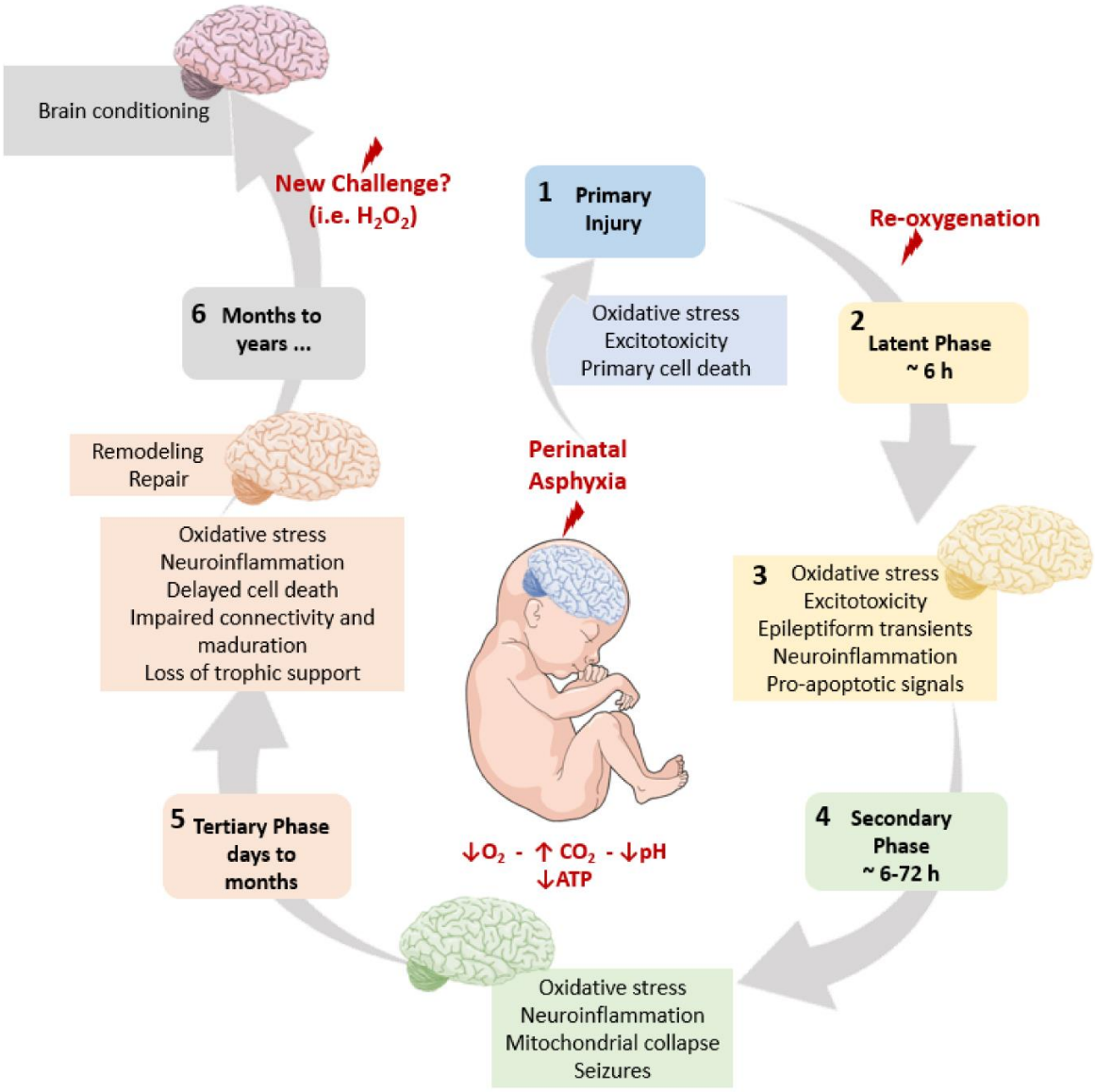

Figure 1: Perinatal asphyxia

Normal Fetal Circulation[16]

"Oxygenated blood from the placenta is delivered to the fetus through the umbilical vein". A significant portion of this blood bypasses the liver via the ductus venosus, subsequently entering the IVC. In the right atrium, the oxygen-rich blood from the IVC preferably shunts through the foramen ovale into the left atrium, thereby avoiding the non-functioning lungs.

From the left atrium, blood flows to the left ventricle, which then pumps it into the ascending aorta. The ascending aorta distributes oxygenated blood into the brain through the carotid arteries and to the upper body. Deoxygenated blood from the brain and upper body returns to the right atrium via the SVC. Blood travels from the right atrium to the right ventricle, where it is pumped into the pulmonary artery; however, only a small portion of this blood reaches the lungs.

Circulatory Changes During Labour and Neonatal Transition

Intermittent Uterine contractions compress placental vessels, reducing placental blood flow temporarily. Foetal adaptations, such as an increased heart rate and redistribution of blood flow to vital organs (heart, brain), compensate for reduced oxygen delivery. The foetus depends on oxygen reserves in the placenta and its blood for brief periods of reduced oxygenation. Stress during labour may stimulate catecholamine release, increasing heart rate and blood pressure to maintain perfusion.

Neonatal Transition (After Birth):

First breaths expand the lungs, replacing fluid with air and lowering pulmonary vascular resistance. Pulmonary blood flow increases, enabling oxygenation in the lungs. Increased blood return from the lungs raises left atrial pressure, closing the foramen ovale, and this prevents the mixing of oxygenated and deoxygenated blood. High oxygen levels and reduced prostaglandins cause the ductus arteriosus to constrict and close, redirecting blood to the lungs instead of bypassing them. Umbilical cord clamping ends placental blood flow, leading to ductus venosus closure and rerouting blood entirely through the liver. Clamping the cord stops placental circulation, prompting an increase in systemic vascular resistance.

Pathophysiology of multiple organ dysfunctions[17]

In HIE, the process of brain injury happens in phases. First, the disruption of the brain's supply of oxygen and glucose results in instantaneous primary neuronal damage. The severity of the damage will determine whether the brain can reroute blood flow to safeguard its most important components, including the brainstem and cerebellum, as doing so would cause harm to the watershed areas. A more severe injury may have a greater impact on the basal ganglia[17].

Cardiovascular Alteration and Multiorgan Dysfunction:

Many biochemical processes cause multiple organs and systems to deteriorate as a result of hypoxia and ischemia[18]. The heart and kidneys are the two most important extracranial organs affected by hypoxia-ischemia, though it can also affect other tissues and systems, including the gastrointestinal (food intolerance, necrotizing enterocolitis), pulmonary (pulmonary hypertension, meconium aspiration), and hepatic (transient transaminase elevation).

"The mechanism of energy metabolism in astrocytes and neurons in the basal ganglia of a neonatal hypoxic-ischemic cerebral damage piglet model was examined" by Zheng and Wang[19,20]. According to their findings, lactate levels rose two to six hours after hypoxic-ischemic damage, while glucose levels peaked six to twelve hours later. In research by Hankins et al.[21] it was found that "hypoxic-ischemic encephalopathy (HIE) was a disorder that developed secondary to renal, cardiac and hepatic failure following hypoxia at birth rather than being caused by low oxygen levels".

Cardiovascular response:

Intrapartum hypoxia can lead to transient foetal bradycardia, peripheral vasoconstriction, centralization of blood flow, and systemic hypertension due to catecholamine release. This can cause hypotension and deplete cardiac glycogen, anaerobic respiration, and metabolic acidosis.[22] If untreated, this can result in myocardial dysfunction, circulatory shock, insufficiency, tricuspid regurgitation, hypotension, and cardiac arrest. Whenever redistribution of cardiac output fails to maintain myocardial oxygenation it leads to reduced cardiac glycogen, metabolic acidosis, and anaerobic respiration, according to Sehgal et al. [23]

Renal changes:[24]

Acute Kidney Injury (AKI) occurs in newborns due to reduced blood supply to the kidney during hypoxic episodes. Between 50-72% of asphyxiated newborns exhibit signs of renal compromise. The kidney's decreased excretory function results in reduced blood volume, electrolyte levels, and acid-base homeostasis. If the kidney injury worsens, other organs, especially the brain, may suffer damage. Liver injury is likely the cause of hypoperfusion secondary to hypoxia. Transaminase levels may correlate with the severity of perinatal asphyxia.[25]

Socio-demographic profile:

The sociodemographic details of maternal age and education level affect the occurrence of birth asphyxia. A study showed that mothers aged twenty or younger experienced three times more newborn asphyxia occurrences than other groups and revealed a direct link between birth asphyxia incidence and incomplete prenatal follow-ups.[26,27]

Birth asphyxia develops from elements that involve maternal health before delivery, alongside conditions that happen during birth and characteristics that affect newborns. Abnormal maternal medical history, such as high blood pressure, gestational diabetes, and anemia, increases the risk of delivery asphyxia. The risk factors that arise during childbirth include instrumental delivery together with meconium-stained liquor and prolonged membrane ruptures. Low birth weight, preterm birth, and small for gestational age do not increase the likelihood of birth asphyxia.

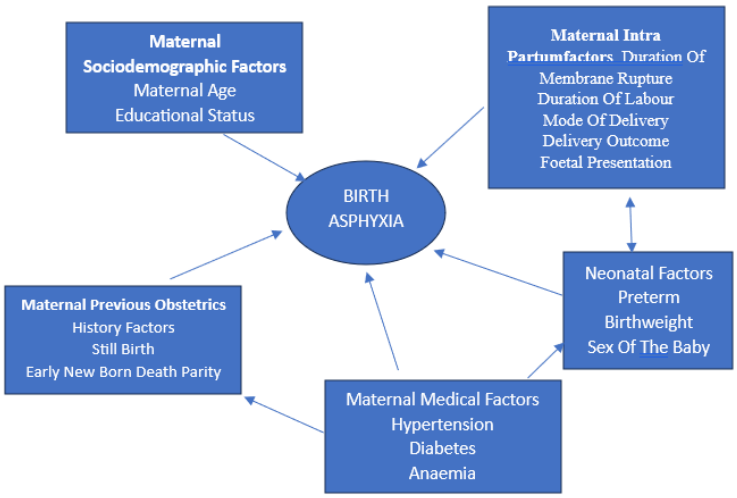

Figure 2: Causes for birth asphyxia

During kidney embryo development, three successive stages are noted, which begin with pronephros during the 4th week, extending through mesonephros from 4th-8th week until metanephros appear in the 5th week. The primitive pronephros contain only non-working tubules together with a pronephric duct. Intermediary mesoderm produces the mesonephros, which achieves temporary blood filtering along with the production of fluid resembling urine. The permanent organ known as the metanephros develops both the ureter and nephrons while creating fetal urine crucially.[28,29]

Anatomy of Kidney:[30]

Each newborn kidney has the same basic adult kidney form, but its functionality remains different because of immature development. The kidneys measure 4-5 cm in length and display a bean shape with rounded edges and several ridges. The kidneys find their position behind the peritoneal cavity while maintaining slightly different elevation levels. The most elevated and lowest parts of the kidney structure are discernible while the renal artery and vein connect to the ureter through the hilum.

The renal cortex presents a thinner composition than the medulla does. Renal veins deliver the bloodstream to the IVC, while renal arteries maintain a size comparable to these veins. The nasal deviation in newborn kidneys results from undeveloped glomeruli and tubules, which create decreased GFR while making newborns more vulnerable to fluid and electrolyte disorders.

Through the renal arteries, the kidneys receive blood until each artery progresses into segmental, interlobar, arcuate, and interlobular arteries to supply filtration blood to the cortex region. The medulla obtains its blood supply through the vasa recta, carrying approximately 10% of the total blood volume for creating urine concentration osmotic gradients. Blood flow fluctuations provide essential metabolic support to the kidney while preserving glomerular filtration and tubular function.

The renal system of newborns faces significant hypoxic risk because their nephrogenesis development is incomplete while their blood flow is poor and their oxygen delivery structures have reached limited growth. Among all kidney regions, the hypoxic-ischemic injury risk is highest for the outer medulla because its low oxygen tension coincides with elevated metabolic requirements. Acute kidney injury becomes more likely in newborns because their autoregulatory mechanisms remain incomplete while oxygen supply is already compromised.[31]

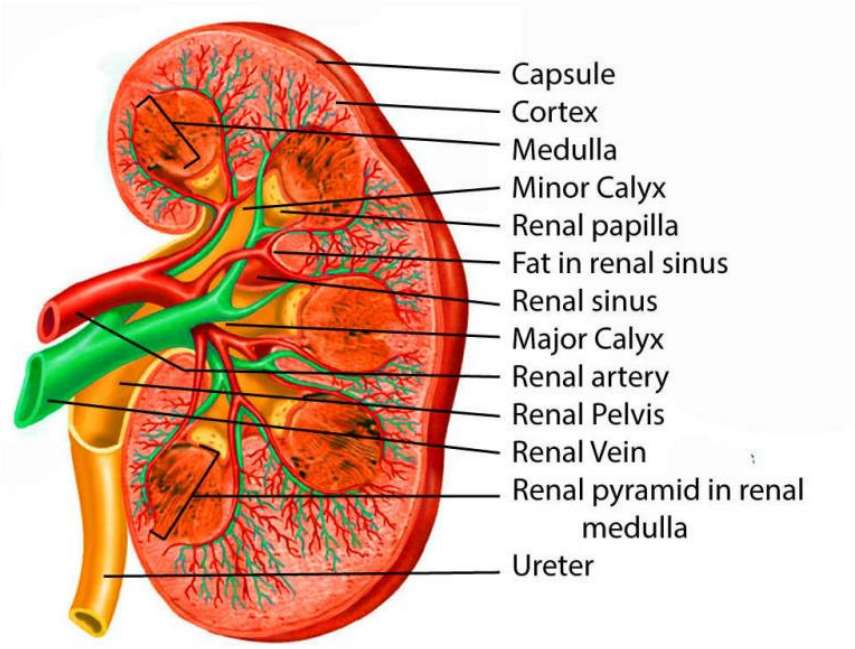

Figure 3: Anatomy of the kidney

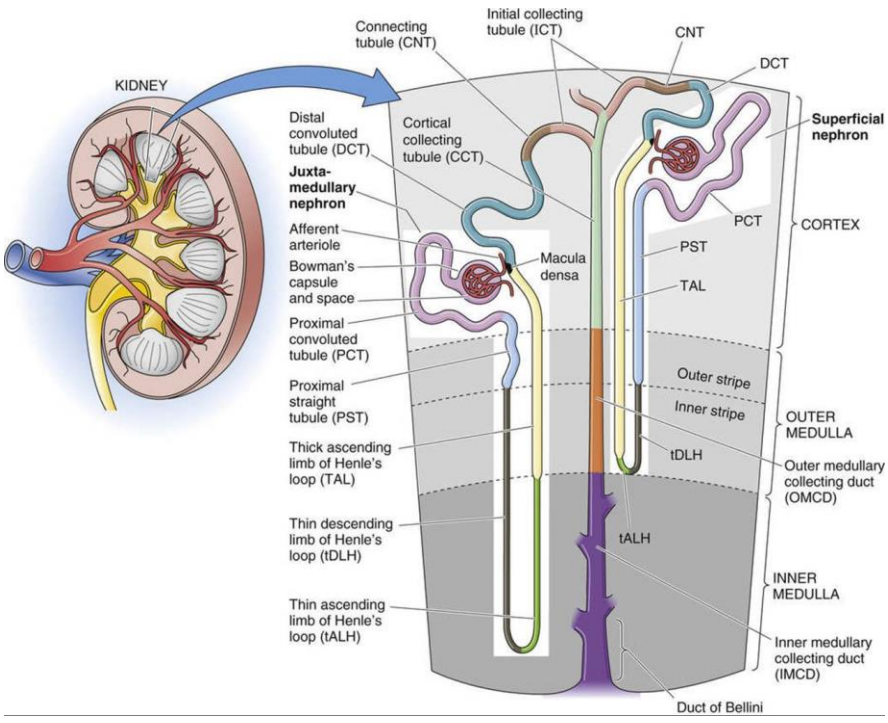

Figure 4: Parts of Nephron

Physiology of kidney function in the newborn:

The foetal kidneys begin to produce urine from 16 weeks of gestation. By 34 to 36 weeks, the kidneys complete their development. The renal vascular resistance decreases simultaneously with increasing blood pressure levels when newborns go through birth. The initial share of renal blood flow from cardiac output ranges from 3% to 7%, which increases to 10% during the first week. Initially, immature tubules produce excessive urine because they have not fully developed. Body weight decreases because excessive water leaves the body through urine.

