B D R News

The official newsletter of the Birth Defect Registry of India,
(A unit of Fetal Care Research Foundation)

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Proceedings of the birth defects registry meeting held on 22.01.2008

The first Birth Defects Registry meeting of the current year was held on 22.01.2008 at the Main Auditorium of Institute of Obstetrics & Gynaecology (IOG) & Government Hospital for Women & Children, Egmore Chennai.

Dr. K.Saraswathy, Director, IOG, extended a pleasant welcome address to the audience gathered. She said that IOG enjoys a long-standing professional relationship with MediScan, Chennai. She disclosed that the Indian Council of Medical Research (ICMR) has proposed a study on Newborn Screening for Congenital Hypothyroidism(CH) & Congenital Adrenal Hyperplasia (CAH) at IOG in association with Fetal Care Research Foundation (FCRF), a unit of MediScan in the near future. She said that FCRF has also conducted a pilot project at IOG that has been approved by the Department of Health & Family Welfare, Government of Tamilnadu. She announced that there would be presentation on the outcome of the BDR data collected & Newborn screening done for Congenital Hypothyroidism in the newborns delivered at IOG over a period of one year. This would be followed by a CME on birth defects by the BDR member hospitals in Chennai, she added.

Dr. S. Suresh, Director BDRI, presented briefly about the vision & mission of BDRI. He said that from a humble beginning of one Nodal Center in Chennai in 2001, now the BDR Nodal Centers have increased 20 folds with 22 Nodal Centers across the country. The number of births analyzed has also subsequently increased from a few thousands to more than a lakh & twenty five thousand in the last year. He hoped that the ongoing ICMR project on the Genetic Polymorphism of Neural Tube Defects (NTD) would help us understand the etiology of NTD in our population & ultimately help the authorities concerned to evolve preventive strategies at the national level. He ended saying that India should not only rise in volume but also achieve academically & contribute large data on medical research to the world.

Dr. Sujatha Jagadeesh, Clinical Geneticist, FCRF, proposed the vote of thanks at the end of the CME session. She appealed to all Government Maternity Hospitals in Chennai to furnish data on birth defects to the registry. This would facilitate complete coverage of births in the city. She hoped that if this could be achieved, Chennai registry would set a model BDR to all other states in the country. The excerpts, of the presentations from the member hospitals are as follow

Analysis & Outcome of Birth Defects Registry & Newborn Screening project at IOG, Chennai.

(Dr. G. Thangavel Epidemiologist, Mediscan Systems, Chennai)

Dr.G. Thangavel while acknowledging Dr. Suresh for conceiving the BDRI project said that, very few disease surveillance programs exist in India. Although birth defects contribute significantly to infant mortality in our country, they have not been given due consideration in the existing surveillance programs, he added. India is undergoing an epidemiological transition & birth defects also contribute significantly to infant mortality apart from infections as always thought to be. He briefly explained about the functioning modalities of BDRI & discussed the statistics derived with the data collected at IOG from August 2006 - July 2007.He said that BDRI has planned to function in phased manner by first concentrating on data collection on the incidence of various birth defects from member hospitals & would embark on the etiological study of birth defects in the future. He also mentioned that BDRI is one of the few registries in the world to have adopted ICD 10 classification of coding of birth defects. By this classification birth defects of structural & chromosomal origin are only taken in to consideration. Following tables give a precise view of the data analyzed on birth defects at IOG.

