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# A RARE CASE RECURRENT ALOBARHOLOPROSENCEPHALY

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## ABSTRACT

Holoprosencephaly (HPE), a congenital induction disorder, occurs due to failed segmentation of neural tube and subsequent incomplete separation of the prosencephalon. Because of the defect in the ventral induction, HPE is also associated with multiple facial abnormalities. Mortality correlates with the severity of brain malformation and facial phenotype. Frequent causes of death include respiratory infections, dehydration due to uncontrolled diabetes insipidus, intractable seizures, and brainstem malfunction. In AH, there is a failure of cleavage of the prosencephalon sagittally into cerebral hemispheres, transversely into telencephalon and diencephalon, and horizontally into olfactory tracts and bulbs. As a result, a small monoventricular cerebrum lacks interhemispheric division. The thalami and the corpora striata are fused across the midline. Olfactorytracts and bulbs, corpus callosum is absent. Alobar holoprosencephaly (AH) usually has various facial dysmorphisms which have higher incidence as 80% in such patients and may be nondiagnostic in 20% of the patients.There are very few reported cases of AH with normal facies in the literature. We are reporting a female with reccurent pregnancies with Alobar holoprosencephaly.

## INTRODUCTION

Holoprosencephaly (HPE) is an abnormality of brain development in which the brain does not divide properly into the right and left hemispheres. There are 4 types of HPE, distinguished by severity. From most to least severe, the 4 types are alobar, semi lobar, lobar and middle interhemispheric variant (MIHV).

HPE occurs between the 18th and 28th day of gestation, indicating that it is a disorder of gastrulation.

HPE is estimated to occur in 1 in 16000 live births.

This is a case of recurrent Alobar holoprosencephaly in the fetus of a 22 yr old suggestive of absence of midline division defects of brain development with facialabnormalities in both the pregnancies.

## CASE REPORT

A 22year old Primigravida at 5 months of amenorrhoea with no comorbidities cameto OPD with Anomaly scan.

The Ultrasonogram was suggestive of a single live intrauterine fetes correspondingto 20 weeks with good cardiac activity and body movements.

Fetal brain showed absence of Falx and Corpus callous with midline thalamusfusion.

Facial abnormalities noted showing hypotelorism with midline maxillary cleft and absence of

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nose. Features were suggestive of Holoprosencephaly Alobar type. The fetal cranium, spine, stomach bubble, kidneys, bladder, three vessel cord and fetal four chambers view seen and appeared normal.

Anterior abdominal wall and cord insertion appeared normal.

Patient underwent medical termination of pregnancy and following which patient had genetic counselling at Fetal Medicine centre.

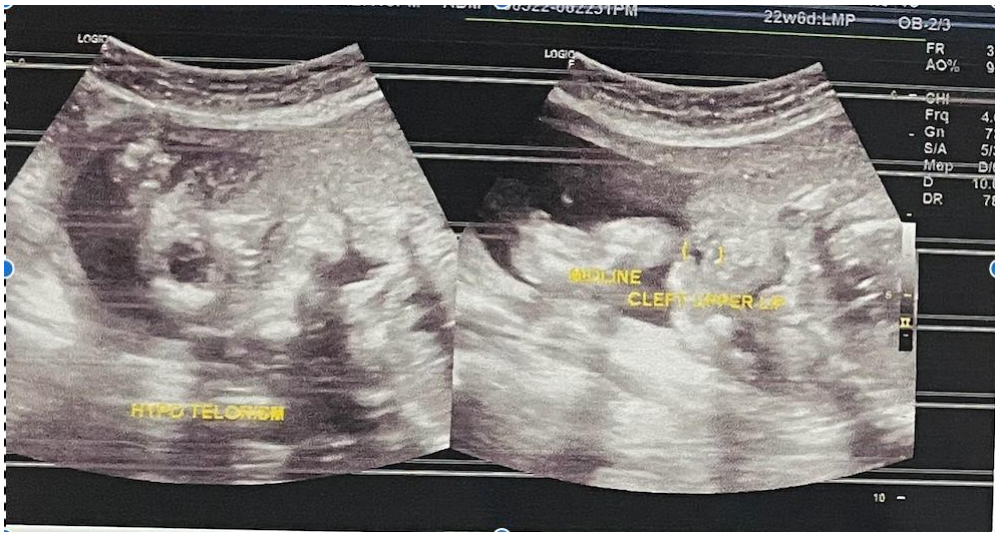
Patient was advised to start periconceptional folic acid 5mg, check her glycemic status and suggested as low risk in the future pregnancy. Patient was suggested review at 12weeks in subsequent pregnancy for detailed scan.