The enzyme xanthine oxidase transforms purine metabolism to uric acid, yet creatinine arises as a degradation product of muscle creatine phosphate breakdown. When hypoxia depletes ATP during perinatal asphyxia, uric acid production from purine metabolism becomes rapid, thus increasing uric acid concentration in the body. Elevated serum creatinine is due to hypoperfusion in the kidneys along with tubular dysfunction, which decreases creatinine clearance. Researchers have identified the ratio of urinary uric acid to creatinine as a possible method to determine the severity of perinatal asphyxia.[11]

The kidney achieves normal functioning during the period from 5 to 7 days. Glomerular filtration rate (GFR) in infants varies with gestational and postnatal age. In term neonates, GFR is approximately 20 mL/min/1.73 m² at birth and doubles within the first two weeks of life. In preterm (27-31 weeks gestation), "median GFR values range from 7.9 - 30.3 mL/min/1.73 m² on day 7, increasing to 15.5 to 37.9 mL/min/1.73 m² by day 28". Neonatal GFR rests between 20% and 30% of adult levels, due to which drug elimination becomes slower. Prescribed fluid amounts for neonates with reduced RBF and GFR must be individualized to their weight along with their clinical situation because of their significant fluid loss threat from their large body surface area.[32]

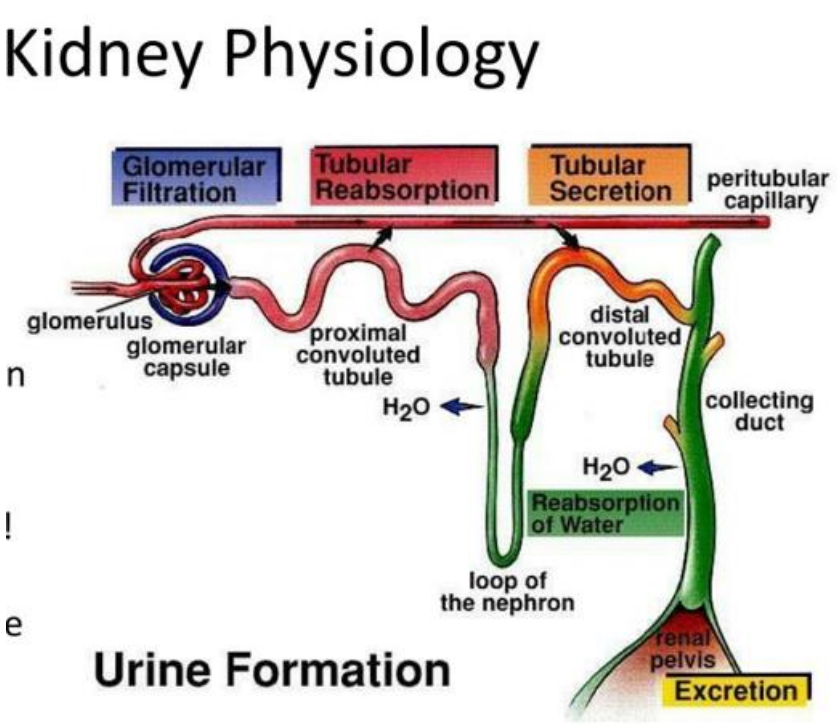

Figure 5: Physiology of Kidney

Acute kidney Injury(AKI) [33,34]

Circulatory shock with hypoxia can result in renal insufficiency within 24 hours, which could cause irreversible damage if it continues. This is because the kidneys are particularly vulnerable to hypoxia. AKI is characterized by a swift deterioration in renal function, disrupting fluid, electrolyte, and acid-base balance. It affects 8% to 24% of critically ill neonates, with mortality rates ranging from 10% to 61%.

Neonatal infections, **birth asphyxia**, respiratory distress syndrome, dehydration, heart failure, and renal anomalies are among the common conditions that lead to kidney injury in neonates, the first two being the most common causes. Asphyxia is one of the primary causes of renal failure in the neonatal period, it's not looked for, as up to 33% of neonates with AKI do not exhibit oliguria, which is frequently the primary indicator that leads to suspicion of renal failure. In critically ill newborns, the presence of AKI is a significant risk factor for adverse outcomes.[35] Neonates who survive acute renal failure are likely to suffer from long-term renal complications.

Whether there is a reduction in urine output (UOP) to oliguria/anuria or not, sudden and reversible rises in serum creatinine (SCr) levels are suggestive of acute kidney injury (AKI). Minor damage to complete renal failure is among the clinical signs and symptoms of this complex illness. AKI has superseded ARF[36] as it was used to describe an anuric, dialysis-dependent state and because treatment interventions may not always be initiated until after the onset of such a state, which increases mortality. AKI in both adult and pediatric patients does not yet have a standard definition. However, most definitions now in use involve a shift in the SCr level.

The definition of AKI in newborns combines "the neonatal modified kidney disease: Improving Global Outcomes (KDIGO) criteria through serum creatinine (SCr) level increases with urine output (UOP) decreases". AKI severity depends on evaluating two parameters as outlined by this classification system:

a) The condition progresses from the **first stage** "when SCr raises to ≥ 0.3 mg/dL within 48 hours or reaches 1.5–1.9 times baseline levels with UOP dropping below 0.5 mL/kg/h for 6–12 hours".
b) The **second stage** "corresponds to an SCr level increase of 2.0–2.9 times baseline and UOP drops below 0.5 mL/kg/h for at least twelve hours".[37]
c) The clinical scenario falls into the **third stage** of AKI "when SCr rises to 3.0 times baseline values or exceeds 2.5 mg/dL or when renal replacement therapy starts and UOP drops below 0.3 mL/kg/h for 24 hours or longer or persists at an anuric state for 12 hours".

The appearance of neonatal AKI leads to poor outcomes, such as higher mortality alongside longer hospital stays and a possible evolution to chronic kidney disease. The normal range of serum creatinine in newborns depends on their gestational and postnatal ages and spans between 0.3 and 1.0 mg/dL. The filtration rate of glomeruli (GFR) starts low after birth yet gradually increases until it reaches about 20 mL/min/1.73 m² during the neonatal period in both term and preterm.

Safa et al. found that 12% of children with AKI in birth asphyxia died, whereas 75% of them recovered completely. Ten kids (21.7%) had Sr creatinine levels between 1.5 and 2 mg/dl, 29 kids (64.04%) had levels between 2 and 3 mg/dl, and seven kids (15.2%) had levels between 3 and 4 mg/dl. This indicates that most patients arrived at the point of injury. [38]

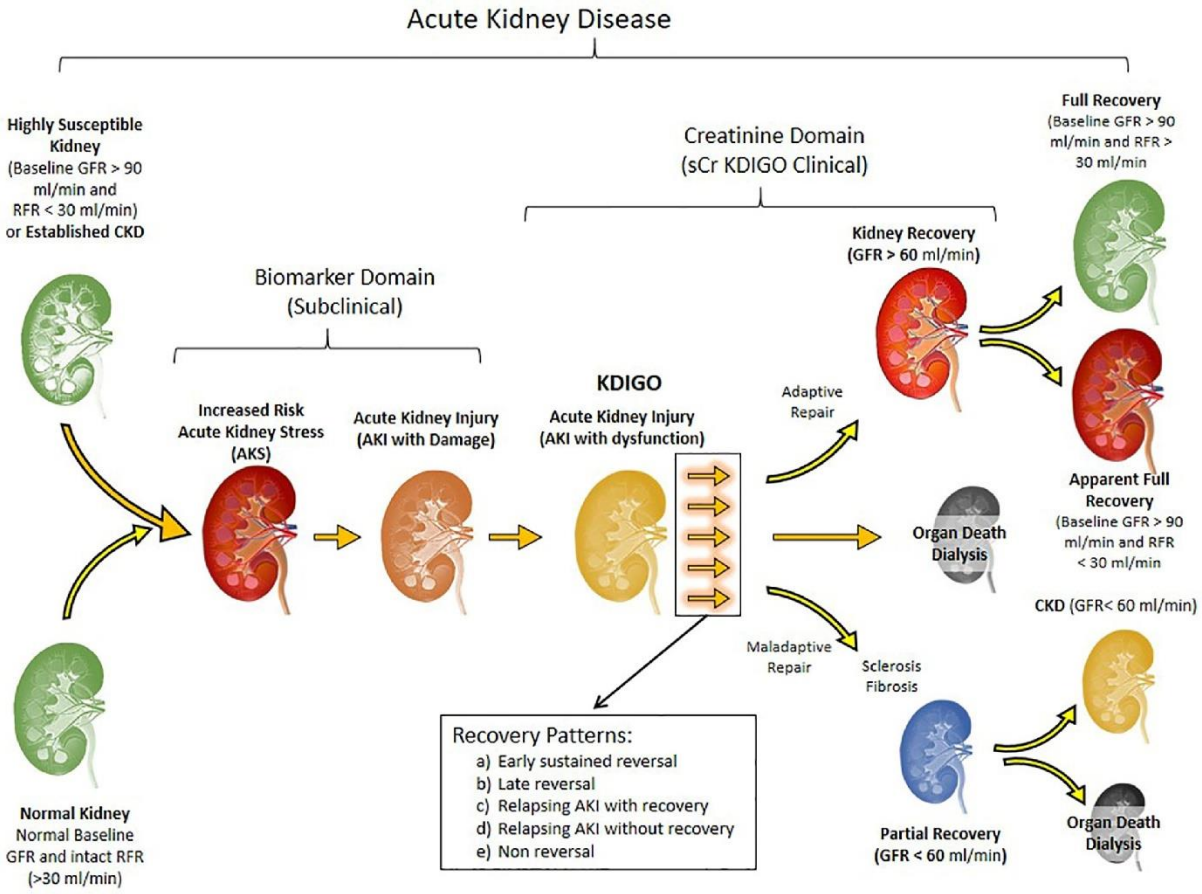

Figure 6: Acute kidney injury

In comparison to cases of mild and moderate asphyxia, a study by Meena et al. found that newborns with severe birth asphyxia had lower urinary output, although this difference was not statistically significant. One known condition that results from perinatal hypoxia is non-oliguric renal failure. [39]

The level of oxygenation in neonates determines their urine output measurement. Normal newborns produce urine at a rate of > 1 mL/kg/hr. The development of hypoxia during asphyxia causes oliguria when U/O remains below 1 mL/kg/hr, and this leads to higher mortality rates as well as hypoxic-ischemic encephalopathy. The prediction of both mortality and severe morbidities in very preterm infants can be determined through U/O measurement of <2 mL/kg/hr. Urine output monitoring plays a critical role in the observation of neonates because hypoxic events require extra attention to urine output measurements.[40]

A study by Krishnan E et al. [41] found that asphyxiated babies had a significantly higher urine uric acid to creatinine ratio than non-asphyxiated newborns (0.78-4.94 vs. 0.42-1.96). In the Gulati K et al. [42] study, 51.1% of babies who were asphyxiated had a urine uric acid to creatinine ratio higher than 1.96. In neonates, the ratio of Urinary UA/Cr was significantly higher in severe HIE (3.18±0.61) than in mild HIE (2.19±0.32).

In a study by David et al.[43], the urinary uric acid & creatinine ratio and the APGAR were found to be positively correlated. Additionally, early spot urine samples from asphyxiated full-term infants showed a significant increase in the ratio. According to a study by Pallab Basu et al.[9] "on 31 asphyxiated and 31 normal neonates, ratios of urinary UA/Cr were significantly higher in patients than in controls (3.1± 1.3 vs. 0.96± 0.54; $p < 0.001$). An APGAR score can be used to clinically correlate urinary uric acid/creatinine ratio, which can be used as a biomarker of birth asphyxia. In both cases and controls, uric acid and creatinine levels were measured in spot urine on the first day of birth".

The urinary uric acid to creatinine ratio is a non-invasive, simple test that serves as an early biomarker for perinatal asphyxia, assisting in clinical diagnosis and severity assessment[7]. The urinary UA/Cr ratio was evaluated among both cases and control groups, revealing significantly higher levels in the case group (3.1 ± 1.3 vs 0.96 ± 0.54; $P < 0.001$). Additionally, a strong linear correlation was found among the ratio and the severity of birth asphyxia in neonates ($r = -0.857$, $P < 0.001$).

In a cross-sectional study by Karthika Gulati et al. on Urinary UA/Cr ratio as a biomarker of perinatal asphyxia on 100 infants with perinatal asphyxia as cases and without asphyxia as controls, urine was collected on the first day of life, Urinary Uric acid and Creatinine were measured. The results showed the Mean UA/Cr ratio was profoundly higher in cases (3.41) than in controls (1.99). Along with this Urinary UA/Cr was compared with umbilical cord blood pH and APGAR. The study concludes Urinary UA/Cr is a reliable marker with good predictive value[37].

In a prospective study by Abhilipsa Acharya et al., titled "Clinico-Biochemical Correlation in Birth Asphyxia and Its Effects on Outcome," researchers analysed 150 term neonates over 2.5 kg diagnosed with perinatal asphyxia. The results indicated that 57.33% of these infants had moderate hypoxic-ischemic encephalopathy (HIE-II), while only 15.33% were classified as having mild or severe forms. Significant associations were found between severe birth asphyxia and factors such as prolonged labour (87.8%) and meconium-stained amniotic fluid (63.4%) ($p < 0.001$).

Clinical signs of HIE III included respiratory distress, lethargy, and hypothermia. Biochemical analysis showed that neonates with HIE III had significantly lower serum sodium and calcium levels and higher serum potassium levels compared to those with HIE I. Additionally, increased severity of HIE correlated with elevated serum uric acid and creatinine levels. While neonates with mild asphyxia fully recovered, all 29 fatalities (19.3%) occurred in those with moderate or severe asphyxia. The study concluded that perinatally asphyxiated neonates exhibited hyponatremia, hypocalcemia, hyperkalemia, and increased serum urea and creatinine levels, all linked to the severity of birth asphyxia, with prolonged labour and meconium-stained amniotic fluid as key contributing factors.[9]

Methodology:

This study was conducted in a Level III-A NICU in North Karnataka.

Study design: Prospective Cohort Study.

Study period: From MARCH 2023 to NOVEMBER 2024.

Inclusion criteria: All neonates born with: APGAR ≤7 at 37 weeks of period of gestation.

Exclusion criteria: Neonates with major congenital anomalies.