Results overview – Denominator

Duration: August 06 – July 07

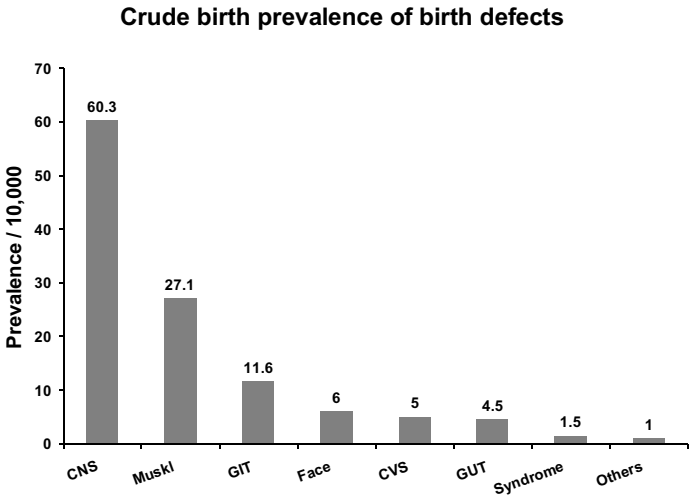
Categories	N	%
Live births (LB)	19648	98.7
IUFD/SB (IUD)	213	1.1
MTP for anomaly (MTP)	44	0.2
Total births (T)	19905	100

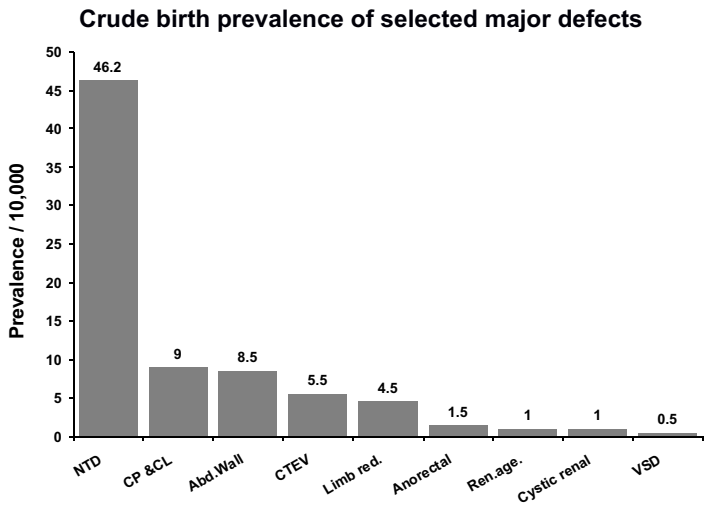
Results overview - Numerator

Categories	N	%
Live births (lb)	91	48.4
IUFD/SB (iud)	53	28.2
MTP for anomaly (mtp)	44	23.4
Total CM* (t)	188	100

Prevalence of Birth Defects

Prevalence Categories	Prevalence / 10,000
Live births alone (lb / LB)	46.3
IUFD/SB alone (iud / IUD)	2488.3
Contribution of MTP for anomaly (mtp / T)	22.1
Crude birth prevalence (t / T)	94.4





Salient features of the statistics were:

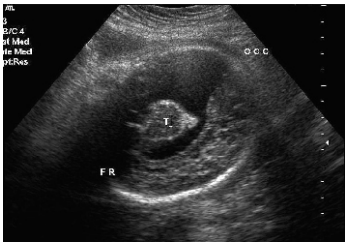
- The crude birth defects prevalence accounted to 9.4/1000 births.
- The incidence of NTD stood at 4.6/1000. It was relatively a little high as IOG is a referral center. Among the Central Nervous System anomalies, anencephaly, spina bifida, encephalocele & hydrocephalus constituted 3/4th & the rest were like microcephaly, holoproscencephaly, agenesis of corpus callosum etc.
- With the advent of ultrasound imaging 30% of specific syndromes & neural tube defects were detected & terminated antenatally.
- Cardiovascular system (CVS) anomalies were found to be the least, which probably was underestimated. If postnatal data had been collected from the Newborns & Paediatric sections, more accurate picture of CVS anomalies would have been obtained. Since CVS anomalies were seen in the last trimester, they were found more in the live birth category.
- Cleft lip & palate were the commonest among the gastro intestinal anomalies.

