A Successful Feto-Maternal Outcome In Pregnancy With Wilsons Disease: An Extremely Rare Case Report With Review Of Literature

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Abstract: Wilson's disease, also known as hepato-lenticular degeneration, is one of the very rare autosomal recessive disorder of copper metabolism. There is impaired liver metabolism of copper thereby causing decreased biliary excretion and deposition of ceruloplasmin levels mainly in the liver, corneas of eyes and brain. Untreated Wilson's disease has been associated with menstrual irregularities, amenorrhoea, miscarriages and infertility. Hence proper chelation with strict antenatal surveillance will lead to a successful feto-maternal outcome. [Katke R Natl J Integr Res Med, 2021; 12(2):78-81]

Key Words: Wilsons disease, pregnancy, feto-maternal outcome, high risk

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Introduction: Wilson's disease, also known as hepatolenticular degeneration, is a very rare autosomal recessive disorder of copper metabolism. In 1921 Kinnier Wilson was the first to describe the disease. It has a prevalence of 1:50,000-1:100,000 live births[1]. It occurs due to mutation of the ATP 7B on chromosome 13q14[2].

This accumulation causes liver cirrhosis and nervous system manifestations like movement disorders and ataxia. The disorder commonly shows its manifestations in the early twenties. Without appropriate treatment, the chance for a successful pregnancy is notably decreased due to the impaired fertility caused by liver insufficiency.

If Wilson's disease is left untreated, it causes subfertility and in cases where pregnancy does occur, it often results in spontaneous miscarriage[3]. If the levels of copper increase, it may lead to preeclampsia, intrauterine growth restriction and neurologic damages in the foetus.

In a pregnant woman with decompensated liver cirrhosis, there are chances of more serious complications like bleeding from oesophageal varices, liver failure, encephalopathy, and rupture of the splenic artery. Successful decopperizing leads to ovulatory cycle restoration and enables pregnancy. Use of Penicillamine, zinc salts, has resulted in successful pregnancy outcomes in patients with Wilson's disease[4].

Treatment for Wilson disease include medications of three types, 1- Penicillamine (Cuprimine) and Trientine dihydrochloride (Syprine) - These remove (chelate) copper from the body by urinary excretion , 2- Zinc salts – These prevent the gut from absorbing copper from the diet, and 3- Tetrathiomolybdate – This prevents both, absorbing copper and binds up toxic copper in the blood making it nontoxic, however Tetrathiomolybdate is not indicted during pregnancy. Treatment for Wilsons disease should be maintained during pregnancy, and patients should be monitored closely for hepatic and neurological symptoms

Material & Methods: A 24 years old female, Married since 1 year, spontaneous conception, with 9 months gestation, presented to casualty Grant Government Medical College, Mumbai, referred from a Maternity Child Health, as a case of Primigravida with BD 36 wks BS 35.2 wks with known case of Wilsons disease with threatened preterm.

Patient was registered and immunised at a PHC, had regular antenatal visits there. Patient had normal congenital anomaly scan.Patient was diagnosed as a case of Wilsons disease with Parkinsons disease at the age of 18 years. Patient had complains of dysarthria, slowing of activities, mask like facies and increased salivation.

Her father noticed slowing at activities like walking and writing. There was slurring of speech and tremors in the hand. Her ceruloplasmin and 24 hour urinary copper were confirmatory for wilsons disease.

KF ring was seen. Patient was stared on Decoppering agents following which her symptoms improved. Patient was on tab Penicillamine 500 mg twice a day and Tab zinc 40 mg twice daily.

After 1 year, patient had neuropsychiatry symptoms like irritability, depression, cognitive impairment and involuntary jerky movements. Patient was started on Tab Escitalopram and tab Tetrabenazine which was continued throughout pregnancy.

Her dose of Penicillamine was decreased to 250 mg twice daily and increased dose of tab zinc to 200 mg twice daily.

Patient was admitted in antenatal transit ward of our hospital. In view of covid pandemic, a covid swab was urgently sent and patient tested Covid RT PCR negative. Her antenatal course was uneventful.

On examination patient's General Condition was fair, afebrile, Pulse – 86 beats / min, regular, Blood Pressure 120/70 mmHg.

No pallor, icterus, cyanosis, clubbing, lymphadenopathy, oedema.

CVS – S1, S2 normal, no murmur, Respiratory System – air entry bilaterally equal.

Per abdomen uterus corresponded to 36 weeks, cephalic presentation, head was engaged, FHS + 144 bpm, relaxed.

On PS examination there was no leak or bleed.On PV examination os was 2 cms, 20-30 % effaced, vertex presentation, membranes present, station (-2), pelvis was adequate. Steroid prophylaxis was given for fetal lung maturity.

