B D R News

The official newsletter of The Birth Defects Registry of India,
(A Unit of Fetal Care Research Foundation)
(A Mediscan Group Organisation)

Volume 3 Issue 1: January 2003

Proceedings of the Chennai Birth Defects Registry meeting held on the 31st of January 2003

Chennai Birth Defects Registry is stepping into its third year with unstinting support from the member hospitals. The CME session of the year was held on the 31st of January. Dr. S. Suresh extended a warm welcome to the members and talked about the launching of Erode Birth Defects Registry at a grand function on 11th November 2002. He expressed his hopes saying that many more institutions including the Government Hospitals would follow the example of Erode and join our team to accomplish the goal of formulating statistics on birth defects. He also explianed about the change in the coding system (member identity code) to the members which has expanded from 3 characters to 7 characters. The present coding system has been changed to 6 0 0 N/P 0 0 1- the first three digits denote the pin code of the centre, the alphabet N/P denotes the status of the member i.e nodal or participatory and the last three digits denote the specific identity code of the hospital. Dr. Suchitra Ravishankar proposed vote of thanks in the end with a special mention about Kinesis Pharmaceuticals Private Ltd for sponsoring the present issue of BDRI newsletter. This was followed by an informative session of case presentations from various member hospitals. The excerpts of case presentations are given below:

EXCERPTS OF CASES PRESENTED AT THE MEETING

PRESYMPTOMATIC DIAGNOSIS OF A METABOLIC PROBLEM IN A NEONATE

(Dr.Sujatha Jagadeesh, Consultant Dysmorphologist, Fetal Care Research Foundation)

Dr.Sujatha Jagadeesh started her presentation with a brief note on inborn errors of metabolism. She said that anabolism alone takes place in fetal life whereas both catabolic and anabolic activities commence immediately after the child is born resulting in the manifestation of various metabolic disorders. These may be classified into three types according to the effects they produce 1) Cellular intoxication where small molecules like amino acids , organic acids and large molecules as in lipid storage disorders get accumulated in the cells, 2) Energy deficiency where the cells are deprived of energy for normal functioning due to some defect in mitochondrial and fatty acid oxidation and 3) Peroxisomal disease where errors are present in mixed forms mentioned above. In these cases genetic mutations alter the biochemical pathways leading to slight variations in the products to be produced or production of useless substrates or causing lack of essential substances..

Case Report:

A thirty year old mother with an obstetric history of G3P2A0L0 came for genetic counseling and prenatal diagnosis. Her first child was a full term male baby with 3 kilograms (Kg) birth weight. He cried well at birth, took breastfeeds and acquired normal developmental milestones till 11 months of life. Suddenly he developed respiratory distress and was hospitalized . The baby died after two days. His echocardiogram (Echo) and fontanelle scan showed no abnormality. The second was a female child , born at 34 weeks with a birth weight of 1.7kilograms. She also had normal milestones of development till 14 months of life. She developed sudden respiratory distress and was reported to have had respiratory failure, ketosis, acidosis, hypoglycemia and hyperammonemia. The child was ventilated and peritoneal dialysis was done and she expired one month later.

The mother was advised cordocentesis in her subsequent pregnancy. When she conceived for the third time, she came to our centre for the procedure. Since the exact etiology of the problems in the previous children was not known, and the diagnosis could be ? Metabolic problem, cordocentesis was not done in this pregnancy. Serial monitoring with scans was done and delivery was planned in a hospital with good neonatal support. Postnatal work up for the baby was planned.

Mother had normal full term delivery. A female baby weighing 2.4 Kgs was delivered vaginally. The baby cried well at birth. Neonatal period was uneventful. In view of previous siblings' history, urine screening for the baby for organic acidemia was done at Willink Laboratory, Manchester, United Kingdom(U.K). The results showed increased Tiglycine and 2 methyl 3 hydroxybutric acid. Uracil and Thymine were also increased. The cause probably may be, an error in the isoleucine pathway. On repeat requests from the laboratory , blood and urine samples were sent again to U.K, where the diagnosis was confirmed to be 2 methyl 3 hydroxy butryl CoA hydrogenase deficiency. Very few cases with this problem have been reported in the world. This has? Xlinked inheritance and our case happened to be a female child.