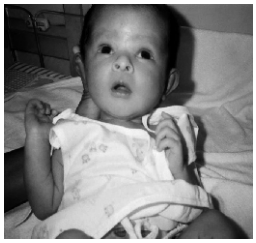
While speaking about the **Newborn Screening data on Congenital Hypothyroidism,** he said that from July 2006-December 2007, 854 newborn babies delivered at IOG were screened. There was not a single case positive for congenital hypothyroidism. This probably goes well with the general incidence of 1/1500 - 1/2500 baby in India. Since the numbers screened in this study were not sufficient, No conclusion could be drawn at present, he ended. **During discussion**, it was suggested that autopsies on Still Birth / IUD fetuses would help in picking up more number of CVS & other birth defects.

A CASE OF AQUEDUCTAL STENOSIS

Dr. K. Saravanan, Paediatrician, Vijaya Hospital

Dr. K. Saravanan discussed about a case of aqueductal stenosis presented late in pregnancy & managed appropriately after birth by surgical intervention. He said that, a mother with an obstetric history of G2P1L1 visited the center for antenatal check up. She had gestational diabetes & was on insulin. Her dating & anomaly scans were normal. At 34 weeks, the mother came with complaints of reduced fetal movements. Her USG revealed dilated lateral & third ventricles & narrow aqueduct. Rest of the fetus was normal.





The parents were counseled regarding the outcome of this pregnancy by the Sonologist, Obstetrician & the Paediatrician. The Neorosurgeon's opinion was also sought & the couple was advised regarding the prognosis & the surgical implications.

Mother later delivered normally a full term female baby weighing 3.14 kilograms. The child was on breast feeds and her head circumference (HC) measured 38 cms. The neurosonogram done on the second day was suggestive of aqueductal stenosis. CT brain on the 6th day revealed gross hydrocephalus with aqueductal stenosis. The HC was closely monitored as shown below and the child was put on ventriculoperitoneal shunt on the 10th day. Postoperative period was uneventful.

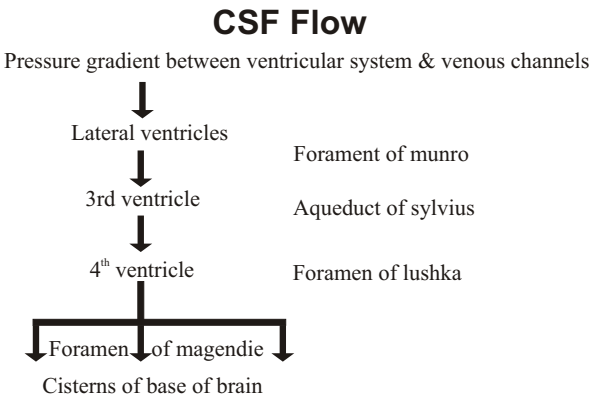
Head circumference measurements

Date	Birth 13.11.07	Day 6	Day 10	Post Surgery	1 mth	1m 13d	7.01.08
Weight (Kg)	3.14	3.09	3.3	3.2	3.6	4.2	4.8
H C	38 CM	39 CM	41 CM	38 CM	37 CM	37.5 CM	38 CM

As observed from the table the HC decreased significantly after surgery & measures 38cm at about 2 months. This is consistent with the age of the baby who is growing well & has attained social smile.The baby is being followed up at present.

Talking about the literature of congenital obstructive hydrocephalus, Dr. Saravanan said that aqueductal stenosis is the most important cause. Hydrocephalus is caused due to

increased volume of cerebro spinal fluid (CSF) which may be due to increased production or obstruction in its pathway or impaired absorption resulting in increased ventricular size. CSF is produced from choroid plexus in lateral, third & fourth ventricles. The speaker explained with the following illustration the pattern of flow of CSF which is due to the pressure gradient between the ventricular systems & venous channels.



The **etiology may be congenital, acquired or idiopathic**. It is congenital when there is mal development of aqueduct due to stenosis, atresia, septal formation or gliosis due to maternal infections during antenatal period.X-linked recessive inheritance of this condition is known with male preponderance in a family. It may be acquired following intracranial hemorrhage, post meningitis, space occupying lesion or asphyxia during delivery.