Sample size: The sample size is calculated by using the "formula n=z2pq/d2 where z=1.96, p=prevalence of asphyxiated neonate admissions, q=(1-p) d=95% confidence interval. The sample size, as calculated by the above formula, is 126.

Hence, a total of 129 neonates are included in the study".

Study population: All term neonates born with perinatal asphyxia. Neonates were admitted to the NICU and were given treatment as per standard protocol.

Neonates were monitored for:

- Duration of oxygen therapy and the modes of respiratory support.
- Electrolyte disturbance within the first 48 hours.
- Length of hospital stay in hours.
- Improvement/worsening/complications, follow-up till discharge or death.
- All asphyxiated babies in the NICU were evaluated for serum and urinary Uric acid and creatinine ratio within 24-48 hours of delivery.

Duration of oxygen therapy, renal function, duration of NICU hospital stay, safety, efficacy, duration of respiratory support (including ventilation), and any complications during NICU stay were evaluated.

Statistical analysis:

Data were input into an Excel spreadsheet for descriptive statistics of both explanatory and outcome variables. Qualitative data were analysed using frequency and percentage, while quantitative data were evaluated for median and interquartile range. Spearman's correlation was assessed, and scatter plots illustrated the relationship between the two groups. The Chi-square test evaluated associations among qualitative variables, and the Mann-Whitney U test analysed mean differences between the two quantitative groups, with a significance level of 5%.

RESULTS

Table 1: Distribution of sex among cases and controls

Sl. no	Sex	Cases n(%)	Control n(%)
1	Male	44(64.7%)	22(36.1%)
2	Females	24(35.3%)	39(63.9%)
3	Total	68(100%)	61(100%)

This table presents the sex distribution among infants with perinatal asphyxia. A total of 68 cases and 61 controls were analyzed. Most of the infants in the case groups were male, comprising 64.7% (n=44).

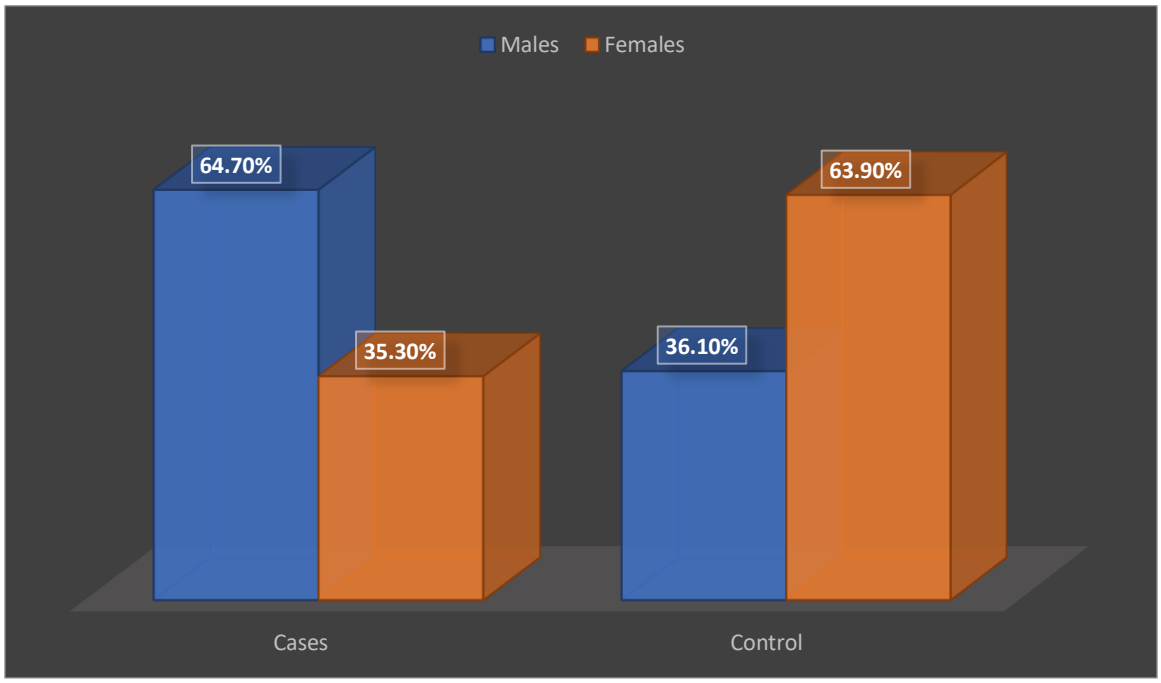

Figure 7: Distribution of sex among cases and controls

Table 2: Distribution of Significant Maternal history among cases and controls

Sl. no	Significant Maternal history	Cases n(%)	Control n(%)
1	Present	22(32.4%)	12(19.7%)
2	Normal	46 (67.6%)	49(80.3%)
3	Total	68(100%)	61(100%)

This table presents the distribution of significant maternal history among infants with perinatal asphyxia. It was observed that 32.4% (n=22) of the cases had a significant maternal history of conditions such as **pre-eclampsia**, **premature rupture of membranes**, and **gestational diabetes**, compared to only 19.7% (n=12) in the control group.

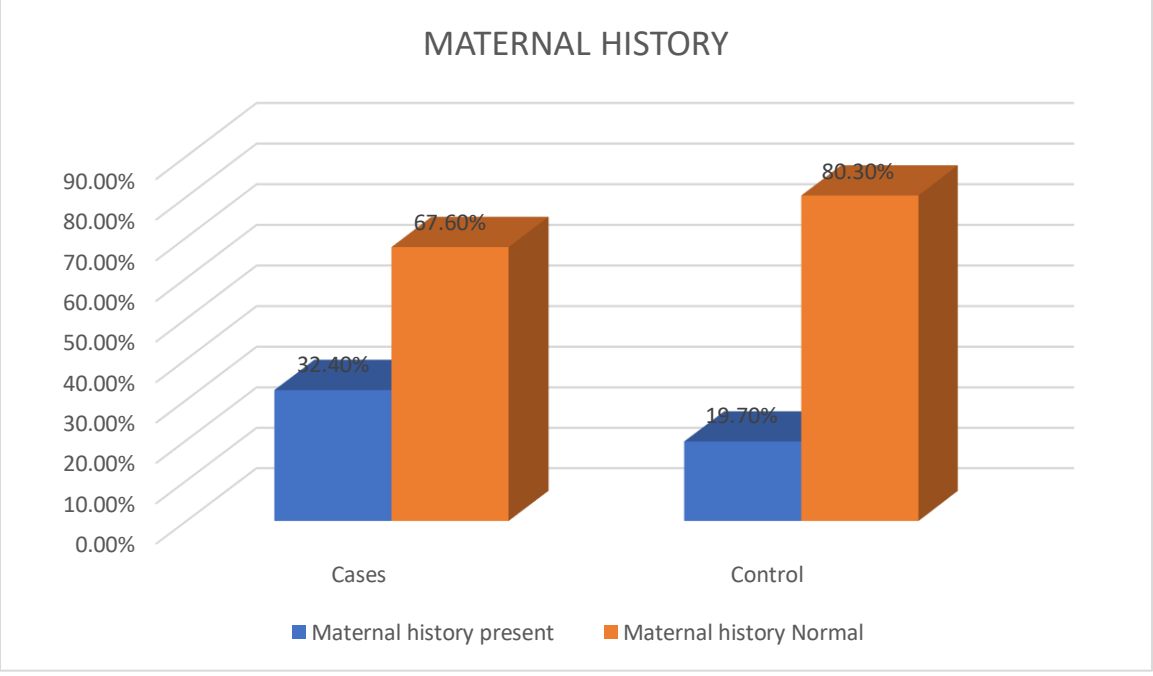

Figure 8: Distribution of Significant Maternal history among cases and controls

Table 3: Distribution of Mode of delivery among cases and controls

Sl. no	Mode of delivery	Cases n (%)	Control n (%)
1	C section ➢ Primigravida ➢ Multigravida	25(36.8%) 13 (52%) 12 (48%)	33(54.1%) 11 (33.3%) 22 (66.6%)
2	Vaginal delivery ➢ Primigravida ➢ Multigravida	43(63.2%) 25(58.1%) 18(41.8%)	28(45.9%) 11(39.2%) 17(60.7%)
3	Total	68(100%)	61(100%)

This table presents the mode of delivery among mothers of perinatally asphyxiated infants. Among the cases, 36.8% (n=25) underwent caesarean section (out of which 52%(n=13) were primigravida and 48%(n=12)), while 63.2% (n=43) had a vaginal delivery (out of which 58.1%(n=25) were primigravida and 41.8%(n=18)). In contrast, among the controls, 45.9% (n=28) had a vaginal delivery, and 54.1% (n=33) underwent LSCS. This distribution is illustrated in the accompanying bar diagram.

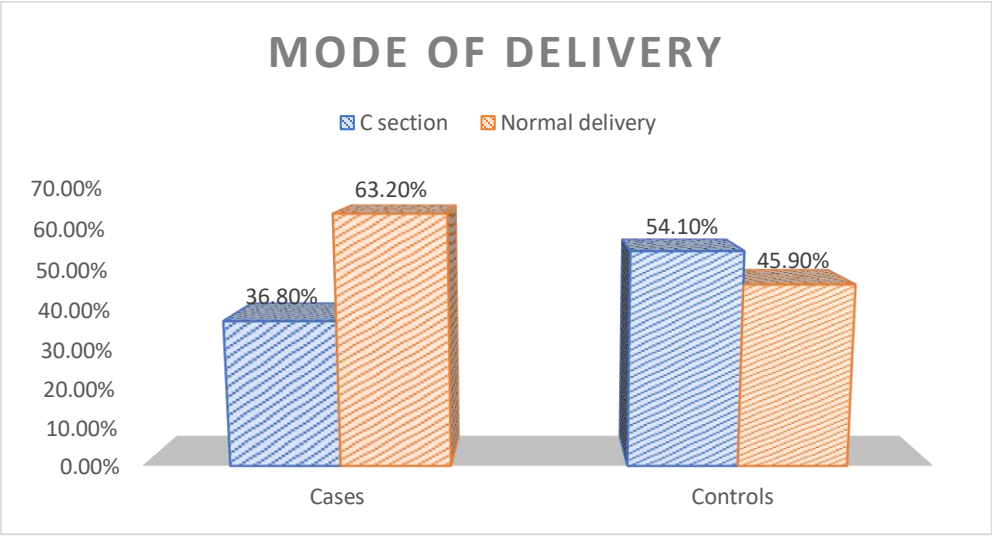

Figure 9: Mode of delivery among cases and controls

Table 4: Distribution of Birth weight among cases and controls

Sl. no	Birth weight (Kgs)	Cases n (%)	Control n (%)
1	<2.5	17(25%)	13(21.3%)
2	>2.5	51(75%)	48(78.7%)
3	Total	68(100%)	61(100%)

This table presents the birth weight distribution among asphyxiated infants. It was observed that 25% (n=17) of the cases and 21.3% (n=13) of the controls had a birth weight of less than 2.5 kg. This distribution is illustrated in the accompanying bar diagram.

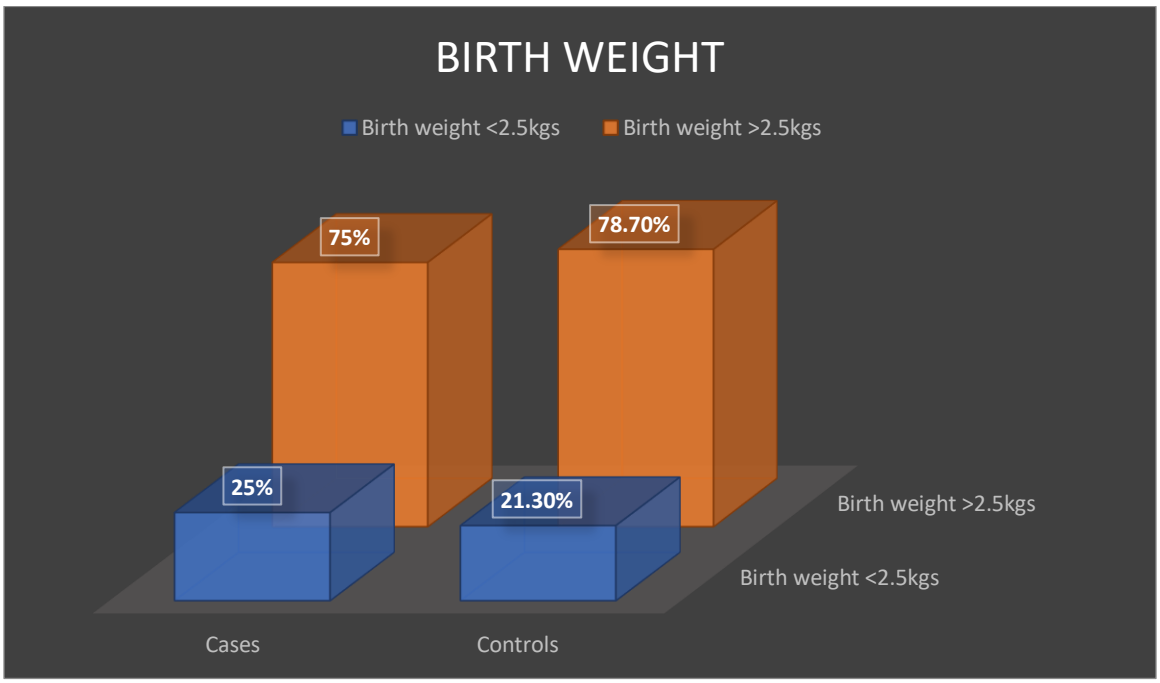

Figure 10: Distribution of Birth weight among cases and controls

Table 5: Distribution of APGAR Score at 1 min and APGAR Score at 5 min among cases and controls

Sl. no	APGAR Score	Cases n (%)	Controls n (%)
APGAR At 1 min	0-3	13(19.1%)	0
	4-6	35 (51.4%)	0
	≥7	20 (29.4%)	61 (100%)
APGAR At 5 min	0-3	7 (10.2%)	0
	4-6	28 (41.1%)	0
	>7	33 (48.5%)	61(100%)

This table presents the distribution of APGAR scores at 1 min among perinatally asphyxiated infants. It was observed that among the cases, 19.1%(n=13) had an APGAR score between 0-3 followed by 51.4%(n=35) with an APGAR score of 4-6 and then 29.4%(n-20) had >7 APGAR score. In contrast to control all had APGAR >7. The mean and SD is 6.46(0.609) among cases, and with control, it is 8.

Among the cases, 10.2% (n=7) had an APGAR score of 0-3, while 41.1% (n=28) had an APGAR score between 4-6, and later, 48.5% (n=33) had an APGAR score greater than 7. In contrast, all infants in the control group (100%, n=61) had an APGAR score greater than 7. Notably, there was an improvement in APGAR scores among cases after 5 minutes compared to at birth. The mean APGAR score for both cases and controls was 8, with a standard deviation of 0.667. The mean and standard deviation among cases was 6.13 ± 0.667, while among controls, it was 9.