The geneticists at the laboratory have requested for skin biopsy for fibroblast culture and more urine sample for further confirmation. Since this is a rare case, they are doing the tests free of cost and they also have plans to publish it in world literature. Presently, baby is stable and on breast feeds supplemented with low protein food (conjee) and fruit juices. Child has to be maintained on Isoleucine free diet to defer precipitation of symptoms. Plans are on to import amino acid mixtures from abroad to facilitate normal

Brain development. Skin biopsy has been withheld to avoid chances of infections and catabolic status in the baby.

Following is the suggested protocol for perimortem specimen collection in IEM :

Often patients with IEM present in a morbid state and do not survive. It is important for genetic counseling to diagnose the IEM. Organs rapidly deteriorate after death, particularly the liver. Specimens should be collected within 1- 2 following death or diagnostic studies may be impossible. A suggested protocol for perimortem specimen collection (done in conjunction with the pathologist) includes:

1. Obtain 10 - 20 cc of blood. Freeze 1 - 2 cc aliquots of serum and plasma at -20 C. (Store erythrocytes at 4 C and leukocytes at - 20 C)

2. Freeze 20 - 30 cc of urine at -20C.

3. Freeze vitreous humor at -20 C.

4. Skin biopsy for fibroblast culture.

5. Tissue biopsy of liver, muscle and other sites depending on the illness (such as heart, brain, etc.) Take samples for quick freezing with liquid nitrogen, glutaraldehyde fixation for electron microscopy and formalin fixation for light microscopy.

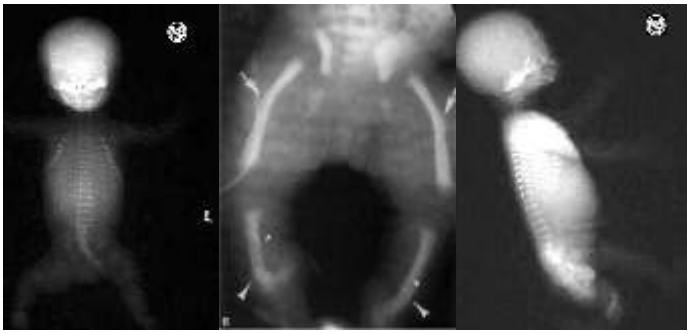
LETHAL SKELETAL DYSPLASIA

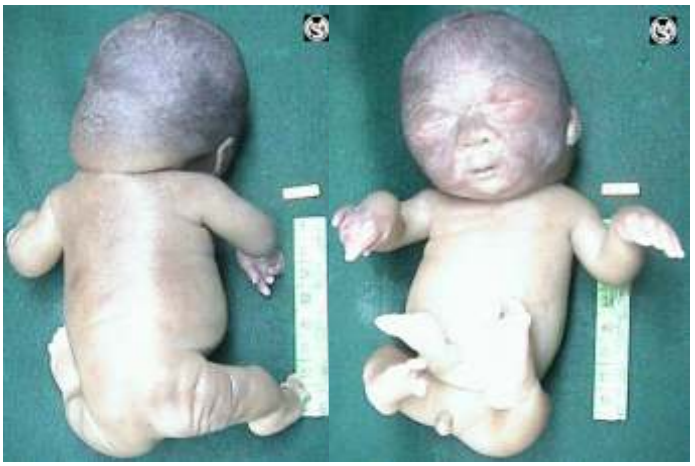
(Dr.Arnab Basak, Consultant - Obstetrician, E.V.Kalyani Medical Centre)

Dr. Arnab Basak presented a case of Lethal Skeletal Dysplasia

Case Report:

Mrs VA 23 years, G2A2P0L0 (non consanguineous) had two pregnancies terminated for lethal skeletal problems in the fetuses. Her first pregnancy was confirmed at 6 weeks by ultra sonogram (USG). Targeted scan at 23 weeks showed head circumference, biparietal diameter and all long bones below 5th percentile. Femur was bowed and spine showed diminished mineralisation. Cystic Hygroma was also seen in the nape of the neck. Detailed genetic counseling regarding the prognosis and recurrence risk in subsequent pregnancies was done to the couple. Fetal blood sampling for karyotype & complete haemogram was done to rule out chromosomal anomalies. Postmortem examination of the fetus revealed dysmorphic features short neck with marked nuchal and rhizomelic type of shortening of both upper and lower Limbs suggesting that the fetus had Camptomelic Dysplasia.





Karyotype and complete haemogram were normal and within limits respectively. Fetal X-Ray showed well ossified skull and vertebra.

She was on periconceptional folic acid supplementation.The second pregnancy was confirmed around 7 weeks. At 11th week there was an increased nuchal thickness. After consultation with the dysmorphologist, a decision was taken to repeat USG after 14 weeks as any skeletal abnormalities would show up by then. Repeat scan at 14 weeks showed Cystic Hygroma with shortening of all long bones, with acute bowing of femur and humerus. Patient was counseled and pregnancy was terminated.

Discussion:

Lethal skeletal dysplasias are of relatively rare occurrence, overall incidence estimated between 1in 5000 to 1 in 11000 live births. Diagnosis is made usually in majority of cases by second trimester by antenatal ultrasound around 16 weeks, and most of them by 24 weeks. The first clue to a possible skeletal dysplasia is shortened femur length. There is also severe shortening of all long bones of the limbs, more than 4 SD below the mean for gestational age. Another characteristic feature is hypoplastic lungs. Thoracic circumference, obtained by USG around the outer perimeter of the ribs at the level of the four chamber view of the heart, is less than 5th percentile for gestational age, with an abnormally high cardiac to chest circumference ratio(60%). Severe bowing of long bones, either generalized or focal, are seen in thanatophoric dwarfism and camptomelic dysplasia. Varying degrees of mineralisation are seen in achondrogenesis. Identification of specific features that are associated with a particular lethal dysplasia would help to define the anomalies. Associated anomalies include cystic hygroma, cleft lip/palate, severe to moderated micrognathia, bell shaped chest, club foot with brachydactyly, ventriculomegaly, cardiac anomaly and ambiguous genitalia.

The differential diagnosis in this case could be achondrogenesis. It was excluded here as spinal ossification was present. Spinal ossification is typically absent in lethal achondrogenesis. Though 2-D, B-mode ultrasound is fairly sensitive in picking up skeletal dysplasias, 3D ultrasound allows better comprehension of precise relationship of complex limb anomalies. Magnetic Resonance Imaging(MRI)now has the potential in assisting diagnosis of skeletal dysplasia.

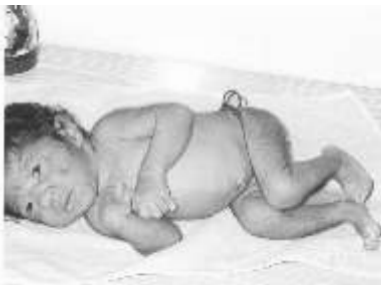
AN INTRESTING CASE OF TRISOMY 18 WITH CHOROID PLEXUS CYST

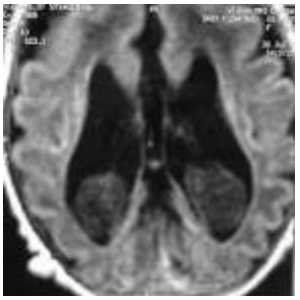
Dr. Chakrapani, Kanchi Kamakoti Childs Trust Hospital

Dr. Chakrapani presented a case of Trisomy 18 with Choroid plexus cyst(CP cyst).

