**METABOLIC DISORDERS IN NEW BORNS**

Metabolic disorders in newborns, characterized by genetic defects that impair the body's ability to process nutrients, represent a critical health issue that necessitates prompt screening and intervention to avert potentially life-threatening complications and ensure optimal long-term development.

1. **PHENYLKETONURIA (PKU)**

It is an inborn error of phenylalanine metabolism, associated with the inability to convert phenylalanine to tyrosine. The phenylketonuria is inherited in an autosomal recessive manner. The incidence of phenylketonuria is about 1 in 20,000 newborns. In phenylketonuria, there is an accumulation of phenylalanine in tissues and blood and results in its increased excretion in urine.

Since phenylketonuric patients cannot convert phenylalanine to tyrosine, by normal pathway, some minor pathway of phenylalanine becomes prominent in phenylketonuric and accumulation of toxic metabolites of phenylalanine such as, phenylpyruvate, phenylacetate, phenyl lactate and phenylacetyl glutamine.

The disease acquired its name (PKU) from the elevated levels of the keto acid, phenylpyruvate in urine. All untreated phenylketonuric are severely mentally retarded. Untreated phenylketonuria is life threatening; half are dead by age 20 and three quarters by age 30.

**Classification of Phenylketonuria (PKU)**

Phenylketonuria may be classified into three broad groups. PKU caused by deficiency of phenylalanine hydroxylase, is the most encountered error.

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| **TYPE OF PHENYLKETONURIA (PKU)** | **DEFECT** |
| Classic phenylketonuria or hyperphenylalaninemia type 1 | Defect in phenylalanine hydroxylase |
| Atypical phenylketonuria or hyperphenylalaninemia type 2 | Defect in dihydrobiopterin reductase |
| Hyperphenylalaninemia type 4and 5 | Defect in dihydrobiopterin synthesis |

**Characteristics of Phenylketonuria (PKU)**

• Increased level of: Phenylalanine, phenylacetate, phenyl lactate, phenylpyruvate and phenylacetylglutamine, in tissues, plasma and urine. Phenylacetate gives the urine a mousy Odor.

• Neurological symptoms: Mental retardation, failure to walk, to talk, seizures, psychoses, tremor and failure to grow.

• Hypopigmentation: Phenylketonuric have a lighter skin colour, fair hair and blue eyes due to deficiency of pigment melanin. The hydroxylation of tyrosine by tyrosinase is the first step in the formation of the pigment melanin is competitively inhibited by the high levels of phenylalanine in PKU.

**Treatment of Phenylketonuria (PKU)**

The therapy for PKU is a low phenylalanine diet. The aim is to provide just enough phenylalanine to meet the needs for growth and replacement.

• Proteins that have a low content of phenylalanine such as casein from milk, are hydrolysed and phenylalanine is removed by adsorption.

• A low phenylalanine diet must be started very soon after birth to prevent irreversible brain damage.

In recent years, advancements in treatment options have emerged. These include:

1. **Pharmaceuticals:** Medications like sapropterin dihydrochloride (Kuvan) can enhance residual PAH activity in some patients with mild forms of PKU.
2. **Gene Therapy:** Research into gene therapy aims to correct the underlying genetic defect by delivering functional copies of the PAH gene.
3. **Enzyme Replacement Therapy:** This approach seeks to provide patients with a synthetic version of the PAH enzyme.

**Contribution of Knowledge about Phenylketonuria (PKU)**

Understanding PKU has significant implications across various fields:

1. **Public Health Initiatives:** Knowledge about PKU has led to widespread newborn screening programs globally. Early detection allows for timely dietary interventions that prevent cognitive impairment.
2. **Nutritional Science:** Research into dietary management strategies informs nutritional guidelines not only for individuals with PKU but also contributes insights into amino acid metabolism relevant for broader populations.
3. **Genetic Counselling:** Awareness of PKU’s genetic basis enables healthcare providers to offer informed counselling for families at risk of having children with this condition. This includes discussing reproductive options and prenatal testing.
4. **Research Advancements:** Ongoing research into novel therapies fosters innovation in treating metabolic disorders more broadly, potentially benefiting other conditions linked to metabolic dysfunctions.
5. **Patient Advocacy and Support Networks:** Increased awareness leads to better support systems for individuals living with PKU and their families through advocacy groups that promote education and access to resources.

**Diagnostic tests for Phenylketonuria (PKU)**

• In the past years, the urine of newborns was assayed by the addition of FeCl3 which gives an olive colour in the presence of phenylpyruvate.

• The phenylalanine level in blood is detected by screening by using Guthrie test.