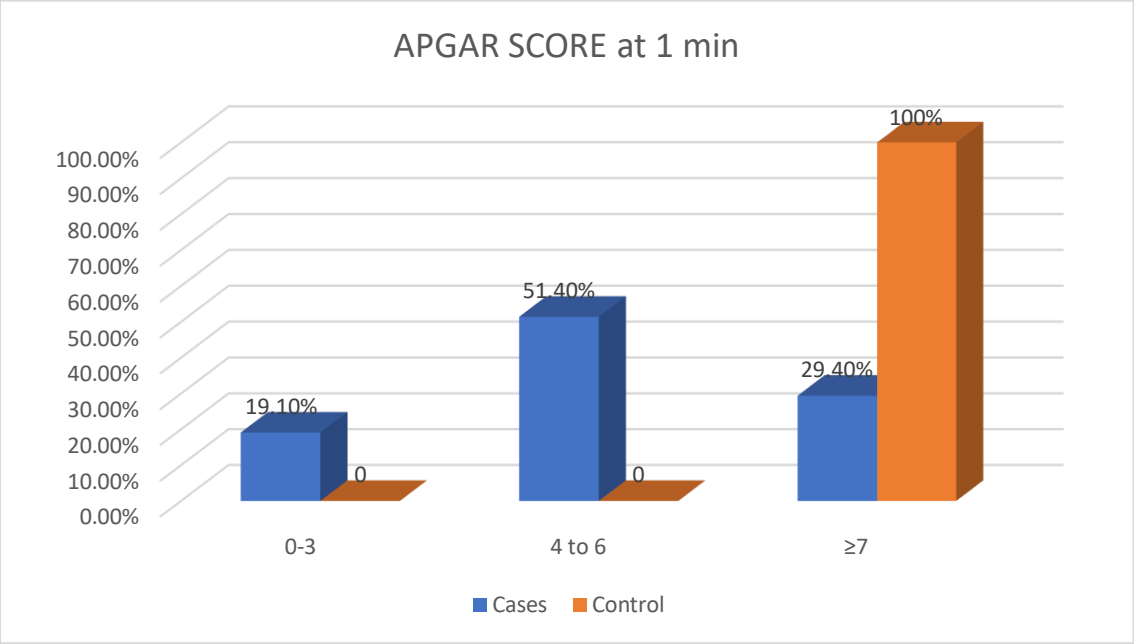

Figure 11: Distribution of APGAR Score at 1 min among cases and controls

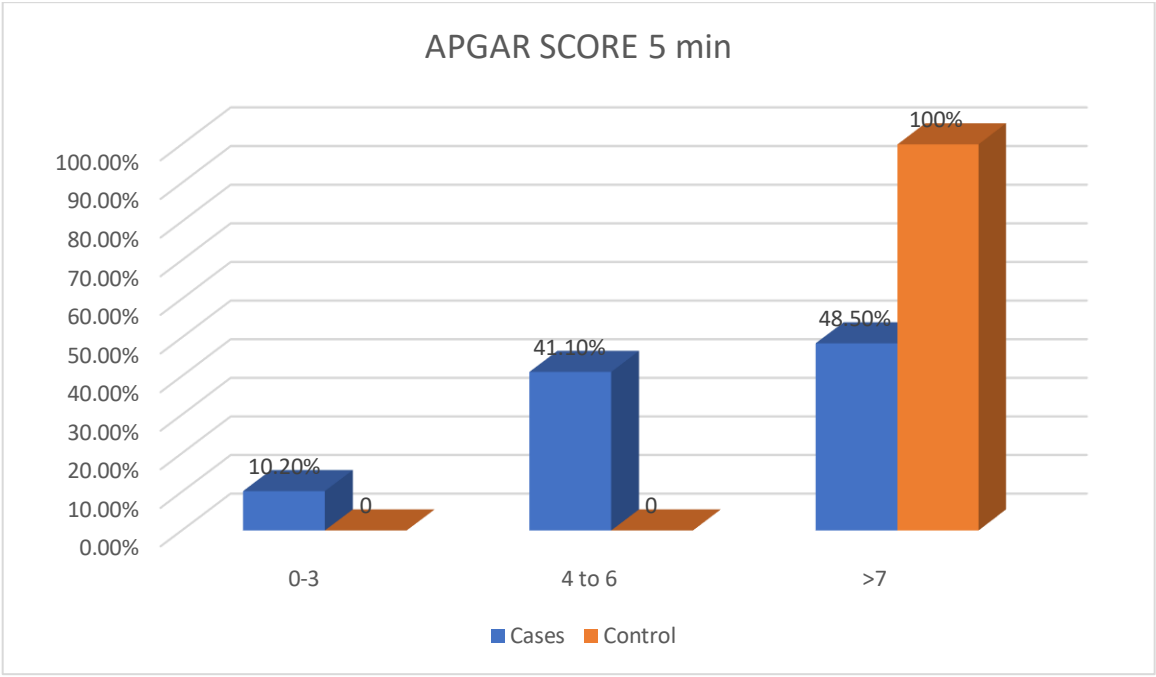

Figure 12: Distribution of APGAR Score at 5 min among cases and controls

Table 6: Distribution of DOWNE's score at admission among cases and controls

Sl. no	DOWNE's score	Cases n (%)	CONTROL n (%)
1	2	0	61(100%)
2	3	2(2.9)	0
3	4	26(38.2%)	0
4	5	33(48.5%)	0
5	6	7(10.3%)	0
6	Total	68(100%)	61(100%)

This table presents the distribution of DOWNE's scores at birth. Among the cases, 48.5% (n=33) had a DOWNE score of 5, followed by 38.2% (n=26) with a score of 4. In contrast, all infants in the control group (100%, n=61) had a DOWNE score of 2 at admission.

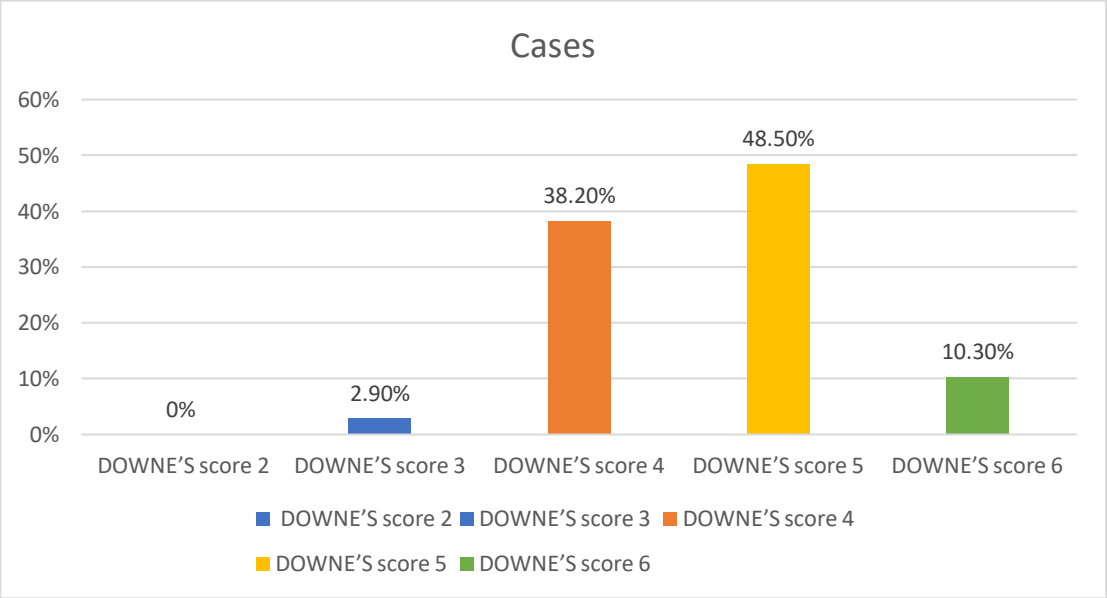

Figure 13: Distribution of DOWNE's score at admission among cases and controls

Table 7: Distribution of Meconium aspiration among cases and controls

Sl. no	Meconium aspiration	Cases n (%)	Control n (%)
1	No	26(38.2%)	68(100%)
2	Yes	42(61.8%)	0
3	Total	68(100%)	61(100%)

This is the table showing the distribution of meconium aspiration among cases and control in perinatal asphyxiated infants. It showed that 61.8%(n-42) had Meconium aspiration among cases compared to control in which no infants had Meconium aspiration as shown in the pie diagram.

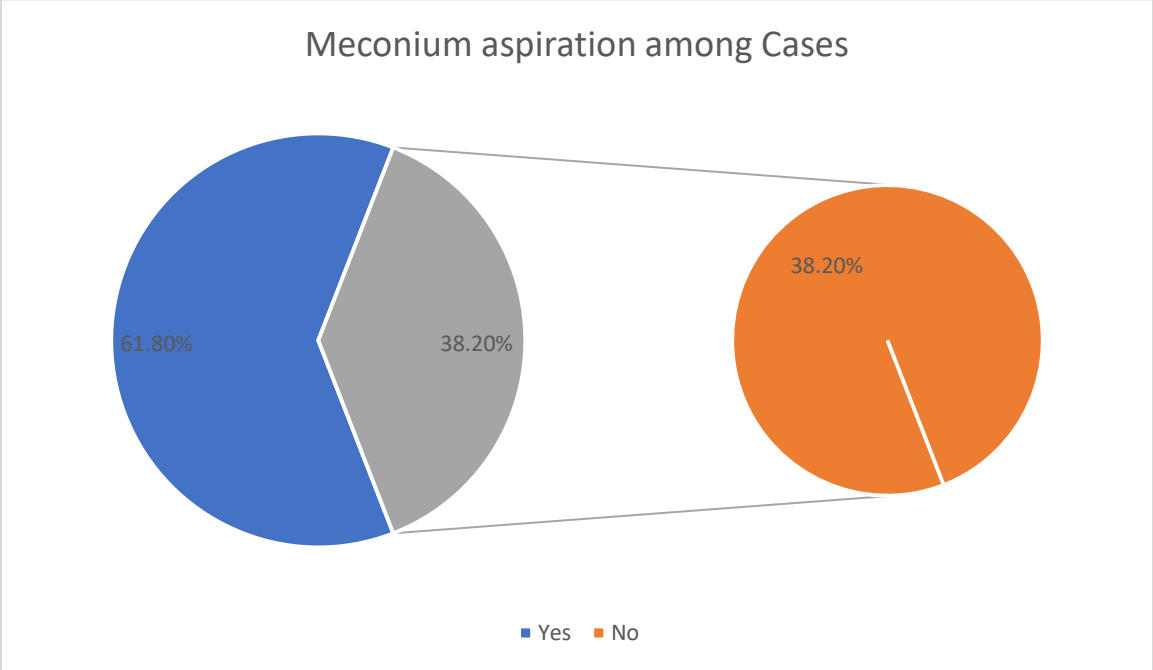

Figure 14: Distribution of Meconium aspiration among cases and controls

Table 8: Distribution of SARNAT scoring among cases and controls

Sl. no	SARNAT Scoring	Cases	Controls
1	HIE 0	0	61(100%)
2	HIE I	42(61.7%)	0
3	HIE II	18(26.4%)	0
4	HIE III	8(11.7%)	0
5	Total	68(100%)	61(100%)

This table presents the SARNAT score among cases and found that the majority in HIE stage I, i.e. 61.7% (n-42) followed by 26.4%(n-18) with HIE II and then 11.7%(n-8) with HIE III and it is shown in the pie diagram.

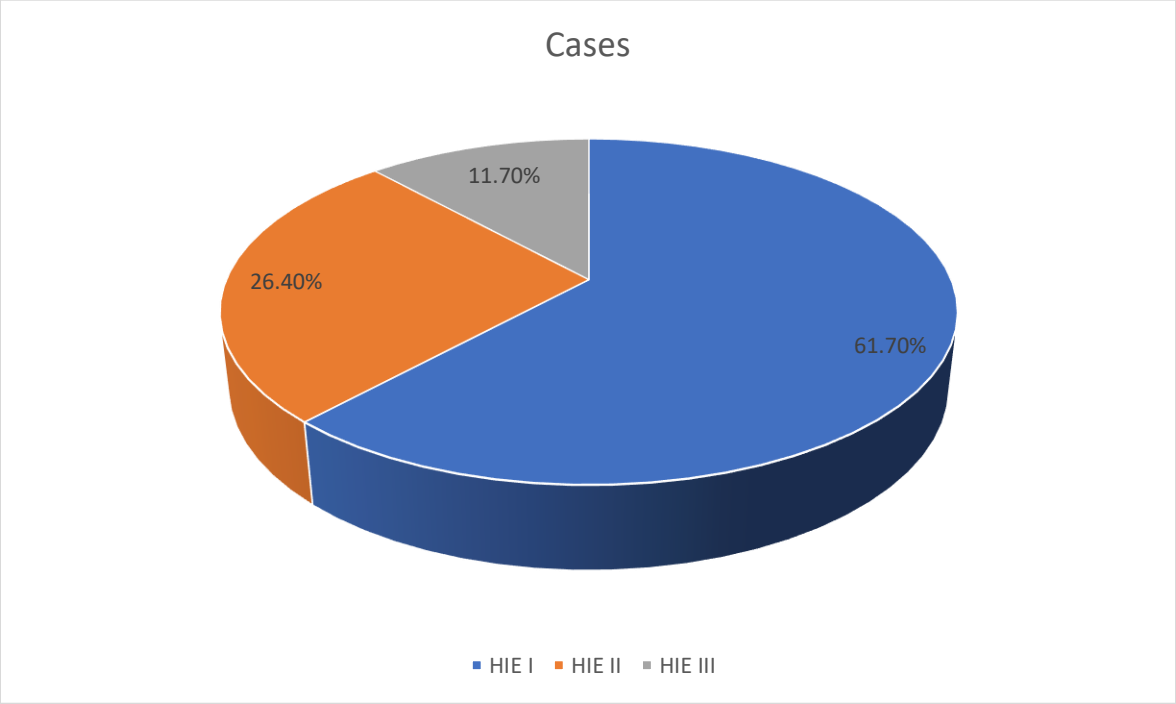

Figure 15: Distribution of SARNAT scoring among cases and controls

Table 9: Distribution of Neonatal convulsions among cases and controls

Sl. no	Neonatal convulsion	Cases n(%)	Control n(%)
1	Absent	36(53.5%)	61(100%)
2	Present	32(46.5%)	0
3	Total	68(100%)	61(100%)

This table shows the distribution of neonatal convulsions in both groups. It was found that 46.5% (n=32) of the neonates in the case group had convulsions, while none of the neonates in the control group experienced convulsions. This distribution is represented in the pie chart.