The **clinical features** include increased head circumference, wide open & bulging anterior fontanelle, dilated scalp veins & broad forehead. It can be **diagnosed** by fetal USG, clinical features after birth,serial measurement of HC, Neurosonogram, CT Brain & MRI. The **treatment** lies in correcting the cause. Medical treatment offers only temporary relief. **Definitive treatment** is surgical repair by VP shunt or Ventriculostomy. The **prognosis** depends on the cause & long term complications can not be ruled out. **Recurrence** of the defect is high if it is due to single gene or X linked inheritance in the index child. If it is due to other causes, it is between 1-5% in subsequent conceptions. The speaker ended saying that developmental defect like aqueductal stenosis can occur in late trimester despite the targeted anomaly scan being normal at 5th month of gestation. Hence antenatal screening & growth scans are a must in all pregnancies.

Discussion

1. How do you monitor the case discussed above in future?
   Since the problem was identified in antenatal period itself, the baby is being followed up every month to look for any problems
2. Does morbidity affect the long term prognosis of such cases? Is cortical thinning detrimental to prognosis?
   The prognosis depends on the cause of aqueductal stenosis. If it is due to infections during antenatal period, it is rated poor. It does not always depend on cortical thinning. The time of intervention is important after birth. Cortical thinning occurs due to pressure inside if the AF is closed. In the above case discussed, the neurosurgeon assured better outcome & hence early intervention was resorted to. The prognosis in 50% of such cases is good & they do well. When the discussion continued with issues regarding the skeptical prognosis of this condition, Dr. Suresh intervened and said that the case presented was a classical example of a late evolving problem in pregnancy & its appropriate management after birth. In such cases where prevention was not possible, best supportive care should be offered to the baby. He also mentioned that there are children who live well with VP shunt for many years. Dr. Indrani Suresh added saying that right approach to such problems becomes crucial in saving a life. She said that parents need to be counseled in detail and they should be informed about the need to deliver the baby in a tertiary center & intervened at the right time after birth. Mode of delivery & early intervention would help in reducing morbidity.

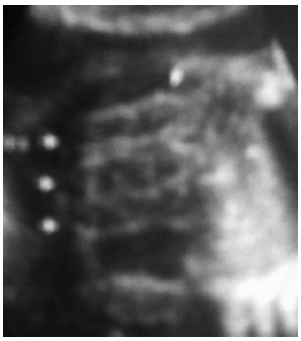
3. What is the option for late evolving problems like microcephaly?
   To this Dr. Suresh said that the law in UK allows the administration of intra cardiac potassium chloride & termination of pregnancy in such cases. Since we do not have specific laws here, such action may be misinterpreted for female feticide, if it happens to be a female fetus.

Antenatal bowel gangrene-a timely intervention

Dr. Deepthi Venugopal & Dr. Jaffer Saleem
(Post graduates OBGYN & Paediatric surgery)
SRMC hospital & RI

Dr. Deepthi Venugopal & Dr. Jaffer Saleem presented a case of antenatally diagnosed bowel gangrene that was successfully managed after birth.

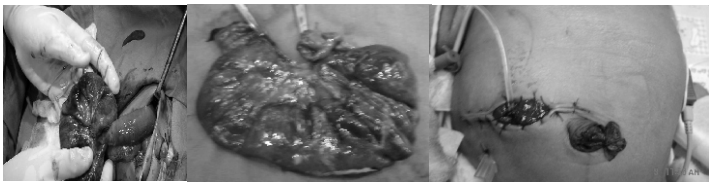
Dr. Deepthi began with the case report. A 22 year old primi was referred at 38 weeks of gestation for safe confinement, with scan findings suggestive of fetal intestinal obstruction & possible diagnosis of Volvulus. Antenatal period was uneventful & fetal movements could be perceived well. She had no history of hypertension / thyroid disease or diabetes mellitus. She has had two scans done at 18 & 32 weeks with normal findings.



