CONGENITAL CNS MALFORMATIONS
IN 3 DISTRICTS OF GUJARAT

(DIAGRAM NO.1, FOR TABLE-7)

1. ANAND, 2. GODHARA, 3. AHMEDABAD, 4. OVERALL
ANENCEPHALY AND SPINA BIFIDA RATES IN 3 DISTRICTS OF GUJARAT

(DIAGRAM NO. 2, FOR TABLE-8)

<table>
<thead>
<tr>
<th>SERIES</th>
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<tbody>
<tr>
<td>1. ANAND</td>
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<tr>
<td>2. GODHARA</td>
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</tr>
<tr>
<td>3. AHMEDABAD</td>
<td>2.7</td>
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<td>4. OVERALL</td>
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CONGENITAL CENTRAL NERVOUS SYSTEM MALFORMATIONS - A PROSPECTIVE STUDY
HYDROCEPHALUS (SERIES 1), MENINGOMYELOCELE (SERIES 2) and ENCEPHALOCELE (SERIES 3) IN 3 DISTRICTS OF GUJARAT

(DIAGRAM NO. 3, FOR TABLE NO-9 AND 10)

1. ANAND, 2. GODHARA, 3. AHMEDABAD, 4. OVERALL
AGE DISTRIBUTION OF MOTHERS OF FETUSES STUDIED
(DIAGRAM NO. 5, FOR TABLE NO. 25)

1. 15-20 YEARS
2. 21-25 YEARS
3. 26-30 YEARS
4. 31-35 YEARS

RESULTS
RESIDENTIAL BACKGROUND OF MOTHERS OF AFFECTED FETUSES
(DIAGRAM NO. 6, FOR TABLE NO. 26)
EDUCATIONAL BACKGROUND OF MOTHERS OF AFFECTED FETUSES
(DIAGRAM NO. 7, FOR TABLE NO. 26)

1-LITERATE
11%

2-ILLITERATE
89%
ECONOMIC STATUS OF MOTHERS OF AFFECTED FETUSES

(DIAGRAM NO. 8, FOR TABLE NO. 27)

PERCENTAGE

0% 10% 20% 30% 40% 50% 60% 70% 80% 90%

1. CLASS I, 2. CLASS II, 3. CLASS III, 4. CLASS IV, 5. CLASS V

89.13%

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ANTENATAL HISTORY

(DIAGRAM NO. 9, FOR TABLE NO. 28)

PERCENTAGE

1. PRIMIGRAVIDA
2. 2nd GRAVIDA
3. 3rd GRAVIDA
4. 4th GRAVIDA

RESULTS
ANTENATAL HISTORY CONTINUED

(DIAGRAM NO. 10, FOR TABLE NO. 29)

73.90%

13.04%

13.04%

1. VAGINAL DELIVERY, 2. LSCS, 3. ABORTION

PERCENTAGE
PERIOD OF GESTATION OF FETUSES
(DIAGRAM NO. 11 FOR TABLE NO. 30)

1. LESS THAN OR EQUAL TO 20 WEEKS, 2. 21-28 WEEKS, 3. 29-36 WEEKS, 4. 37-40 WEEKS
SEX OF FETUSES
(DIAGRAM NO. 12, FOR TABLE NO. 31)

1. FEMALE, 2. MALE, 3. AMBIGUOUS
APPARENT CNS MALFORMATIONS

(DIAGRAM NO. 13, FOR TABLE NO. 32)

1. ANENCEPHALY, 2. ANENCEPHALY WITH SPINABIFIDA, 3. ANENCEPHALY WITH MENINGOMYELOCELE, 4. ENCEPHALOCELE, 5. HYDROCEPHALUS, 6. MENINGOMYELOCELE
OTHER APPARENT DEFECTS IN FETUSES STUDIED

(DIAGRAM NO. 14, FOR TABLE NO. 33)

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<td>1.00%</td>
</tr>
<tr>
<td>10</td>
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</table>