Case Report:

A one month old female child with birth weight of 2.4Kg was brought to the hospital for abnormal facies and failure to thrive. She was the second child born to a non consanguinous couple. Her mother's antenatal period was uneventful. She had a weak cry and feeding difficulty initially. On clinical examination , the child weighed 2.4 Kg with head circumference 32.5 cm, low set ears, coarse skin, hypertrichosis, wedge of bone over root of nose, cliteromegaly, umbilical hernia and hepatosplenomegaly.





Her urine screen for Inborn errors of metabolism, Echo & USG abdomen were normal. Computerised tomography(CT) scan of the brain showed non lissencephalic cortical dysplasia, partial agenesis of corpus callossum, microcephaly and grey matter heterotopia. MRI of the brain revealed agenesis of corpus callossum,bilateral intraventircular SOL and Choroid plexuscyst cyst. Karyotyping revealed Trisomy 18. No active neurosurgical intervention was attempted. The child was lost for follow up later. She was said to have expired at 60 days of age.

Discussion:

Trisomy 18 is the second most common multiple malformation syndrome with an incidence of 0.3/100 newborns. The female to male ratio is 3:1. Among the affected, 95% constitute full trisomies and 5% constitute mosaic trisomies. Associated malformations would include many systems like craniofacial anomalies (cleft lip/palate, microcephaly, micrognathia, dolicicephaly), central nervous system anomalies (C.P cyst,agenesis of corpus callosum, hydrocephalus, cerebellar hypoplasia, meningomyelocele),cardiovascular anomalies (ventricular septal defect, auricular septal defect,double outlet right ventricle,bicuspid outflow tract valves, single umbilical artery), gastrointestinal anomalies (esophageal atresia, tracheo easophagial fistula,omphalocele, diaphragmatic hernia) genito urinary anomalies (renal dysplasia, horse shoe kidney, ureterovesical obstruction) and skeletal anomalies (clenched hands/arthrogryposis, overlapping digits, rockerbottom feet, short extremities, radial dysplasia). Regarding prognosis of this condition, neonates with trisomy 18 have 40% chance of survival up to one month, infants have 5% chance of survival up to 1 year and children have 1% chance of survival up to 10 years.CP cyst in general remain a normal variant in 2% of babies. It is associated with trisomy 18 in 3.47% of individuals. Antenatally, if the cyst is bilateral and is more than 10mm in size, risk of carrying a fetus with trisomy is 5%. Risk of aneuploidy increases with age.

It was discussed that CP cyst is a common finding in antenatal ultra sonogram. Postnatal cranial USG would have been effective in picking up the intra cranial problems of this baby. It was emphasized that isolated CP cyst is not a pointer of chromosomal anomaly but only when it is associated with other markers and structural anomalies , aneuploidy should be thought of.

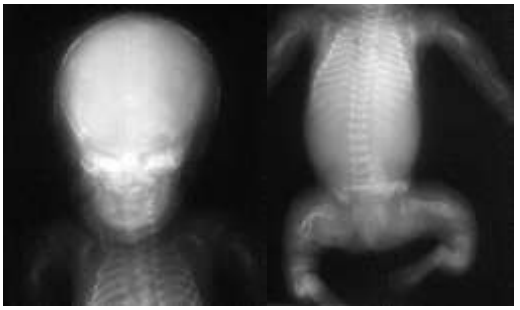
DILEMMAS IN MULTIPLE PREGNANCY

(Dr. Suma, Resident, Vijaya Hospital)

Dr. Suma presented a case of twin pregnancy with a lethal anomaly in one of the fetuses.