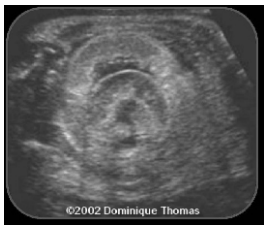
At 37 - 38 weeks of gestation, scan revealed a cystic mass of 7.6x6.9 cms with internal echoes in lower end of vertebral column, overlapping the abdomen with possible diagnosis of meningocele.

A repeat scan on the following day showed scan features suggestive of intestinal obstruction with dilated aperistaltic loops of bowel with absent blood flow. Midgut volvulus with gangrene was considered in this case. Hence, the patient was posted for emergency LSCS on the same day. A girl baby with good APGAR, weighing 2.6 kg was delivered. The baby cried immediately after birth. Dr. Deepthi ended saying that the baby was handed over to the Paediatric surgical unit for further management. Dr. Jaffer Saleem took over & said that the Paediatric surgical team that was kept alert, acted quickly

and successfully operated on the child the same day. X ray was taken an hour after birth. Part of stomach & small bowel were visualized and the rest of the abdomen was gasless. This was the classical presentation of intestinal obstruction. Clinically the baby presented with distended abdomen with shiny stretched skin & dilated bowel loops. NG tube was inserted and bilious secretions were aspirated. Double Barrel Ileostomy was performed & the gangrenous loops were resected.



The take home messages were as follow:
Fetal midgut volvulus has a specific clinico-echographic presentation:



- The main complaint of the pregnant woman is the absence of fetal movement.
- The ultrasound examination usually gives the diagnosis by the typical image of whirlpool or snail configuration, without peristalsis.
- The absence of blood flow by Doppler exploration in the centre of the mass suggests gut ischemia.
- Delivery must take place in a tertiary center because immediate surgical correction of this anomaly is indispensable.

Discussion

1.What is the sensitivity of Ultrasound in detecting bowel gangrene during antenatal period ?

To this question Dr. Suresh said that it is quite difficult to diagnose this problem by doing antenatal USG. In general volvulus presents late in third trimester. Value of color doppler may or may not be that useful as small mesenteric vessels can not be not be picked up. Peristalsis also can pick up color. Hence absence of color in doppler alone is not diagnostic of bowel gangrene. In USG some pattern as shown in the presentation may be seen which would be suggestive of distended/dilated bowel/meconium ileus or aperistaltic bowel. When there is bowel torsion there is aperistalsis and the fetus experiences pain & tends to remain quiet. It is wiser to deliver the baby early once the problem is suspected to avoid vascular insufficiency /perforation of intestine & meconium leak.

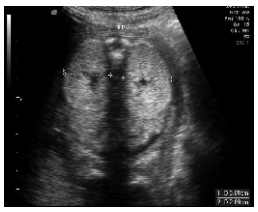
2.Echogenic bowel is generally seen in the case of PIH / IUGR. Can compromised blood supply due to these problems in early gestation be the cause of bowel atresia?

Compromised blood supply can contribute to bowel atresia but it presents much earlier in gestation and not in last trimester. In the case presented it was clearly due to meconium ileus.

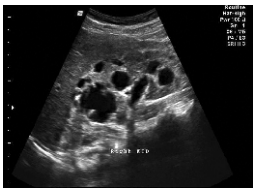
Autosomal dominant polycystic kidney disease

Dr. Neelam Chhajed, Fellow, Fetal Medicine,
MS. Jerene Abraham, Trainee, Genetic Counseling - MediScan,

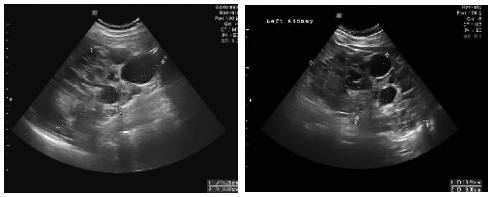
Dr. Neelam presented a case with Autosomal Dominant Polycystic Kidney Disease (ADPKD) and discussed in detail about fetal presentation of echogenic kidneys. A primi mother with 3rd degree consanguinity was referred at 24-25 weeks of gestation for an ultrasound. Her mother in law was said to have cysts in the kidney & was supposed to be normotensive. Her USG findings revealed normal liquor & fetal biometry and bilateral enlarged echogenic kidneys.