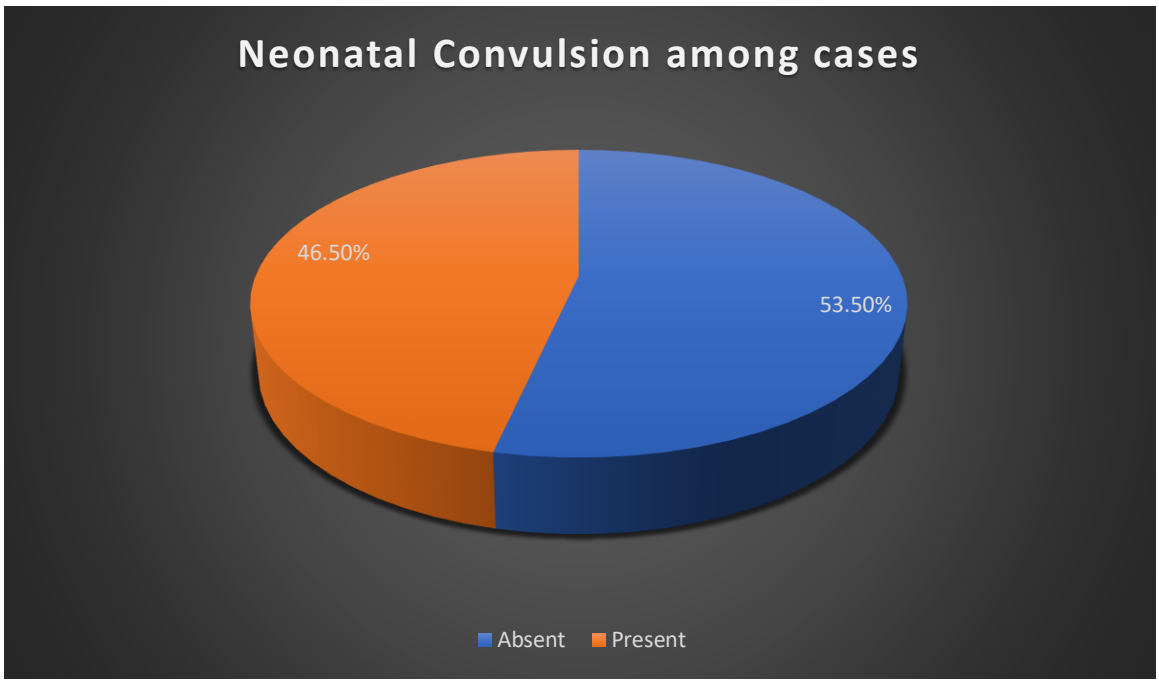

Figure 16: Distribution of Neonatal convulsion among cases and controls

Table 10: Distribution of serum sodium among cases and controls within 48 hours of life

Sl. no	Serum sodium (135-145mEq/L)	Cases n (%)	Control n (%)
1	Hyponatremia	9 (13.2%)	11 (18%)
2	Normal	39 (57.3%)	48 (78.6%)
3	Hypernatremia	20 (29.4%)	2(3.2%)

This is the table showing the Serum sodium level among cases and found that 13.2%(n-9) had serum sodium levels <135mg/dl and 57.3%(n-39) had serum sodium levels 135mg/dl-145 mg/dl. Among cases, the mean serum sodium level is 142.47 with a standard deviation of 6.35. Among control mean and SD are 138.39±3.19.

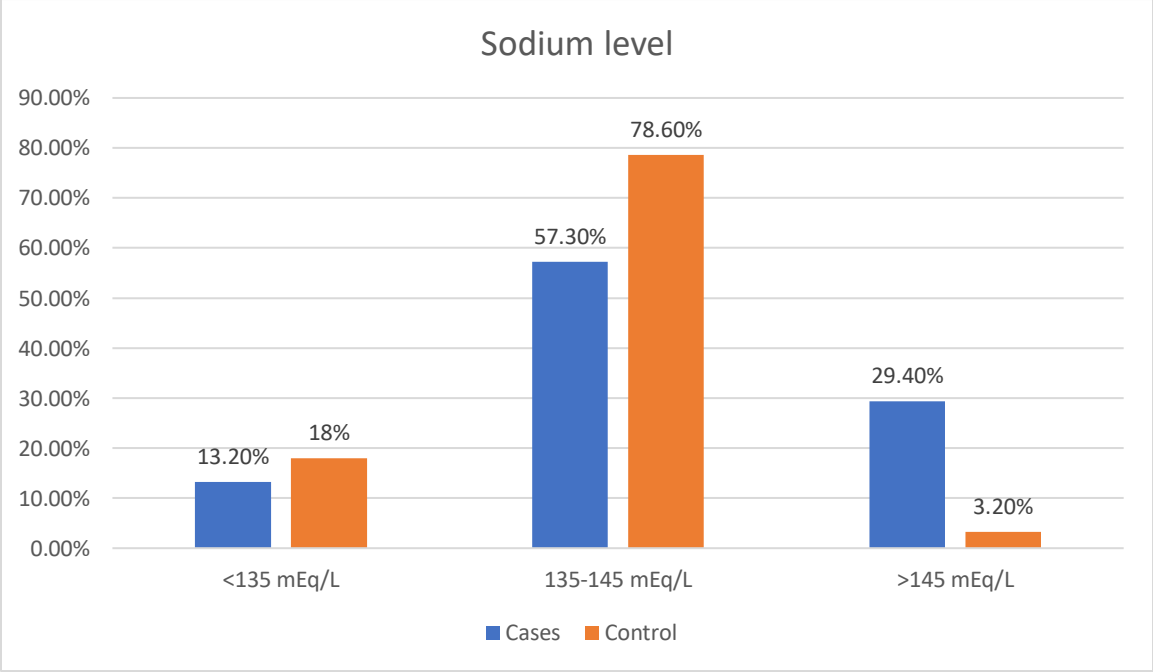

Figure 17: Distribution of serum Sodium level among cases and controls within 48 hours of life

Table 11: Distribution of serum potassium level among cases and controls within 48 hours of life.

Sl. no	Potassium (3.5–5.5mEq/L)	Cases n (%)	Control n (%)
1	Hypokalaemia	8(11.7%)	1(1.6%)
2	Normal	58(85.2%)	60(98.3%)
3	Hyperkalaemia	2(2.9%)	0

This table presents the serum potassium levels among neonates. It was found that 85.2% (n=58) of the cases had normal potassium levels (3.5–5.5mEq/L), while 11.7% and 2.9% had hypokalaemia (<3.5mEq/L) and hyperkalemia (>5.5mEq/L), respectively. The mean potassium level among the cases was 4.50, with a standard deviation of 4. In contrast, 98.3% of the control group had normal potassium levels. With mean and SD are 4.17±0.505.

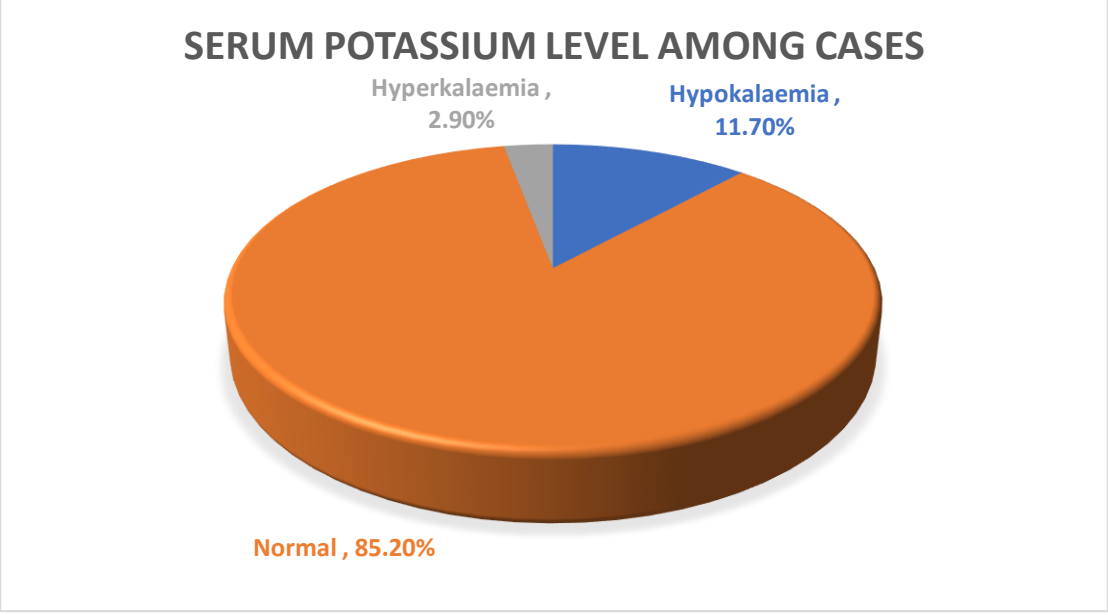

Figure 18: Distribution of serum potassium level among cases and controls within 48 hours of life

Table 12: Distribution of Serum Lactate level among cases and controls within 12 hours of life.

Sl. no	Serum Lactate (<2mmol/L)	Cases n (%)	Control n(%)	P value
1	Increased	60(88.8%)	20 (32.7%)	**<0.001**
2	Normal	8 (11.7%)	41 (67.2%)	
	Total	68 (100%)	61 (100%)	

X^2= 8.3 Df-1

This table presents serum lactate levels among cases and controls and found to be significant.

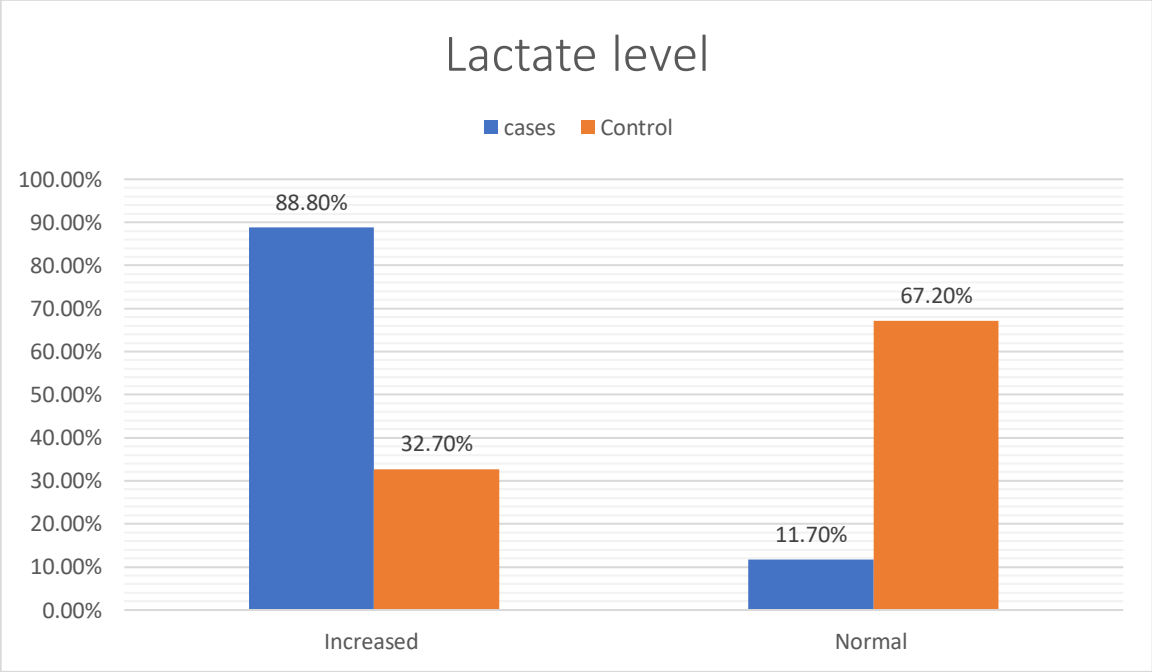

Figure 19: Distribution of Lactate level among cases and controls within 12 hours of life

Table 13: Distribution of serum uric acid level among cases and controls within 48 hours of life.

Sl. no	Serum uric acid level (2-6.2 mg/dl)	Cases n (%)	Control n (%)	P value
1	Normal	48(70.5%)	60 (98.3%)	**P value-<0.001**
2	Increased	20 (29.4%)	1 (1.6%)	
	Mean ±SD	6.40±2.28	4.13±1.2	

X^2= 18.2 Df-2

This table presents the serum uric acid levels among the case and control groups. Among cases, the mean serum uric acid level was 6.40, with a standard deviation of 2.28. Additionally, 29.4% (n=20) of the cases had an elevated serum uric acid level. In comparison, only 1.6% (n=1) of the control group had increased serum uric acid levels. The p-value was found to be significant, with $p < 0.005$.

Table 14: Distribution of serum creatinine level among cases and controls within 48 hours of life.

Sl. no	Serum creatinine level (0.6-1.2 mg/dl)	Cases n (%)	Control n (%)	P value
1	Normal	60 (88.2%)	59 (96.7%)	**<0.05**
2	Increased	8 (11.7%)	2 (3.2%)	
	Mean ±SD	1.04±0.20	0.95±0.311	

X^2= 3.2 Df-2

This table presents the serum creatinine values among perinatally asphyxiated neonates in both the case and control groups. It was found that 11.7% (n=8) of the cases had an increased serum creatinine value, compared to only 3.2% (n=2) in the control group. The mean serum creatinine level among the cases was 1.04, with a standard deviation of 0.207. This difference was found to be statistically significant after applying the chi-square test, with a 95% confidence interval.

Table 15: Distribution of Random Urinary Uric Acid among cases and controls within 48 hours

Sl. no	Random Urinary uric acid (16-22 mg/dl)	Cases n (%)	Control n (%)	P value
1	Normal	46 (67.6%)	61 (100%)	**<0.001**
2	Increased	22 (32.3%)	0	
	Mean ±SD	48.5±5.5	18.66±4.15	

X^2= 23.79 Df-2

This table presents the random urinary uric acid levels among perinatally asphyxiated neonates in the case and control groups. It was found that 32.3% (n=22) of the cases had an increased random urinary uric acid level compared to the control group. The mean random urinary uric acid level among the cases was 48.5, with a standard deviation of 5.5. This difference was found to be statistically significant, with a p-value < 0.001, after applying the chi-square test with a 95% confidence interval.

Table 16: Distribution of Random urinary creatinine among cases and controls within 48 hours

Sl. no	Random urinary creatinine (2-20 mg/dl)	Cases n (%)	Control n (%)	P value
1	Normal	46 (67.6%)	61 (100%)	<0.001
2	Increased	22 (32.3%)	0	
	Mean ±SD	42.21 ±4.7	17.48 ±3.78	

Df-1

This table presents the random urinary creatinine levels among perinatally asphyxiated neonates in both the case and control groups. It was found that 32.3% (n=22) of the cases had increased random urinary creatinine levels, compared to 32.7% (n=20) in the control group. The mean random urinary creatinine level among the cases was 42.21, with a standard deviation of 4.7. This difference was found to be significant statistically, with a p-value < 0.001, after applying the chi-square test with a 95% confidence interval.