Case report:

Mrs X, 28years old, married non consanguinously and had an obstetric history of P1L1A1.She was on ovulation induction treatment and visited the hospital with complaints of pain in the abdomen following 30 days of amenorrhoea.Her LMP was on 02/03/02 and her USG on 01/04/02 showed twin pregnancy which was later confirmed to be diamniotic dichorionic twins at 13 weeks. Her targeted scan at 20 weeks showed a normal fetus-A and fetus B with skeletal anomaly. Fetus B had abdominal circumference and femur length falling less than 5th percentile, calvarium was compressed and the long bones appeared short and bent. The diagnostic possibilities were camptomelic dysplasia or



Osteogenesis imperfecta. As it was not ethical to do selective fetal reduction in late pregnancy, it was planned to continue pregnancy till term and post natally evaluate the baby with skeletal dysplasia. Mother delivered a live male baby with 3.22 Kgs and a dead female baby with 1.98 Kgs.

Discussion:

Skeletal dysplasias are a group of heterogenous disorders with a wide variety of clinical and radiological manifestations. Primary abnormalities lie in the formation of bones and cartilage. It is quite difficult to recognize the type of presentation. It requires a careful study of various disciplines like clinical, radiological, pathological evaluation, biochemical and molecular assays and inheritance pattern in the family. A number of possible differential diagnosis for this condition were enumerated. The baby reported here, had Osteogenesis Imperfecta (OI) type-II type of skeletal dyaplasia and it is characterized by fractures both during antenatal or postnatal period. The incidence rate is 1 in 50,000 and it is due to mutation in collagen1A1/collagen1A2 genes. The inheritance mode may be both autosomal dominant or recessive.

Differential diagnosis is hypophosphatasia. On concluding her talk, she said that USG has improved the detection rate of skeletal dysplasias and more so in case of lethal type OI. Management involves multidisciplinary approach with detailed genetic and psychosocial counseling of the affected. Dr.S. Suresh discussed the ethical issues involved in fetal reduction in late pregnancy and how policies differ in various countries in the world.

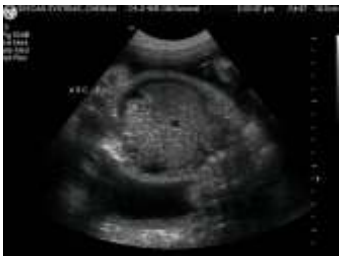
NON IMMUNE HYDROPS FETALIS

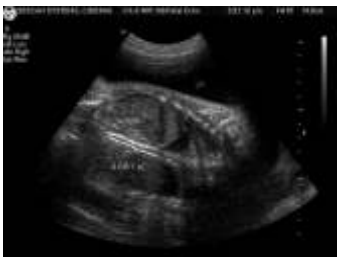
(Dr. R.Sangeetha,(DNB) CSI Rainy Multi Specialty Hospital)

Dr.R.Sangeetha presented a case of non immune hydrops fetalis (NIHF) and its management in detail.

Case Report:

Mrs. S. 24 yrs, with an obstetric history of G 4 P 3 L 1 A0 , II degree consanguinity was booked for her fourth pregnancy antenatal check ups. Her first pregnancy was a stillborn at 8 months due to eclampsia, second child was a healthy male child at 3 years and her third pregnancy was terminated due to neural tube defect in the fetus. Her pedigree details did not have any significant features in the family. USG impression at 22 - 23 weeks was normal at 29 weeks, the scan revealed fetal ascites with bilateral pleural and pericardial effusion, aortic wall calcification and placentomegaly. The diagnosis assigned was NIHF. Elective LSCS with





Sterilization was done after 10 days. A live male baby was delivered. The APGAR score was 3/10. The child was put on intermittent positive pressure ventilation and was transferred to NICU. On examination he had dysmorphic facies and peripheral cyanosis. Heart rate was less than 80/minute. Per abdomen, mild distension, free fluid accumulation and bilateral hydrocele were seen. Baby expired one hour after birth. X-Ray showed minimal ascites.