Patient in the next pregnancy was followed up and subjected for detailed firsttrimester ultrasound at 12weeks.

Ultrasound suggestive of Uncleaved thalami and cortex, absent fall, monoventricle.Facial abnormalities were noted- midline cleft lip and palate, absence of nose, hypotelorism, mid facial hypoplasia.

The fetal 4 chambered view of heart, great vessels, thorax, lungs, abdominal wall,stomach, bilateral kidneys, bladder, spine, bilateral upper and lower limbs and skeletal system appeared normal for the gestational age.

The fetus was diagnosed with Alobar holoprosencephaly with facial abnormalities. Hence patient underwent Medical termination of pregnancy




USG FINDING-S/O HYPOTELORISM AND MIDLINE CLEFT UPPERLIP

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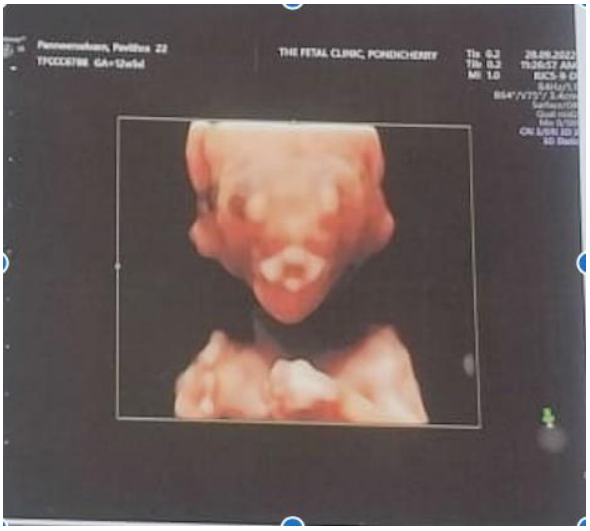
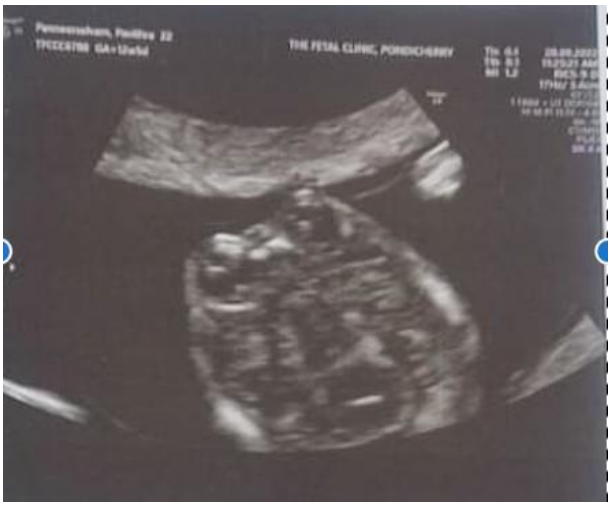



USG FINDING- S/O ARRHINIA AND HYPOTELORISM

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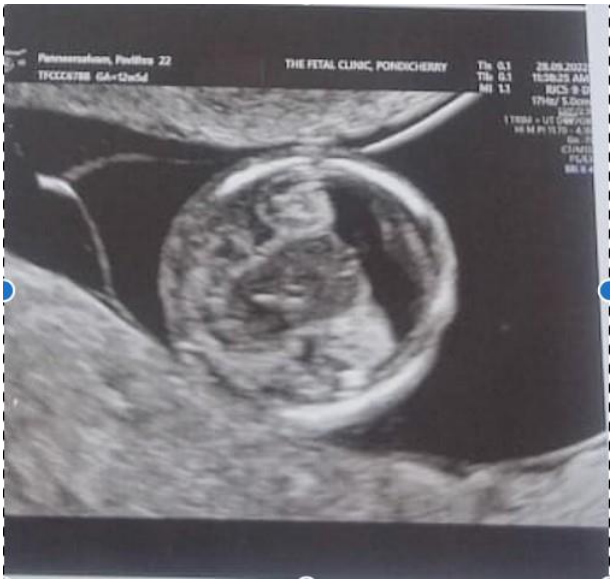