Table 17: Distribution of Serum Uric acid /serum creatine ratio among cases and controls within 48 hours of life

Sl. no	Serum Uric acid/creatine ratio (3.33 to 5.16)	Cases n (%)	Control n (%)	P value
1	Normal	25(36.7%)	50(81.7%)	<**0.001**
2	Increased	43(63.3%)	11(18.5%)	
	Mean ±SD	6.62 ±1.65	5.06 ±1.46	

X^2= 5.479 Df-2

This table shows the **Serum urine /serum creatine ratio distribution among cases and controls in perinatal asphyxia infants. Among the cases, 63.3% had an increased ratio compared to the control group, which is significant.**

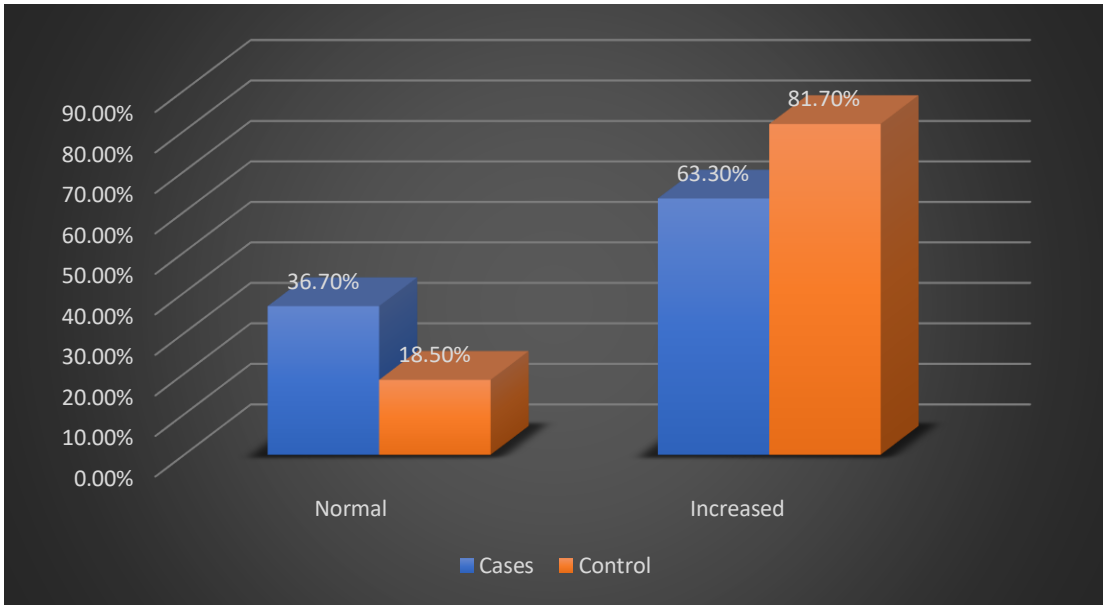

Figure 20: Distribution of Serum uric acid /creatine ratio among cases and controls within 48 hours of life

This table presents the serum urine/serum creatinine ratio among perinatally asphyxiated neonates in both the case and control groups. It was found that 98.5% (n=67) of the cases had an increased serum urine/serum creatinine ratio, compared to 96.7% (n=59) in the control group. The mean serum urine/serum creatinine ratio among the cases was 6.62, with a standard deviation of 1.65. This difference was found to be significant statistically, with a p-value < 0.001, after applying the chi-square test with a 95% confidence interval.

Table 18: Distribution of Random Urinary uric acid / Random urinary creatinine ratio among cases and Controls within 48 hours of life

Sl. no	Random Urinary uric acid/urinary creatinine (0.3 to 3.4)	Cases n (%)	Control n (%)	P value
1	Normal	0	58 (95.06%)	**<0.001**
2	Increased	68 (100%)	3 (4.9%)	
	Mean ±SD	3.78 ±1.52	0.7 ±0.49	

X^2= 11.62, Df-2

This table presents the random urinary UA/Cr ratio among perinatally asphyxiated infants in both cases and control groups. It was found that 100% of the cases had an increased random urinary uric acid/urinary creatinine ratio, compared to only 4.9% (n=3) in the control group. The mean random urinary UA/Cr ratio among the cases was 3.78, with a standard deviation of 1.52. This difference was found to be significant statistically, with a p-value < 0.001, after applying the chi-square test with a 95% confidence interval.

Table 19: Distribution of Primary Mode of respiratory support in cases

Sl. no	Primary Mode of respiratory support	Cases n (%)
1	HFNC	34(50%)
2	CPAP	4(5.8%)
3	LFNC	10(14.7%)
4	VENTILATOR	20(29.4%)
5	Total	68(100%)

X^2= 28.38, Df-3

This table represents the mode of respiratory support in cases and found 50% (n-34) need HFNC, followed by 29.4% (n-20) who required ventilator support, 14.7% (n-10) on LFNC, and 5.8% (n-4) were on CPAP.

Table 20: Distribution of the No of days of O_2 support required among cases and controls

Sl. no	No of days of O_2 support	Cases n (%)	Control n (%)	P value
1	<6 days	30(44.11%)	60(98.36%)	**<0.001**
2	7 days and above	38(55.88%)	1(1.6%)	
	Mean ±SD	8.40 ±5.2	4.03 ±1.16	

X^2= 44.51, Df-2

This table compares the oxygen support needed by neonates with perinatal asphyxia in case and control groups. The analysis revealed that 44.11% of cases required oxygen for fewer than 6 days, while 98.6% of controls did. Conversely, 55.88% of cases needed oxygen for over 7 days. This difference was significant statistically, with a p-value of < 0.001, as shown by the chi-square test at a 95% confidence interval. The average duration of oxygen support was 8.40 days (SD = 5.2) for cases, compared to 4.03 days (SD = 1.16) for controls.

Table 21: Distribution Outcome among Cases and Controls

Sl. no	Outcome	Cases n (%)	Control n (%)
1	Dead	2(2.9%)	0
2	Discharged	66(98.1%)	61(100%)

This is the table showing the distribution of outcome results among cases and controls in perinatal asphyxiated babies and showed that 2.9% (n-2) died and 98.1% (n-66) were discharged among cases, and all were discharged in control groups.

Table 22: Distribution of Clinical status among cases and controls

Sl. no	Clinical status	Cases n (%)	Control n (%)
1	Convulsion	29(42.6%)	0
2	Improved	39(57.4%)	61(100%)

This is the table showing the distribution of Clinical status among cases and control in perinatal asphyxiated baby and showed that among cases, 42.6% (n-29) developed convulsions and 57.4% (n-39) improved during their admission time and in the control group, all improved.

Table 23: Distribution of patients taking anticonvulsants

Sl. no	Clinical status	**Anticonvulsants Yes**	**Anticonvulsants No**
1	Discharged	27 (40.9%)	39 (59%)

This is the table showing the distribution of patients taking anticonvulsants. It found that 40.9% of patients were on Anticonvulsants at the time of discharge.

Table 24: Association between HIE and APGAR Score at 5 min among cases in perinatal asphyxia baby

Sl. no	SARNAT SCORING	APGAR SCORE at 5 min			P value
		0-3	4-6	>7	
1	I	0 (%)	12 (42.8%)	30 (90.9%)	**<0.001**
2	II	4 (57.1%)	11 (39.2%)	3 (9.9%)	
3	III	3 (42.8%)	5 (17.8%)	0 (%)	
4	Total	7 (100%)	28 (100%)	33 (100%)	

X^2= 28.99, Df-4

This table presents the association between SARNAT score and APGAR SCORE at 5 min and after the statistical test, this value was found to be significant.

The given table 25 shows the association between renal parameters and APGAR score at 5 min and found that there is a statistical significance between all these after applying the chi-square test (p-value < 0.001).

Table 25: Association between APGAR Score at 5 min and renal parameters among cases and control in perinatal asphyxia neonates

VARIABLES		APGAR Score at 5 min			P value
		0-3	4-6	>7	
Serum Uric Acid Level	Normal (2-6.2 mg/dl)	2(4.2%)	15(31.2%)	31(64.6%)	**<0.001**
	Increased	5 (25.0%)	13 (65.0%)	2 (10.0%)	
Serum Creatinine Level	Normal (0.6-1.2 mg/dl)	3 (5.0%)	18 (30.0%)	39 (65.0%)	**<0.001**
	Increased	4(50.0%)	6 (50.0%)	0 (0.0%)	
Random Urinary Uric Acid Level	Normal (16-22 mg/dl)	2(4.3%)	14 (30.4%)	30 (65.2%)	**<0.001**
	Increased	5 (22.7%)	14 (63.6%)	3 (13.6%)	
Random Urinary Creatinine Level	Normal (2-20 mg/dl)	2(4.3%)	14 (30.4%)	30 (65.2%)	**<0.001**
	Increased	5 (22.7%)	14 (63.6%)	3 (13.6%)	
Serum Uric acid/Serum Creatinine Ratio	Normal (3.33 to 5.16)	1 (4.0%)	6 (24.0%)	18 (72.0%)	**<0.001**
	Increased	6 (14.0%)	22 (51.2%)	15 (34.8%)	
Random Urinary Uric Acid/Urinary Creatinine Ratio	Normal (0.3 to 3.4)	1 (14.2%)	10 (35.7%)	31 (93.9%)	**<0.001**
	Increased	6 (85.7%)	18 (64.2%)	2(6.06%)	

DISCUSSION

Perinatal asphyxia is one among the leading causes of morbidity and mortality in neonates, asphyxiated newborns are more likely to have AKI, which might impact the prognosis overall. Because the kidneys are extremely susceptible to hypoxia, a hypoxic shock can cause renal insufficiency within 24 hours, which could cause irreparable damage if it persists. A low APGAR score is the most widely recognized diagnostic and prognostic marker of asphyxia in neonates. The current study evaluated the serum and urinary" UA/Cr" ratio in Asphyxiated and control neonates and identified AKI in asphyxiated babies based on the abnormal ratio.

Sociodemographic profile:

A total of 129 newborns were enrolled, out of which 68 were cases and 61 were controls. In Both the group's majority were male, with 64.7% (n=44) of the cases and 63.9% of the controls being male. A significant maternal history, such as pre-eclampsia, premature rupture of membranes, and gestational diabetes was found in 32.4% (n=22) of the cases, while this percentage was only 19.7% (n=12) in the control group. It was found that 25% (n=17) of the cases and 21.3% (n=13) of the controls were born weighing less than 2.5 kg. Among cases, 36.8% (n=25) had a lower-segment caesarean section (LSCS)(out of which 52% are primigravida and 48% are multigravida) and 63.2%(n=43) had a vaginal delivery(58.1% are primigravida & 41.8% are multigravida).

APGAR Score

In our study among perinatally asphyxiated neonates, APGAR score at 1 min 19.1%(n-13) between 0-3, followed by 51.4%(n-35) score of 4-6, and then 29.4%(n-20) had score >7. The APGAR at 5 min 10.2%(n-7) had 0-3, followed by 41.1%(n-28) had 4-6 and 48.5%(n-33) had >7 score. Certain neonates, despite achieving an APGAR score of ≥7 at both 1 and 5 minutes, were classified as cases due to their respiratory patterns and type of cry. Neonates exhibiting abnormal respiratory activity or a weak cry were categorized as cases, and normal patterns of respiration or cry were categorized as controls.

A case-control study by **Manoj et al.** found that the "APGAR score of cases taken at 1 minute were <3 score for 60 babies (75%), 4-6 score in 20(25%) babies, and 6-7 score in nil babies. At 5 minutes <3 score in 11 (13.75%) newborns, 4-6 score in 55 (68.75%), and 6-7 score in 14(17.5%) babies were noticed. The Apgar score in 10 minutes was <3 in 06(7.5%), 4-6 score in 30(37.5%), and 6-7 score in 11 (13.75), whereas in controls, the Apgar score was > 7 at 1 minute and 5 minutes were 56 and 60 respectively indicating that all babies were good around 5 minutes after birth. The Apgar Score of cases and controls were significantly different (4.9±1.624 and 8.633±0.604)". [42]

Electrolyte and Asphyxia

According to the current study, Serum sodium levels among cases found that 13.2%(n-9) had serum sodium levels <135mEq/L; 57.3%(n-39) had serum sodium levels 135mEq/L -145mEq/L and 29.4%(n-20) had serum sodium levels >145mEq/L. Among cases, the mean serum sodium level is 142.47 with a standard deviation of 6.35. Among control mean and SD are 138.39±3.19.

In our research, hyperkalemia (levels over 5.5mEq/L) with AKI was observed in only 2.9% of cases (n=2) which later improved within 48 hours, contrasting with **Ananta Jayaswal's** study[43], which found a prevalence of 39.13% in acute renal failure (ARF) patients. The causes of hyperkalemia in ARF are linked to decreased glomerular filtration rate (GFR) in prerenal failure and hypoxic damage to renal tubules in intrinsic renal failure.

Serum Lactate

Our study found elevated serum lactate (>2mmol/L) levels in 88.8% of patients with perinatal asphyxia and 32.7% of the controls while revealing a statistically significant difference ($P < 0.01$). Another study by **Abdelbaseer et al.** performed research to understand how serum lactate and enzymes (LDH, CK-MB, AST, and ALT) work together to detect perinatal asphyxia cases. Asphyxiated neonates demonstrated statistically significant elevated serum lactate levels when compared to non-asphyxiated controls according to their analysis ($P < 0.001$). According to this study, serum lactate testing becomes an important tool to identify cases of perinatal asphyxia. [44]

Another research conducted by **Shah et al**. confirmed that the "initial lactate levels were significantly higher (p=0.001) in neonates with moderate-to-severe HIE (mean±SD=11.09±4.6) as compared to those with mild or no HIE (mean±SD=7.1±4.7). They found that elevated serum lactate levels strengthened the risk of negative consequences in newborns experiencing asphyxia".[45]

Renal parameters

In our study, we evaluated serum uric acid levels (Normal: 2-6.2 mg/dl) at 24 - 48 hours of life, elevated in 29.4% (n=20) of the cases, the mean and SD is 6.40±2.28 in cases and 4.13±1.2 in controls (raised in only 1.6% of the controls). Serum Creatinine (Normal: 0.6-1.2 mg/dl) at 24 - 48 hours of life, elevated in 11.7% (n=8) of the cases, the mean and SD is 1.04±0.20 in cases and 0.95±0.311 in controls (raised in only 3.2% of the controls). We found that the mean Serum UA/Cr ratio was 6.62 ±1.65 vs 5.06 ±1.46 among cases and controls respectively, and this value was found to be significant statistically ($p<0.001$).

We have also evaluated random urinary uric acid levels (normal: 16-22 mg/dl) at 24 - 48 hours of life, elevated in 32.3% (n=22) of the cases, the mean and SD is 48.5±5.5 in cases and 18.66±4.15 in controls (raised in only none of the controls). Random urinary Creatinine (Normal: 2-20 mg/dl) at 24 - 48 hours of life, elevated in 32.3% (n=22) of the cases, the mean and SD is 42.21 ±19.7 in cases and 32.48 ±14.78 in controls (raised in none of the controls). We found that the mean urinary UA/Cr ratio was 3.78 ±1.52 vs 0.7 ±0.49 among cases and controls respectively, and this value was found to be statistically significant($p<0.001$).

The study by **Kinjal et al.** shows that the "mean UA/Cr ratio (2.75±0.18 vs 1.78±0.23) is significantly higher in the asphyxiated group than in the control group ($p<0.0001$). Urinary UA/Cr ratio had a negative correlation with blood pH ($r= -0.27$, $p=0.18$), which was not significant ($p>0.05$)".[46]

A study by **Gubbala et al.** on 80 full-term neonates enrolled, out of which 40 asphyxiated newborns had higher urinary UA/Cr ratios than 40 control subjects with statistical significance ($P < 0.001$). The research showed that the UA/Cr ratio measured in urine serves as an easy and dependable method to screen and evaluate asphyxiated neonates early on. [47]

A case-control study by **Rai et al.** enrolled 84 neonates, 42 newborns who developed asphyxia, along with 42 newborns who did not experience such events. This study confirmed that the early urinary measurement of UA/Cr ratio adds to clinical diagnoses by providing non-invasive support for assessing asphyxia severity through APGAR score evaluation. [48]

Association between ratios of serum uric acid/creatinine and urinary uric acid/creatinine ratios and APGAR score at 5 min

Our study shows a correlation between 5-minute APGAR scores and means of different biochemical markers between cases and controls, like serum uric acid (6.40 vs 4.13), serum creatinine (1.04 vs 0.95), urinary uric acid (48.5 vs 18.66), urinary creatinine (42.21 vs 32.48), serum UA/Cr (6.62±1.65 vs 5.06±1.46) and urinary UA/Cr (3.78±1.52 vs 0.7±0.49). Interestingly, when these markers are higher, the APGAR scores at 5 min tend to be lower, hinting that they could potentially indicate the severity of perinatal asphyxia (p-value <0.001).