All routine investigations were sent. Blood group A Rh positive. HIV HBsAg, HCV VDRL were negative. HB 10.3 total leucocyte counts 9700 platelet 209000, Total Bilirubin 0.5 SGOT/SGPT 44/38. Creatinine 0.7 Urea 44

Fasting Blood Sugar- 87, Post Prandial Sugars-102.

Urgent ultrasound with doppler was done s/o Single Live intrauterine gestation of 37.3 weeks, cephalic, anterior placenta, 3.2 kg baby weight with adequate AFI and normal doppler study.

Close antenatal foetal surveillance including foetal heart rate, non stress test monitoring was done. Patient was given complete bed rest.

Patient went in spontaneous labour , labour partographic monitoring done and was delivered vaginally with episiotomy .A female healthy child of 2.6 kg baby weight with APGAR score 8 was delivered. Post delivery patient was monitored and was stable.

Post delivery haemoglobin was 9 gm %. A slit lamp examination by an experienced ophthalmologist was done suggestive of Keiser Fischer ring. 2D ECHO was done suggestive of normal study with no cardiac changes.

Ultrasound abdomen suggestive altered echotexture of liver with mild parenchymal echogenicity.

Neurology opinion was taken and tab Penicillamine was increased post delivery with increased dose to 250 mg 2-0-1. Patient was advised to avoid breast feeding. Patient was given breast milk suppressants and baby was started on top feed. Baby was advised to follow up for work up after 6 months age and yearly follow up to check for early changes of Wilsons disease if any.

Discussion: In Wilson's disease neurological symptoms and liver damage at an early age and reduce the probability of marriage[6]. The primary storage organ for copper is liver. From here it can be distributed in circulation to other tissues such as nervous system, eyes and kidneys. Decreased excretion leads to excessive copper accumulation which can adversely affect these tissues leading to hepatic injury and cirrhosis, neurological symptoms such as dyskinesias and tremors, kayser-fleishcer ring around limbus and renal tubular damage.

When pregnancies do occur in untreated Wilson's disease, most result in spontaneous abortions.

These are induced by the excessive concentration of free intrauterine copper. Hepatotoxicity may lead to menstrual irregularities and copper deposition in the uterus in women in reproductive age group may lead to recurrent

miscarriages. Many women with Wilson's disease may require infertility treatment but some patients may also conceive spontaneously.

A change has been observed in the serum copper and ceruloplasmin levels as the pregnancy progresses. The levels have shown increase till 24 weeks of gestation followed by some decline probably due to fetal intake of copper[5].

Approximately 12 mg of copper may be present in a neonate and the fetus is thought to remove 0.044 mg of copper per day from the maternal serum on an average, due to which improvement in symptoms of Wilson's disease have also been reported[4] Untreated, Wilson's disease may lead to early pregnancy complications. Penicillamine and zinc are increasingly being used as a therapeutic option in managing Wilson's disease.

Penicillamine is an active chelating agent that binds to copper and forms an inert complex which is excreted in the urine. Zinc causes interference in the absorption of copper from the gastrointestinal tract. Zinc prevents serosal transfer of copper into the blood by induction of intestinal cells metallothionein which has a high affinity for copper.

Deposition of zinc in the endometrium is hypothesized to be associated with increased abortion risks.Previous studies have reported that clinical and biochemical signs of Wilson's disease have not worsened during pregnancy[7].

Some investigators have even demonstrated clinical improvements during pregnancy and for several months after delivery, possibly because of a rise in serum ceruloplasmin. This rise would be probably induced by the high levels of estrogen, since ceruloplasmin does not cross the placenta.

In our case the serum ceruloplasmin did not increase during pregnancy. This suggests that changes in serum ceruloplasmin may not be responsible for the clinical improvement of a Wilson's patient during pregnancy[8,9,10].

Pregnancy in Wilsons disease, in general is associated with pre-eclampsia, abortions and poor wound healing due to chelating agents.Birth defects have been reported in patients taking penicillamine and include generalised connective tissue diseases e.g. cutis laxa, micrognathia, low set ears and inguinal hernias etc. , however, the overall teratogenic risk of penicillamine is low and studies support continuing treatment throughout pregnancy to avoid the risk of relapse in the mother. Fetal development was normal and a normal infant subsequently delivered.

According to previous studies, serum levels of ceruloplasmin reach adult normal at 6 months of age. Although children of Wilson's patients will be heterozygous for the autosomal recessive Wilson's disease gene, homozygous abnormal infants are rare. Early diagnosis can be made in an infant of one year of age and the illness controlled.

Conclusion: A pregnant women with Wilsons disease is to be considered a high risk obstetric case in which a successful outcome is possible with a multi-disciplinary approach and a close antenatal monitoring with appropriate use of drugs like D-penicillamine and Zinc.

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