Discussion:

NIHF may be an associated problem in cardio vascular anomalies like congenital heart block, tachyarrythmia, septal defects, hypo plastic left heart syndrome, pulmonary valve insufficiency, tetralogy of fallot and Ebstein anomaly or in chromosomal anomalies like trisomies, triploidy or in lysosomal storage disorder or in some types of skeletal dysplasias or twin-twin transfusion or in respiratory anomalies like diaphragmatic anemias , cystic adenomatoid malformation, or in urinary anomalies such as urethral stenosis, posterior neck obstruction, ureterocele and neurogenic bladder or in garointestinal anomalies like jejunal atresia midgut volvulus and malrotation of intestines or in parvovirus and other infections or in amniotic band syndrome and cystic hygroma.

Dr.Sangeetha explained the standard protocol for NIHF with variying causes. By ultrasound, detailed anatomy and liquor volume could be evaluated. Echo and Doppler could provide information regarding structural and functional abnormalities of heart. Fetal blood sampling should be done to assess the karyotype, fetal blood count , viral infection, blood gases and serum protein. If ascites is due to primary pleural effusion, Thoraco amniotic shunt may be offered. If it is due to Parvovirus infection and subsequent anemia, Intra uterine blood transfusion could be done. It was reported that in Japan, Intra peritoneal administration of albumin was done for idiopathic NIHF.Therapeutic amniocentesis could be sought for in pregnancy with Twin to twin transfusion . If ascites is arising out of associated cardiac anomaly, like arrythmias direct and indirect drug therapy are available. In the former, transplacental drug therapy with drugs like digoxin, verapamil and amiodarone is followed and in the latter fetal drug therapy is done by intra peritoneal, intramuscular or intra vascular methods. If pregnancy is terminated, it is essential to do a detailed postmortem examination of the fetus. It was discussed that idiopathic arterial calcification should be thought of as a cause for NIH in the case reported above.

EPIDERMOLYSIS BULLOSA

(Dr.Vijaya Ganesh, Consultant Obstetrician, Fertility Research Centre - G.G. Hospital)

Dr.Vijaya Ganesh in her presentation discussed a case of Epidermoysis Bullosa.

Case Report.

A 25-year-old lady, visited the hospital for secondary infertility. Hers was a third degree consanguinous marriage. Her pedigree details did not have significant features. She had a bad obstetric history of G3 P 3 L 0 . Her first child was a full term male child with delayed milestones, mental retardation and seizures. He died at 1 ½ years of age. Her second child was a live female child died after 10 days postnatally The cause assigned was? Epidermoysis Bullosa. She conceived with IUI for the third time. She had gestational diabetes mellitus and hypothyroidism and was on treatment for the same. Her antenatal ultrasound showed PUV obstruction and bilateral hydronephrosis. She delivered normally, a male child at full term, who also seemed to have? Epidermoysis Bullosa and died after some days.

Epidermoysis Bullosa (EB) is a group of inherited bullous disorders, characterized by blisters formation in response to mechanical trauma. Inheritance mode is both autosomal dominant and recessive. It is classified into non scarring EB (EB simplex, EBlethalis) or scarring EB (Recessive dystrophica EB,Dominant dystrophica EB) according to the types of lesions produced. The complications arising out of EB may be secondary infection local or systematic, contracture deformities,swallowing difficulties perioral esophagus scarring, gastric outlet obstruction, failure to thrive / anemia, squamous cell carcinoma and early death. Diagnosis is made by clinical examination by evaluating the distribution of blisters, eliciting relevant family history, and by electron / immunofluorescent microscopic studies of the skin(EM). Electron microscopy of skin biopsy of the affected will show the level of blistering and basement membrane zone morphology. Genetic work up by DNA analysis will confirm the type of EB. Prenatal diagnosis is done by electron microscopic study of fetal skin biopsy sample. Chorionic villi sample or amniotic cells are required for DNA mutation analysis /carrier detection among the family members.