A study by **Gulati et al.** carried out a cross-sectional study that looked at 100 term neonates with perinatal asphyxia and another 100 without it. They discovered the "mean urinary UA/Cr ratio was greatly higher in the asphyxiated group (3.41±0.68) compared to the controls (1.99±0.23) ($P < 0.001$). They noticed a strong negative correlation between the urinary UA/Cr ratio and the 5-minute APGAR score ($r=-0.8806$, $P < 0.001$), which means that higher UA/Cr ratios are linked with lower APGAR scores".[39]

Outcome of Enrolled Neonates

In our study, 42.6%(n=29) of asphyxiated neonates had convulsions, the mortality rate was 2.9%(n=2) and 40.9% (n=27) were discharged with antiepileptics. Neonates with seizure control survived. Among two asphyxiated neonates who died, one died at 72 hours of life (on Therapeutic Hypothermia) and the other neonate died on day 5(on the ventilator).

A study by **Chikkanna et al.** looked back at data from 100 newborns who faced birth asphyxia and reported a mortality rate of 21%. The highest mortality (11%) was seen in those babies classified as hypoxic-ischemic encephalopathy (HIE) stage III. The study noted that a majority (22%) of the neonates who survived had some neurological issues, and required long-term anti-seizure medication.[49]

STRENGTH of the study:

1. Prospective Cohort Design: This study keeps track of newborns over time, which helps cut down on **recall bias** and makes it easier to see how perinatal asphyxia links up with changes in biochemical markers.

2. Conducted in a Level III-A NICU With **advanced diagnostic tools** on hand.

3. Use of Both Serum and Urinary Biomarkers: Using both **serum and urine biomarkers** gives us a **complete metabolic profile**, which helps with accurate diagnoses. Since urinary biomarkers are **non-invasive**, they offer a practical way to screen routinely.

4. Well-defined inclusion and Exclusion Criteria

5. Adequate Sample Size (129 neonates). This helps cut down the chances of **type II errors**, where we might miss out on detecting a real effect.

6. Objective and Quantifiable Outcome Measures: The levels of biomarkers we're looking at (like serum and urinary uric acid/creatinine ratios) are **quantifiable**, which helps reduce any subjectivity.

7. Strong Statistical Analysis:

The study uses **P-values, Chi-square tests, and correlation analyses** to pin down real associations.

8. Clinical Relevance: The findings could help with **early diagnosis and timely interventions**, possibly improving outcomes for newborns.

9. Potential for Future Research and Clinical Application: This study sets the stage for **larger multicentric trials.**

Recommendations:

1. **Long-Term Follow-up:** We should consider studying the long-term neurodevelopmental outcomes for infants. This would help us understand how well these biomarkers can predict those outcomes.
2. **Multicentric Studies:** It would be great to see similar research done in different centres. This could help us figure out if the findings apply to various populations.
3. **Additional Biomarkers:** Why not think about including other markers related to oxidative stress? Stuff like lactate dehydrogenase (LDH) and ischemia-modified albumin (IMA) could boost our diagnostic precision.
4. **Machine Learning Models:** Using AI to create predictive models could enhance how sensitive and specific these biomarkers are when diagnosing perinatal asphyxia early on.

Limitations:

1. **Single-Centre Study:** Keep in mind that our findings might not apply to other areas that have different healthcare facilities and management styles.
2. **Limited Follow-up:** We didn't look at long-term neurodevelopmental outcomes, which are super important for understanding the overall effects of perinatal asphyxia.

CONCLUSION:

This study shows that even the serum uric acid to creatinine ratio has the potential as **a** biomarker for grading perinatal asphyxia**,** like urinary levels. Collecting serum at 24 – 48 hours for an asphyxiated baby in NICU may be more feasible than urine. There's an important link between these biochemical markers and low APGAR scores, which help in prognostication of outcome.

Summary:

This **prospective cohort study** was done at a Level III-A NICU in North Karnataka from March 2023 to November 2024. We looked at how **serum and urinary uric acid and creatinine ratios** can act as biomarkers for **perinatal asphyxia**. The study involved **129 neonates born at ≥37 weeks gestation.** Results showed that these biomarkers are closely tied to **low APGAR scores**, indicating they might be really useful for **early diagnosis**. While there are strong points like **a solid prospective design, a good sample size, and thorough biomarker** analysis, the fact that it's a single-centred study and doesn't track long-term neurodevelopment means we need more multicentric research with longer follow-up to back up these findings and understand their significance better**.**

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BLDE (DU)/IEC/ 970/2022-23 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "SERUM AMD URINARY URIC ACID AND CREATININE RATIO AS BIOMARKER IN PERINATAL ASPHYXIA."

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.SASIDHAR KONERU

NAME OF THE GUIDE: DR. R.H.GOBBUR, PROFESSOR,
DEPT. OF PEDIATRICS.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA
MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE – II

RESEARCH INFORMED CONSENT FORM

BLDEA's Shri B.M. PATIL Medical College, Hospital & Research Centre,
Vijayapura, Karnataka -586103.

TITLE OF THE PROJECT

"SERUM AND URINARY URIC ACID AND CREATININE RATIO AS BIOMARKER IN PERINATAL ASPHYXIA"

GUIDE: **DR.R.H.GOBBUR**, MD
PROFESSOR,
DEPARTMENT OF PEDIATRICS

PG STUDENT-**DR. SASIDHAR KONERU**

PURPOSE OF RESEARCH:

To assess the use of Serum and Urinary, Uric Acid, and Creatinine ratio as a biomarker in Perinatal Asphyxia, which helps in assessing the level of HIE in neonates, so an early diagnosis can be established based on these values and treatment to be given can be assessed using them as biomarkers.

PROCEDURE:

I understand that after having obtained a detailed clinical history, thorough clinical examination, and relevant investigations, a final workup of the process and its outcome is planned.

RISK AND DISCOMFORTS:

I understand that I may experience pain and discomfort during the examination or my treatment. It is mainly the result of my condition, and the procedures of this study are not expected to exaggerate these feelings, which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the treatment.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to confidentiality. Information of a sensitive personal nature will not be part of the medical record but will be stored in the investigations research file. Suppose the data are used for publication in the medical literature or teaching. No name will be used in that case, and other identifiers such as photographs will be used only with special written permission. I understand that I may see the picture before giving consent.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time DR. SASIDHAR KONERU at the Department of Pediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the study, which might influence my continued participation. I will be given a copy of this consent form to keep for careful reading.

REFUSAL FOR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that DR. SASIDHAR KONERU may terminate my participation in the study after they have explained the reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to my child resulting directly from the child's participation in this study if such damage were reported promptly, the appropriate treatment would be available to the child. But, no further compensation would be provided by the hospital. I understand that by agreeing to participate in this study and not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks to the best of my ability.

DR. SASIDHAR KONERU
(Investigator)
Date:

BLDE (DEEMED TO BE UNIVERSITY)
VIJAYAPUR, KARNATAKA

"SERUM AND URINARY URIC ACID & CREATININ RATIO AS BIOMARKER IN PERINATAL ASPHYXIA"

A PROSPECTIVE COHORT STUDY

PROFORMA OF CASE TAKING

1. DEMOGRAPHIC INFORMATION

NAME: B/O

SEX:

IP NO:

ADDRESS:

CONTACT NO:

2. PATIENT INFORMATION

DATE & TIME OF DELIVERY:

ADMISSION DATE:

OBSTETRIC HISTORY:

M/H/O: PIH/Preeclampsia/Eclampsia/GDM/others

ESTIMATED GESTATIONAL AGE:

ANTENATAL STEROIDS:

MODE OF DELIVERY / INDICATION OF DELIVERY: DELIVERED

AT: INBORN / OUTBORN

BIRTH WEIGHT:

MOTHER BLOOD GROUP:

BABY BLOOD GROUP:

3. CLINICAL INFORMATION

APGAR SCORE:

1 min	2 min	3 min	4 min	5 min

DOWNE'S SCORE AT ADMISSION:

MODE OF RESUCITATION: TACTILE STIMULATION/ BAG&MASK/INTUBATION

MECONIUM ASPIRATION: YES / NO

AMINOPHYLLINE/ERYTHROPOIETIN:

INOTROPES GIVEN:

ON EXAMINATION: HR: CFT: AF: SpO2:

SYSTEMIC FINDINGS:

CVS:

RS:

CNS:

PA:

PRIMARY MODE OF RESPIRATORY SUPPORT:

SARNET STAGING:

4. INVESTIGATIONS ON ADMISSION

GRBS AT TIME OF ADMISSION:

TC	N/L	Hb	PCV	RBC	PLATELET	CRP	Na	K	Ca

BLOOD GAS ANALYSIS:

DATE			
pH			
pCO2			
pO2			
HCO3			
SO2c			
Lac			

	Serum	**Urinary**
URIC ACID:		
CREATININE:		
RATIO:		

2D ECHO (if done):

5. CLINICAL OUTCOME

ON OXYGEN SUPPORT: NP O2/ HOOD/CPAP/HFNC/VENTILATOR

NUMBER OF DAYS ON OXYGEN SUPPORT:

NUMBER OF DAYS OF NICU STAY:

URINE O/P AT ADMISSION & DISCHARGE:

DAY OF DISCHARGE FROM NICU:

CLINICAL STATUS AT DISCHARGE:

DISCHARGE/DEATH:

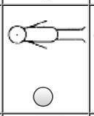
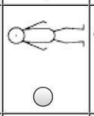
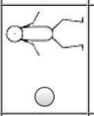
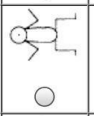
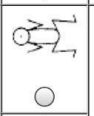
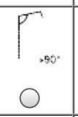
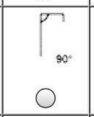
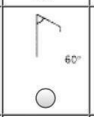
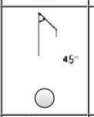
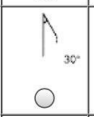
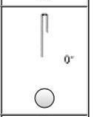
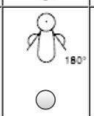
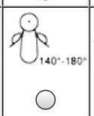
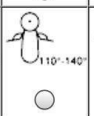
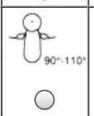
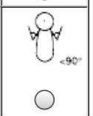
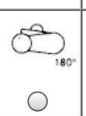
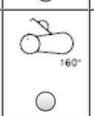
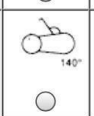
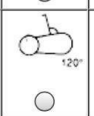
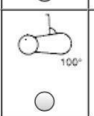
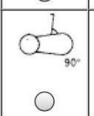
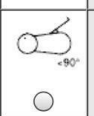
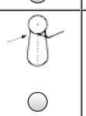
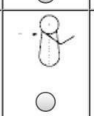
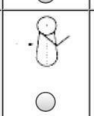
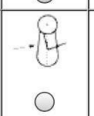
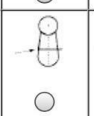
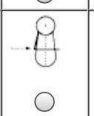
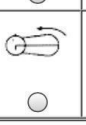
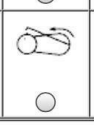
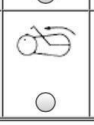
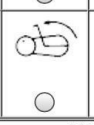
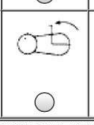
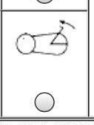
PARENTS / GUARDIAN CONSENT STATEMENT:

We confirm that Dr SASIDHAR KONERU is doing a study on **SERUM AND URINARY URIC ACID AND CREATININE RATIO AS BIOMARKER IN PERINATAL ASPHYXIA** admitted in NICU in Shri B. M. Patil Medical College Hospital, Vijayapura, Karnataka. Dr SASIDHAR KONERU has explained to us the purpose of the research and the study procedure. We are willing to allow our baby to get treated at Shri B.M. Patil Medical College Hospital, Vijayapura. We have explained the study, benefits, and possible discomforts in detail in our native language and we understand the same. We are aware that the child will get the best treatment, and no compensation like financial benefits, will be given if our child's condition deteriorates and any untoward complication happens, and we will not sue anyone regarding this. Therefore, we agree to give our full consent for the child's participation as a subject in this research project.

_____ _____

(Parents / Guardian) Dr SASIDHAR KONERU

DATE:

SIGN	NEUROMUSCULAR MATURITY SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Posture								
Square Window								
Arm Recoil								
Popliteal Angle								
Scarf Sign								
Heel To Ear								

TOTAL SCORE	WEEKS
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44
TOTAL NEUROMUSCULAR MATURITY SCORE	
TOTAL PHYSICAL MATURITY SCORE	
TOTAL SCORE	WEEKS

SIGN	PHYSICAL MATURITY SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Skin	Sticky, friable, transparent	gelatinous, red, translucent	smooth pink, visible veins	superficial peeling &/or rash, few veins	cracking, pale areas, rare veins	parchment, deep cracking, no vessels	leathery, cracked, wrinkled	
Lanugo	none	sparse	abundant	thinning	bald areas	mostly bald		
Plantar Surface	heel-toe 40-50mm: -1 <40mm: -2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
Breast	imperceptable	barely perceptable	flat areola no bud	stippled areola 1-2 mm bud	raised areola 3-4 mm bud	full areola 5-10 mm bud		
Eye / Ear	lids fused loosely: -1 tightly: -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff		
Genitals (Male)	scrotum flat, smooth	scrotum empty, faint rugae	testes in upper canal, rare rugae	testes descending, few rugae	testes down, good rugae	testes pendulous, deep rugae		
Genitals (Female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large, minora small	majora cover clitoris & minora		

BIODATA OF THE GUIDE:

NAME: **DR. R. H GOBBUR**

DOB: 25/03/1962

EDUCATION: MBBS, GULBARGA UNIVERSITY; APRIL 1984.

MD PAEDIATRICS, GULBARGA UNIVERSITY; APRIL 1991.