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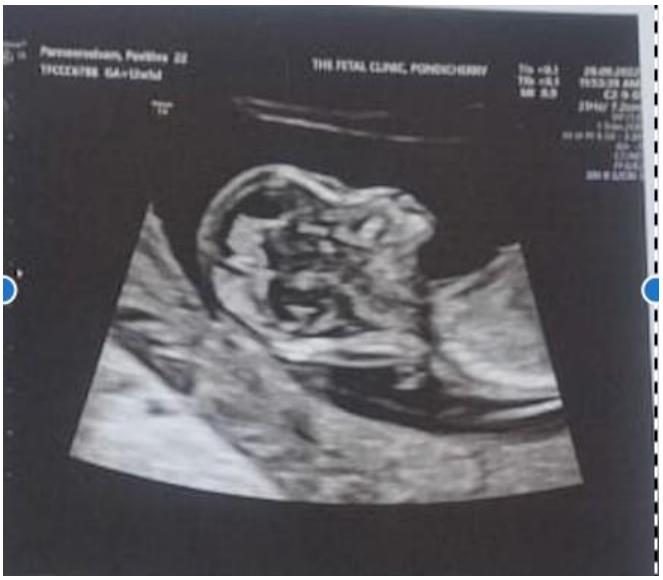


USG FINDING- S/O ARRHINIA AND INCREASED NUCHAL THICKNESS

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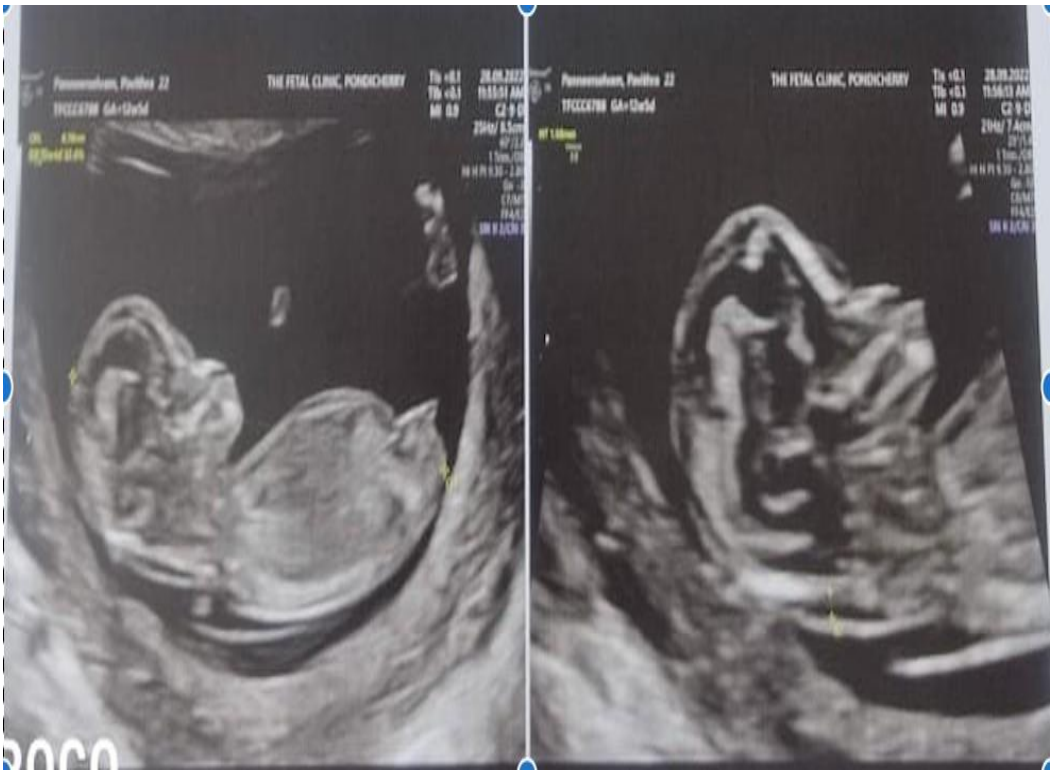