The treatment lies in draining the blisters by puncturing and giving cool water compresses and applying topical antibiotics and dressing. Nutritive requirements need to be met with the help of nutritionists. Nasogastric feeds, semi liquid /soft diets are generally given for easy consumption. Vitamin, iron and protein supplementations are necessary. Surgical intervention may be necessary for problems like oesophageal strictures and mitten deformities. Steroids are quite helpful. Genetic counseling is very essential to the members concerned in a family to know the implications of this disorder and the risk of inheritance in subsequent generations.During discussion a question was raised as to why this couple was not offered prenatal diagnosis work up despite the fact that EB was suspected in the second child. Dr. Sujatha Jagadeesh explained that vesiculo bullous lesions have multivaried etiology and unless the diagnosis is confirmed in the index child, offering prenatal diagnosis may not be the right option. Fetal skin biopsy can be done at 22 - 23 weeks of pregnancy. For prenatal diagnostic work up, it is mandatory to have a confirmed diagnosis of the index case.

NEIGHBOURHOOD NEWS

As predicted the BDR membership fever has now caught on to some more districts in Tamilnadu. Three districts Salem, Dharmapuri and Nammakkal have joined our team. Salem BDR was inaugurated at a grand function on the 16th of February 2003. Dr.Chellammal, practising obstetrician & gynaecologist of Gokulam Hospital, Salem is championing the cause of BDR as the Nodal member of Salem registry.

The dignitaries assembled were Dr.J.Radhakrishnan I.A.S (District Collector) Dr.M.Ganapathy (Dean Govt.Medical College hospital-Salem) Dr. E.Esther (Joint director of Health Services, Salem), Dr.Arunachalam (President Salem I.A.P) Dr.Selvaraj (President I.M.A-Salem) Dr.Chitra Sampath (President OGSSI- Salem) Dr.P.Chellammal (Consultant Gokulam Hospital, Salem) and the doctors from various hospitals of the three districts who were to be inducted in the registry.

Inauguration - Salem BDR 16 / 02 / 2003

Dr. P. Chellammal welcomed the gathering. Dr.S.Suresh (Director, BDRI) started the session. His reminiscences about the inception of BDR by the Fetal Care Research Foundation way back in 1995 was interestingly put across to the audience. He explained that members could reap a lot of benefits from BDR statistics. He emphasized the fact that this baseline statistics will help us institute supportive measures to those affected and alleviate their sufferings to an extent possible. He also called for the support from the Government health officials to provide access to the birth data from Government maternity hospitals / Primary health centers as total births in a region is the denominator value while analyzing the statistics. The district collector Dr.Radhakrishnan spoke convincingly about the need to formulate statistics on birth defects. He said that birth of a child should bring joy and not misery to the family members. He requested the health officials assembled there to carry out effective peri conceptional Folic acid campaign to prevent Neural tube defects. He also promised that the Salem Registry would get all help from the Government. In his presidential address, Dr. Ganapathy (Dean Govt Medical College-Salem) extended his wholehearted support for the cause. He lauded the collaborative efforts of the registry. This was followed by the distribution of BDRI starter kits to the members. About 30 were inducted. Dr. R.Ramalingam proposed vote of thanks.

Dr. G. Thangavel (Epidemiologist-BDRI) during post tea session , explained the methodology of furnishing data, and he also presented the annual (2001-2002) statistics of Chennai BDR. Dr. Sujatha Jagadeesh (Dysmorphologist-BDRI) in her lucid presentation explained how medical advancement has raised the expectations of the public and how people demand assurance of normalcy in the unborn child. She elaborated on a holistic approach to structural anomalies in the fetus depending on the time and mode of presentation. The function came to a close with a lively panel discussion lead by Dr. S. Suresh and the audience participated with great enthusiasm.

Congratulations Members - Erode Birth Defects Registry!!!
The members of EBDR are doing an excellent work of data collection for the registry. Well done and keep it up!!

An appeal:

Help a national cause. Join the Birth defects registry. If you are already a member of the registry, please motivate a friend to become a member of the registry. If you are not a member kindly contact us. Let us work together to build a healthier nation.

Members are most welcome to contribute relevant articles for the news letter.

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