The fetus showed no other structural abnormalities. The USG diagnosis was Autosomal Recessive Polycystic Kidney Disease (ARPKD). The family was referred for genetic counseling. The father was identified to be hypertensive. Renal imaging was not done. The parents were subjected to ultrasound examination.

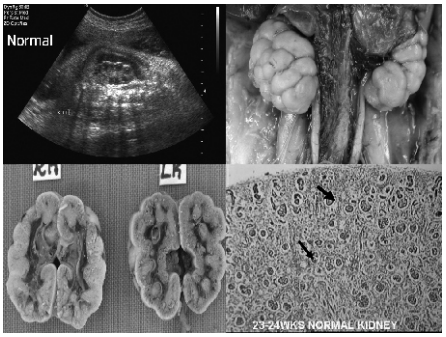


Maternal kidneys

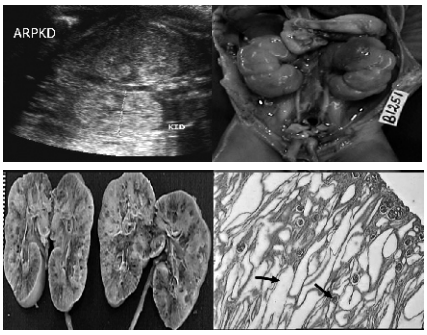


Paternal kidneys

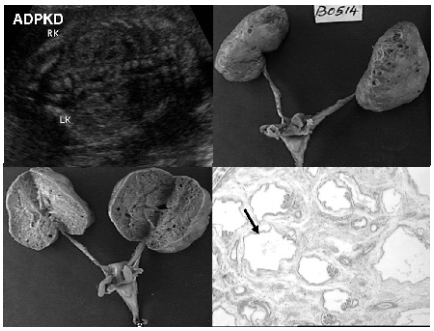
Both the parents had bilateral enlarged & polycystic kidneys. These findings suggested that it was ADPKD and not ARPKD. The parents opted to terminate the pregnancy and no post mortem was done. The speaker after presenting the case discussed in detail about the echogenic presentation of fetal kidneys due to various causes. She said that renal cystic disease might be an **isolated or associated** problem. Urinary tract obstruction has to be ruled out. In the absence of obstruction, it could be a presentation of cystic disease. When it presents as an isolated defect, it may be **classified** as ARPKD, ADPKD or Multicystic Kidney Disease (MCDK) or Renal Cystic Disease with Associated Disorders .The Ultrasound apparently show normal picture of other systems in these cases. Dr. Neelam presented a comparative picture of various cystic renal presentations as shown.



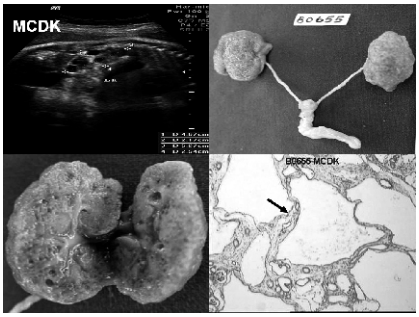
She said that the USG of kidneys in a normal fetus, are reniform shape with fetal lobations. The cortex & medulla are also well differentiated. Histopathological Examination (HPE) of the kidneys shows capsule, cortex made up of glomeruli, tubules & medulla.



In ARPKD, the kidneys are grossly enlarged, but the shape is maintained. In cut section, radially arranged fusiform cysts are seen from medulla to the subcortical area. HPE shows linear tubular arrangement representing the dilated collecting ducts in cortical & sub cortical areas with glomeruli interspread between the tubules.