KMC REGISTRATION NUMBER: 24372

WORK EXPERIENCE: UG – 30 YEARS

PG – 23 YEARS

MEMBERSHIP: LIFE MEMBER IAP

PRESENTLY WORKING AS PROFESSOR, DEPARTMENT OF PEDIATRICS,

SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE,

VIJAYAPURA - 586103

E-MAIL ID: rhgobbur@gmail.com

MASTER CHART:

No	B/O	E/	Mf	D/f	Detric	Final	H.TAL	of	Deve	reigh	Blod	loodR	aR	aore	Resim	Astrop	f	Respt	Stl	Cosort	wmissal	Coils/	Lymog	k(C	Bilet	CRh	Sc	Potzn	Ca	pH	CO2	pO2	CO2	ctU	ina	Creinary	l/Sd	Ur	tofiss	HA
1	ages	M	#	2/236	A.1	3E	clamt	Giv	NVD	O	3	OS	OSIT	6	8	5	&	M	Yes	: &	DITILATE	II/rese	NO	97	###	88/7.9	22	#	7	2,0	#	##	4	6.4	7	15	##	#	99	5	#	#	1	21	9	4	it	#	0	2
2	a Dr	M	#	2/224	A9	wk	PRO	Inknou	NVD	O	3	OS	OSIT	6	9	5	&	M	No	: &	DHFNCE	II/rese	NO	91	###	62/32	19	#	6	3,0	#	##	5.5	8.8	7	30	##	9	95	#	9	#	1	12	8	4	37	1	1
3	ba P	M	#	2/210	Ps	POE	clam	Giver	Sectir	I	3	OS	OSIT	6	9	5	&	M	No	&	DRECPAP	IE I/bse	YES	113	###	61/31	24	#	6	7 4,0	#	##	3.1	8.9	7	25	56	#	98	2	6	#	1	53	6	2	h	#	1	1
4	ma I	M	#	2/200	Pwith	3PRO	lGiver	Sectir	O	3	OS	OSIT	6	9	3	&	M	Yes	&	DRELFNC	HE I/bse	NO	120	###	65/27	17	#	5	7 2,0	#	##	3.8	8.4	7	22	##	#	99	7	5	#	1	11	5	3	tr	3	1	2
5	tekh	F	#	1/246	Pwith	37wee	Giver	NVD	O	3	OS	OSIT	6	8	5	&	M	Yes	: &	DHFNCE	II/rese	NO	74	###	83/9.6	20	#	6	2 1,0	#	##	6	7.8	7	21	99	#	98	8	6	#	1	18	8	5	h	8	1	2
6	a Bi	M	#	2/257	P37	weeks+	Giver	NVD	O	3	OS	OSIT	6	8	5	&	M	No	: &	DHFNCE	II/rese	NO	98	###	59/34	15	#	4	3 6,0	I<5	##	4.8	6	7	20	86	9	98	#	6	#	1	10	6	10	t,	#	1	1
7	ii Ch	M	#	2/2:14	Aweeks + 4	Giver	Sectir	I	3	OS	OSIT	6	8	4	&	M	No	: &	DHFNCHE	I/rese	YES	78	###	44/51	16	#	5	9 2,0	#	##	4.3	8.1	7	34	69	#	97	1	6	#	1	12	6	4	P4	1	1	
8	Polic	M	#	2/2:56	P8weeks +	Giver	NVD	I	3	OS	OSIT	6	8	4	&	M	No	&	DREHFNC	HE I/bse	YES	78	###	35/49	13	#	4	3 6,0	#	##	3.9	6.7	7	27	##	#	97	8	5	#	1	29	7	4	,	4	1	2
9	nant	M	#	3/230	Awith 40	wee	Giver	NVD	O	3	OS	OSIT	6	8	4	&	M	No	: &	DHFNCIE	I/bse	NO	99	###	70/23	13	#	4	3 2,0	#	##	4.1	7.1	7	30	87	#	97	4	6	#	1	54	7	3	\7	1	1	
10	a La	M	#	2/2C:21	Ath 37	weel	Giver	NVD	I	3	OS	OSIT	6	9	4	&	M	No	&	DREHFNC	IE I/rese	YES	74	###	59/32	19	#	5	4 2,0	#	##	4.2	8.2	7	30	##	#	##	3	5	#	1	41	7	3	in	6	1	1
11	urub	M	#	9/235	Aweel	Dther	Giver	NVD	O	3	OS	OSIT	6	8	5	&	M	Yes	&	DREHFNC	IE I/rese	NO	84	###	74/22	21	#	6	5 3,0	#	##	5.1	8.6	7	24	##	#	97	5	5	#	1	27	7	3	.\	4	1	1
12	.axm	M	#	3/2:30	Ath 38	weel	Giver	NVD	I	3	OS	OSIT	6	7	5	&	M	No	: &	DLFNC	IE I/bse	YES	89	###	63/28	17	#	5	3 5,0	#	##	3.8	8.4	7	37	79	#	97	5	5	#	1	37	7	3	>-	#	1	2
13	ama	F	#	4/200	Fth 38	weel	Giver	NVD	O	3	OS	OSIT	6	8	5	&	M	Yes	&	DREHFNC	E II/bse	NO	77	###	76/17	16	#	5	3 3,0	#	##	4.3	8.7	7	23	##	#	99	4	8	#	1	24	7	4	a	3	1	1
14	kara	F	#	3/245	Ath 38	weel	Giver	NVD	O	3	OS	OSIT	6	8	4	&	M	Yes	&	DBUTTILATE	II/bse	NO	110	###	72/15	15	#	4	###	#	##	4.4	7.6	7	25	86	#	98	5	6	#	1	39	5	4	a	#	0	2
15	ha g	M	5	01/2:00	P8 weeks +	Giver	NVD	I	3	OS	OSIT	6	8	5	&	M	Yes	&	DUTILATE	II/bse	YES	113	###	77/24	14	#	4	2 0,0	#	##	5.3	6	7	27	##	#	99	6	7	#	1	134	6	2	R9	1	1	
16	keep	F	#	6/2:30	Ath 3PRO	lGiver	Sectir	I	3	OS	OSIT	6	8	5	&	M	Yes	&	DREHFNC	IE I/bse	YES	117	###	68/32	16	#	6	4 6,0	#	##	6.1	8.9	7	15	##	#	##	2	5	#	1	21	8	4	wi	7	1	1
17	unith	F	#	9/2:31	A weeks	Mot	Giv	NVD	O	3	OS	OSIT	6	9	2	DIAE	No	&	DREHFNC	HE (bse	YES	83	###	72/21	15	#	6	4 0,0	#	##	3.9	7.7	7	36	##	#	##	2	2	#	1	22	2	1	n	4	1	1
18	tekh	F	#	9/225	A2eks	pog	Mot	Giv	NVD	O	3	OS	OSIT	6	9	2	DIAE	No	&	DRELFNC	HE (bse	YES	92	###	47/41	16	#	5	3 8,0	#	##	3.8	8.8	7	36	##	#	##	2	4	#	1	23	2	1	D	3	1	2
19	hwa	M	#	9/2:31	Aeeks	under	known	NVD	I	3	OS	OSIT	6	9	2	DIAE	No	&	DRELFNC	HE (bse	YES	112	###	70/30	16	#	5	3 6,0	6	##	3.9	8.9	7	37	##	#	##	2	1	#	1	17	2	1	o	3	1	2
20	eedi	F	5	69/240	Ai days	pog	Giver	Sectir	I	3	OS	OSIT	6	8	2	DIAE	No	: &	DHFNCHE	(bse	YES	96	###	72/27	18	#	6	1 8,0	#	##	4.3	8.8	7	42	97	#	##	1	1	#	1	26	2	1	ii	5	1	2
21	asw	M	5	69/248	Ath 3E	clam	Giver	Sectir	I	3	OS	POSI	T	6	9	2	DIAE	No	&	DREHFNC	HE (bse	YES	138	###	64/29	18	#	6	3 7,0	#	##	4.8	9	7	37	##	#	##	1	2	#	2	15	2	1	..	4	1	1
22	ihad	M	#	3/237	Ath 37	week	Mot	Giv	NVD	O	3	OS	OSIT	6	9	2	DIAE	No	&	DRECPAP	HE (bse	YES	98	###	51/48	20	#	5	1 5,0	5	##	3.9	8.1	7	37	##	#	99	2	5	#	1	30	5	1	t	4	1	2
23	avith	F	#	3/230	Pwith 39	Mot	Giv	Sectir	O	3	'GA	EGA	T	8	9	2	DIAE	No	&	DREHFNC	HE (bse	YES	97	###	51/46	17	#	5	1 8,0	#	##	3.9	8.1	8	41	##	#	99	2	4	#	1	60	6	0	2	4	1	2
24	abo	F	#	0/2:30	Awith 39	Mot	Giv	NVD	O	3	OS	OSIT	8	9	2	DIAE	No	DOP	LFNC	HE (bse	NO	110	###	51/48	16	#	5	1 7,0	#	##	3.9	8.1	7	39	##	#	##	1	6	#	1	35	6	1	P2	1	2	
25	vale	M	#	0/2:27	Aweeks	unkn	known	NVD	O	3	OS	OSIT	8	9	2	DIAE	No	DOP	LFNC	HE (bse	NO	85	###	70/28	19	#	5	2 7,0	#	##	4.7	7.7	7	29	##	#	##	2	4	#	1	55	5	1	,	4	1	2

26	Aishı	M	#	0/2:33	/eeks und	Not Giv	Secti	O	3	)SI	'OSIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	88	###	71/28	20	#	5	54,0(	<5	##	4.8	8.1	8	46	##	#	98	2	4	#	1	60	4	0	T	4	1	2
27	chitl	F	#	0/230	A eks pog ur	Giver	Secti	I	3	OS	POSI	8	9	2	CIAE	No	OOP/	LFNC	HIE (bsei	YES	84	###	71/28	19	#	5	75,0(	<5	##	3.9	8.1	7	48	##	#	98	3	6	#	1	45	7	0	G	3	1	2
28	Pooj	M	#	0/237	Pweeks und	Giver	Secti	I	3	EG/	OSIT	8	9	2	CIAE	No	ADRE	CPAP	HIE (bsei	YES	110	###	51/48	18	#	5	58,0(	<5	##	4.3	8.9	7	39	##	#	99	1	4	#	1	55	5	0	(	4	1	2
29	iyan	F	#	0/234	Pweel	Others	Giver	Secti	O	3	OS	POSI	8	9	2	CIAE	No	& D	CPAP	HIE (bsei	YES	84	###	60/38	19	#	5	15,0(	#	##	4.3	7.7	7	42	##	#	##	2	4	#	1	48	5	0	vi	5	1	2
30	hobl	M	#	0/2:30	feeks und	Not Giv	Secti	O	3	)SI	'OSIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	79	###	47/42	17	#	4	15,0(	<5	##	3.9	7.8	7	38	##	#	98	2	4	#	1	44	6	0	nt	3	1	1
31	na cl	M	#	0/2:21	Weeks pog	Giver	Secti	O	3	OS	POSI	8	9	2	CIAE	No	ADRE	CPAP	HIE (bsei	YES	94	###	61/37	19	#	5	51,0(	#	##	3.9	7.9	8	48	##	#	99	2	4	#	1	48	5	0	::	5	1	1
32	fsar	M	#	0/2:00	feeks und	Not Giv	NVD	I	3	GA	'OSIT	8	9	2	CIAE	No	& D	HFNC	HIE (bsei	YES	96	###	71/29	16	#	5	13,0(	#	##	3.9	8.7	7	41	##	#	99	2	6	#	1	59	5	0	h	5	1	1
33	Loop	F	#	/20:40	/eeks	PROM	t Giv	Secti	O	3	)SI	'OSIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	84	###	52/47	19	#	5	71,0(	#	##	5.1	8.7	7	49	##	#	##	2	6	#	1	63	6	0	t,	4	1	2
34	Vidy	M	#	/20:43	Fweeks u	Not Giv	NVD	O	3	)SI	)SIT	8	9	2	CIAE	No	Nil	LFNC	HIE (bsei	NO	91	###	61/27	16	#	4	17,0(	5	##	3.9	8.9	7	37	##	#	99	2	4	#	1	40	6	0	,	2	1	2
35	ina r	F	#	/20:41	P2 with 39 w	Giver	Secti	O	3	)SI	'OSIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	79	###	71/29	18	#	5	54,0(	#	##	3.9	7.4	7	37	##	#	99	1	4	#	1	33	5	1	T	4	1	2
36	indh	F	#	/20:41	Aweeks u	Not Giv	NVD	O	3	)SI	'OSIT	8	9	2	CIAE	No	Nil	LFNC	HIE (bsei	NO	84	###	41/47	17	#	5	34,0(	<5	##	3.9	7.9	7	33	##	#	##	1	4	#	1	47	7	0	t	3	1	2
37	aduk	M	#	/20:37	/ks pog u	Not Giv	NVD	I	3	)SI	POSI	8	9	2	CIAE	No	Nil	LFNC	HIE (bsei	NO	88	###	70/28	17	#	4	18,0(	#	##	3.9	8.3	7	26	##	#	98	2	4	#	1	29	7	1	t	3	1	2
38	lash	F	#	/20:37	/eeks pog u	Giver	Secti	O	3	EG	POSI	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	110	###	61/38	15	#	4	26,0(	6	##	3.8	7.8	7	47	##	#	98	1	4	#	1	51	6	0	t	3	1	2
39	Pooj	M	#	/20:30	Aweeks po	Not Giv	NVD	I	3	)SI	)SIT	8	9	2	CIAE	No	& D	HFNC	HIE (bsei	NO	96	###	47/42	18	#	4	78,0(	<5	##	3.9	7.9	7	38	##	#	99	1	6	#	1	55	6	0	T	6	1	2
40	unitl	F	#	/2030	P5 day	PIH	Giver	Secti	I	3	OS	)SIT	8	9	2	CIAE	No	& D	CPAP	HIE (bsei	YES	110	###	60/38	15	#	4	74,0(	#	##	3.3	7.4	7	47	##	#	99	3	6	#	1	53	5	0	T	6	1	1
41	adhil	M	#	0/247	Ath 40 we	Not Giv	Secti	I	3	)SI	'OSIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	97	###	70/28	19	#	5	37,0(	6	##	3.8	7.9	7	44	##	#	99	2	4	#	1	38	5	0	nt	5	1	1
42	npa l	M	#	5/2:30	Fweel	Eclam	Giver	Secti	O	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	NO	110	###	63/30	16	#	6	71,0(	#	##	4.7	8.7	7	38	##	#	99	2	4	#	1	17	5	1	(	5	1	2
43	yash	M	#	5/2:56	/3 weeks u	Giver	Secti	I	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	107	###	56/43	17	#	6	48,0(	<5	##	3.9	8.7	7	44	##	#	98	2	4	#	1	17	5	1	h	4	1	1
44	shal	M	3	7/9/2:32	/ks+4 d po	Giver	NVD	I	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	LFNC	HIE (bsei	NO	112	###	75/18	20	#	6	33,0(	<5	##	4.5	9.5	7	24	##	#	##	3	5	#	1	22	5	1	,	3	1	2
45	urekl	M	#	9/2:55	/+ 5 days p	Giver	Secti	O	3	)SI	'OSIT	8	9	2	CIAE	No	OOP/	LFNC	HIE (bsei	NO	77	###	82/12	16	#	6	77,0(	<5	##	3.8	8.3	7	38	##	#	98	2	6	#	1	16	8	1	r	2	1	1
46	itha	M	#	9/2:47	/+ 5 days	Not Giv	NVD	O	3	)SI	)SIT	8	9	2	CIAE	No	Nil	LFNC	HIE (bsei	NO	112	###	50/36	16	#	4	30,0(	#	##	3.7	8.3	7	30	##	#	##	3	4	#	1	14	5	1	ir	2	1	1
47	gam	M	#	9/2:30	Weeks pog	Giver	Secti	I	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	103	###	49/40	18	#	5	50,0(	#	##	3.7	8.7	7	32	##	#	99	2	5	#	1	32	9	1	C	4	1	1
48	nara	M	#	9/2:50	feeks und	Not Giv	Secti	O	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	LFNC	HIE (bsei	NO	79	###	46/47	12	#	4	41,0(	#	##	4.1	8.2	7	33	##	#	##	1	3	#	1	42	5	0	vi	3	1	2
49	kshı	M	#	9/2:25	Fwith 38 w	Not Giv	NVD	I	3	GA	EGAT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	YES	116	###	53/38	13	#	4	38,0(	#	##	4.5	8.7	7	12	##	#	99	2	4	#	1	26	5	1	tl	5	1	1
50	remı	F	#	9/2:44	Fweeks po	Not Giv	NVD	O	3	)SI	)SIT	8	9	2	CIAE	No	Nil	LFNC	HIE (bsei	NO	87	###	72/21	19	#	5	78,0(	#	##	4.1	7.8	7	33	##	#	##	1	4	#	1	17	5	1	F	3	1	2
51	Salm	M	#	9/247	A+4d pog	Unknov	Secti	O	3	)SI	)SIT	8	9	2	CIAE	No	ADRE	HFNC	HIE (bsei	NO	81	###	56/36	20	#	6	19,0(	#	##	4.2	8.3	7	25	##	#	##	3	7	#	1	18	6	1	)	5	1	2