• The gene for human phenylalanine hydroxylase has been cloned, so that prenatal diagnosis of PKU is now possible with DNA probes.

1. **VERY LONG CHAIN ACYL COA (VLCADD)**

VLCADD or very long chain acyl CoA dehydrogenase deficiency is a condition that impacts the body’s capacity to metabolize specific fats, particularly very long chain fatty acids. This disorder falls under the category of fatty acid oxidation disorders. Is passed down through genes in a recessive manner. People, with VLCADD have levels or no VLCAD enzyme, which plays a role, in converting these fatty acids into energy.

**Genetic basis**

The root of VLCADD can be traced back, to changes, in the ACADVL gene for encoding the VLCAD enzyme. If this gene undergoes mutations, it causes a shortage of the enzyme, which hinders the oxidation of very long chain fatty acids. Consequently, these fatty acids build up in the body triggering a range of health problems.

**Symptoms and clinical presentation**

VLCADD can present with a spectrum of sumptuous that are very based on the age of ones.

1. ***Earl-onset form***

Symptoms usually appear shortly after a baby is born, within days or weeks. Frequent indicators consist of feeling tired being low blood sugar levels (hypoglycaemia) weakened heart muscles (cardiomyopathy) and irregular heartbeats. Babies might also go through metabolic emergencies triggered by fasting or sickness.

1. ***Later-onset form***

Symptoms usually show up a few days or weeks later, in childhood or adolescence. This condition is marked by periods of muscle pain, tiredness and muscle breakdown known as rhabdomyolysis. Patients might also face recurring blood sugar episodes though, with milder heart issues compared to those seen in early onset instances. These symptoms are often brought on by fasting or sickness.

1. ***Adult-onset form***

Symptoms may involve experiencing muscle pain and weakness while engaging in activity or when unwell. The presence of myoglobin, in urine, known as myoglobinuria can result from muscle breakdown.

**DIAGNOSIS**

Diagnosis of VLCADD involves several steps name.

* Newborn screening: Most infants are diagnosed through expanded newborn screening programs using tandems mass spectrometry, which defects elevated levels of specific acylecarnitines in blood vessels
* Biochemical testing: Urine organic acid analysis shows decreased or absent ketone bodies and elevated dicarboxylic acids.
* Genetic testing: Confirmatory testing via the DNA sequencing can identify mutations in the ACADVL

***Measurement and treatment***

Management strategies focus on preventing metabolic crises and ensuring adequate energy supply.

* ***Emergency protocells***

Intravenous glucose infusion during acute bouts or diseases is essential for managing hypoglycaemia.   
To avoid complications, fasting or illness must be carefully monitored.

* ***Dietary Management***

reduce the need for fasting, a low-fat, high-carbohydrate diet is recommended.   
Regular meals and snacks help keep blood glucose levels constant.   
Medium-chain triglyceride (MCT) oil supplements offer an alternative energy source that does not rely on VLCAD for metabolism.

* ***Long term monitoring***

Regular follow-ups with metabolic specialists are required for continuing assessment and management adjustments, as warranted.

* ***Genetic counselling***

Families impacted by VLCADD should seek genetic counselling to better understand inheritance patterns and potential hazards for future pregnancy.

**Prognosis**

Individuals with VLCADD can have healthy lives if they are diagnosed early and treated appropriately. However, untreated cases can result in catastrophic complications such as brain damage or death from metabolic crises.

**Contribution of knowledge on VLCADD**

The Understanding of VLCADD has significant implications for both clinical practice and research which include;

1. *Enhanced Screening Programs*: Knowledge about this disorder has led to improved newborn screening protocols that can identify affected infants early, allowing for timely intervention before severe complications arise.
2. *Personalized Nutrition Plans:* With insights into individual metabolic profiles, healthcare providers can create tailored dietary plans that optimize health outcomes for patients with VLCADD.
3. *Research Advancements*: Ongoing research into the molecular mechanisms underlying VLCADD may lead to novel therapeutic approaches, including gene therapy or enzyme replacement therapies that could restore normal metabolic function.
4. *Increased Awareness Among Healthcare Providers*: Educating healthcare professionals about VLCADD ensures better recognition of symptoms and appropriate management strategies across different medical specialties.
5. *Support Networks for Families*: Increased awareness fosters community support systems that provide resources for families managing this chronic condition, enhancing their quality of life through shared experiences and information.

**CONCLUSION**

In conclusion, metabolic disorders in newborns represent a significant public health concern that necessitates robust screening protocols and immediate medical attention to ensure better health outcomes for affected infants.