In ADPKD, the kidneys are mildly or moderately enlarged & the reniform shape may be maintained. In cut section lobes may be unevenly cystic or it may contain diffusely distributed minute cysts. In HPE reveals that cysts are more rounded than in ARPKD and in addition we find several glomeruli cysts.



In MCDK, the kidneys are enlarged, misshapen & irregularly cystic. The hilum & the pelvis are hypoplastic.Cysts in the cortical areas are seen on HPE. There are no well developed glomeruli.

Dr. Neelam summarized the presentation of the fetal echogenic kidneys as below

Features	ARPKD	ADPKD	MCDK
Echogenicity	+	+	+
Cysts	linear	round	round
Hilum & pelvicalyceal	+	+/-	-
Cortico medullary system	-	+/-	-
Liver	+	+/-	-

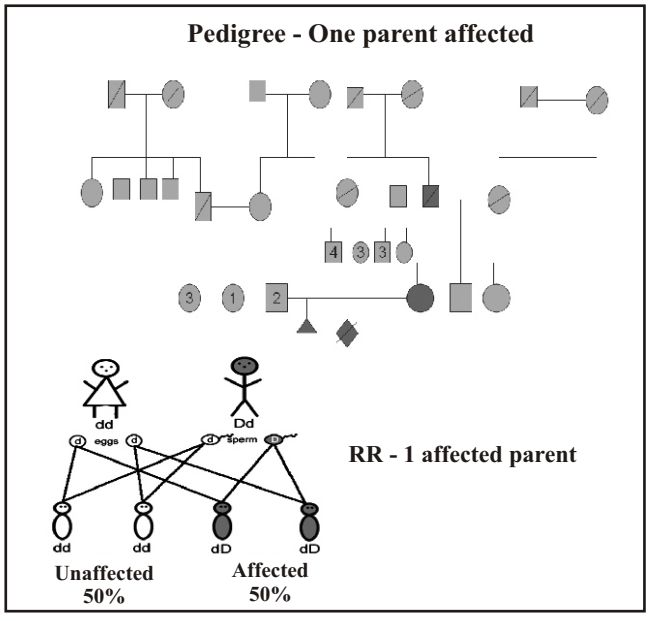
Later she explained about the various conditions associated with echogenic kidneys such as Meckel Gruber syndrome, a case of Trisomy 13 with enlarged, echogenic kidneys with holoprocencephaly, probosis,cryptophalmos,cyclops & large placenta & a case with mildly enlarged echogenic kidneys with large placenta, nuchal edema, AVSD& heart block which turned out to be NIH on autopsy. The **take home messages** were

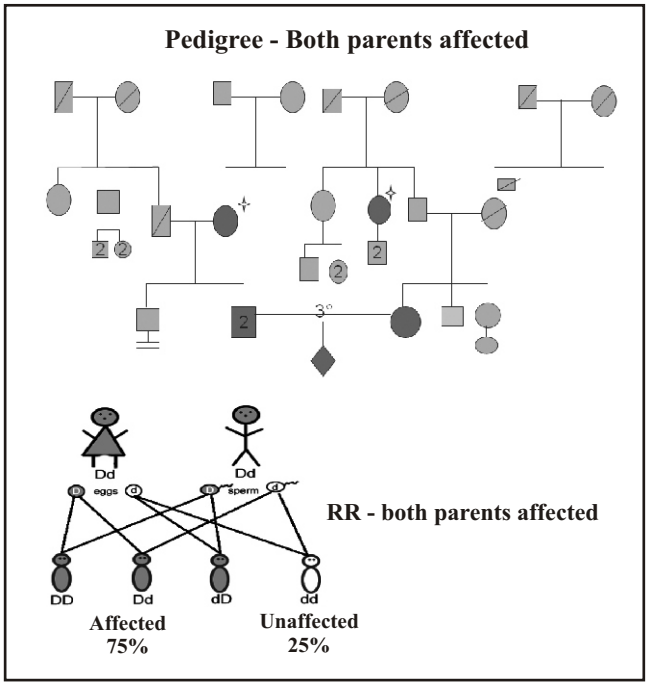
- All echogenic kidneys are not ARPKD
- Final diagnosis of cystic diseases through genetic counseling & perinatal examination is a must for planning subsequent pregnancies.