USG FINDING- S/O ARRHINIA AND INCREASED NUCHAL THICKNESS

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## DISCUSSION

HPE is a congenital induction disorder of the brain occurring at 3-6 weeks gestation, with failed segmentation of neural tube. This leads to incomplete DeMyer and Zeman suggested that this resulted from a defect in the ventral induction and from the patterning of the rostral neural tube by the prechordal mesenchyme. As ventral induction is related to facial development, many HPE cases also demonstrate craniofacial abnormalities

1. Alobar, which means the complete absence of division of the prosencephalon structures, resulting in completely absent interhemispheric fissure and corpus callosum, fused thalami, fused cerebral hemispheres with only one cerebral ventricle, and facial dysmorphism which include such abnormalities as separationof the prosencephalon. leading to so called "holoprosencephaly sequence".

HPE is classified into 4 types
cyclopia, proboscis, ethmocephaly and cebocephaly. It is the most severe form.

2. Semilobar, consisting in incomplete separation of cerebral hemispheres: thereare 2 cerebral hemispheres connected in the frontal area, with a singlular ventricular cavity and partially fused thalami.

3. Lobar, in this case interhemispheric fissure is present, septum pellucidum is absent and frontal horns of lateral ventricles communicate freely, corpus callosumis absent, hypoplastic or normal, with midline fusion of cingulated gyrus. It is the least severe from.

4. MIVH (middle Interhemispheric variant), which means a defect of separation ofthe posterior portions of the frontal lobes and the parietal lobes, with varying lackof cleavage of the basal ganglia and thalami and absence of the body of the corpus callosum but the presence of the genu and splenium of the corpus callosum.

Studying HPE on a molecular level; has led to the identification of the HPE genes:Sonic hedgehog (SHH), ZIC2 and SIX3. To date, at least 12 loci located on 11 different chromosomes contain genes involved in HPE. For 5 of them, a minimal critical region has been
identified: HPE 1 at 21q22.3, HPE 2 at 2p21, HPE 3 at 7q36, HPE 4 at 18 p, andHPE 5 at 13q32.

Multiple environmental factors have also been reported in the pathogenesis of HPE, including: maternal diabetes, a 200 folds increase in the incidence of HPWE in babies of diabetic mothers was reported; radiation or toxin exposure during pregnancy; TORCH infection, cigarette smoking; and retinoic acid. The HPE facies which are characterized by hypotelorism, are grouped into 5 major categories:

(1) Cyclopia, a single eye or partially divided eyes in a single orbit with a proboscisabove the eye;
(2) Ethmocephaly, severe hypotelorism and a proboscis between the eyes;

(3) Cobocephaly, hypotelorism with a single nostril and a blinded nose;
(4) Absent intermaxillary segment with central defect and hypotelorism
(5) Intermaxillary rudiment with hypertelorism.

In general, mortality correlates positively with the severity of the brain malformation and, by extension, severity of the facial phenotype. In contrast to most children with Alobar HPE, children with HPE types other than Alobar may more often survive into adulthood.
Frequent causes of death include respiratory infections, dehydration secondary to uncontrolled diabetes insipidus, intractable seizures, and sequelae of brainstem malfunction, including aberrant control of respiration and heart rate.

## CONCLUSION

In summary, HPE is a major malformation of the central nervous system that should be distinguished from other causes of fetal hydrocephalus. Awareness of the sonographic findings associated with HPE should improve the scope of prenatal diagnosis. Identification of concurrent facial malformations can help predict subsequent fetal outcome.

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