Miss. Jerene Abraham continued the presentation talking in detail about the genetics behind ADPKD. The epidemiological facts of ADPKD suggest that it is the most prevalent single gene disorder with incidence of 1/500-1/1000. It presents clinically between 30-50 years of age in affected individuals. It is found to be more progressive in males & accounts for 3-13% of patients on renal transplant. Earlier diagnosis of this problem is easier with genetic testing now. 2 interesting cases with ADPKD were presented to show the inheritance pattern of this autosomal dominant disease as in the pedigrees shown.

She said that in patients with family history of ADPKD, at least 2 cysts either uni or bilateral will show up by 30 years of age in the affected It presents as large cysts in infants & children. When there is no family history, a finding of bilateral renal cysts with 2 or more of the following features confirms the diagnosis.

1. Bilateral renal enlargement
2. Three or more hepatic cysts
3. Cerebral artery aneurysm
4. Arachnoid cysts
5. Pineal gland cyst
6. Pancreatic cysts
7. Splenic cyst.





Diagnosis may be confirmed by molecular testing. It is done by Linkage Analysis involving a large number of family members identifying the specific mutation. Prenatal testing is available when diagnosis in the index case is confirmed. Talking about genetics of this disorder, 2 types of gene PKD 1 & PKD II are responsible she said. The mutant gene Polycystin 1 Glycoprotein of PKD I is found in the short arm of chromosome 16p13.3. It is a membrane protein receptor seen in the primary cilium of the epithelium. This mutation is found in 85% of cases & it has earlier onset & quick progression. The life expectancy of the affected is 53 years. In PKD II, the mutant gene Polycystin 2 Glycoprotein is found on chromosome 4q21. It is found in 15% of the affected.It is also a membrane protein seen in the calcium channel of the primary cilium.The average life expectancy here is 69 years. The Polycystin genes I & II are responsible for the normal development, organization & functioning of the kidneys. There are about 90 mutations, in PKD I type & 100 mutations in PKD II. Nonsense mutation being the commonest & gene deletion being the least. The protein products of the *PKD* genes, the polycystins, form a calcium-permeable ion channel complex that regulates the cell cycle and the function of the renal primary cilium. Abnormal cilial function is now thought to be the primary defect in several types of PKD including autosomal recessive polycystic kidney disease and represents a novel and exciting mechanism underlying a range of human diseases.

Anticipation is a genetic phenomenon in families with ADPKD, there is an earlier manifestation with increasing severity in successive generations. It is more severe when inherited from the mother.

- Regarding **prognosis,** 50 to 75% of patients with ADPKD land in renal failure requiring dialysis or transplantation.
- Predictors of **more rapid progression to renal failure** include earlier age at diagnosis, male sex, black race, *PKD1* genotype, larger renal volume, gross hematuria, rapid increase in kidney size, hypertension, hepatic cysts (in women), and UTI in men
- ADPKD does not increase risk of renal cancer, but if patients with ADPKD develop renal cancer, it is more likely to be bilateral.
- Without dialysis or transplantation, patients usually die of uremia or complications of hypertension; about 10% die of intracranial hemorrhage from a ruptured cerebral aneurysm.
- With dialysis or transplantation, patients may die of valvular cardiomyopathy, disseminated infection, or ruptured cerebral aneurysm.

The speaker ended the presentation with a positive note saying that early diagnosis of ADPKD facilitates

- Early detection & treatment of disease complications
- Identification of possible kidney donors
- An alert to other family members

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