1. OMPHALOCELE 2. CLEFT LIP
3. EXOPHTHALMOS 4. DEFORMED EAR
5. SHORT/ABSENT NECK 6. PROTRUDING TONGUE
RELATIONSHIP BETWEEN ANENCEPHALY AND PARITY OF MOTHERS

(Diagram No. 15 for Table No. 34)
A total of 18075 consecutive deliveries were screened for congenital central nervous system (CNS) malformations from six different hospitals in three regions of Gujarat namely, Anand, Godhara (Panchmahal district) and Ahmedabad from September 2001 to August 2003 prospectively. A total of 119 fetuses were found to be affected by central nervous system malformations. The observed rate of central nervous system malformations was different in all six hospitals of the three regions (TABLE-7). Congenital CNS malformation rate in S.K. hospital was observed as 4.4/1000 births, in Anand municipal hospital it was 3.2/1000, while a rate of 5.1/1000 births was observed in J S Chauhan hospital, Baria. In PKT nursing home, congenital CNS malformation rate was observed as 12.6/1000 births. In Shamalji Sarvjanik hospital Godhara the rate was 3.4/1000 births. The rate of congenital CNS malformations in B. J. Medical College, Ahmedabad was observed as 7.3/1000 births (DIAGRAM NO.1). The average rate for all six hospitals was observed as 6.5/1000 births (DIAGRAM NO.1). The commonest CNS malformation observed was anencephaly (DIAGRAM NO.2). The average rate of occurrence of anencephaly in the six hospitals was calculated as 2.6/1000 births. Individual anencephaly rates observed were 2.2/1000, 1/1000, 2.3/1000, 8.4/1000, 3.4/1000 and 2.7/1000 respectively in the above mentioned six hospitals (TABLE-8). Anencephaly was followed by spina bifida with an average rate of occurrence as 1.7/1000 births (DIAGRAM NO.2). Rate of occurrence of spina bifida was seen as 1/1000 births in Anand municipal hospital, 0.5/1000 in J S Chauhan hospital, Baria and 2.2/1000 in B. J. Medical College, Ahmedabad (TABLE-8). Other defects encountered were hydrocephalus with an average rate of 1.1/1000 births for all six hospitals, followed by meningomyelocele as 0.9/1000 births and encephalocele as 0.05/1000 births (DIAGRAM NO.3) (TABLE-9, 10).
In J S Chauhan hospital, Baria rate of occurrence of hydrocephalus was calculated as 2.3/1000 births while it was 4.2/1000 in PKT nursing home Godhara and 1.2/1000 births in B. J. Medical College, Ahmedabad. The rate of occurrence of meningomyelocele in S K hospital, Karamsad was 1.4/1000, in Anand municipal hospital it was 1/1000 and in B. J. Medical College, Ahmedabad it was 1.15/1000 births. One single case of encephalocele was observed in S K hospital, Karamsad. Therefore, the observed rate was 0.05/1000 births.

Out of the 119 malformed fetuses, 46 dead fetuses were collected for detailed study. These consisted of 38 female (82.61%) and 7 male (15.22%) fetuses. One fetus (2.17%) had ambiguous genitalia (DIAGRAM NO.12) (TABLE-17, 31). 31 fetuses (67.39%) had primarily anencephaly, 9 had (19.56%) anencephaly with spina bifida and 3 had (6.52%) anencephaly with meningomyelocele. There was one fetus each (2.17%) with hydrocephalus, encephalocele and meningomyelocele (DIAGRAM NO.13) (TABLE-32). All fetuses were born as singleton except one fetus with meningomyelocele who was born as a conjoint twin. The gestational age of these fetuses were varied from 18 weeks to 40 weeks (DIAGRAM NO.11) (TABLE-17, 30). 10 fetuses (21.74%) were between 37 to 40 weeks gestation while 19 fetuses (41.30%) were 29 to 36 weeks. There were 12 fetuses (26.09%) of gestation age 21-28 weeks and only 5 fetuses (10.87) were below the age of 20 weeks. CR length of the fetuses varied from 9cm to 28cm and did not correspond to the gestational age (TABLE-17).

On external examination, short or absent neck was observed in 7 fetuses (15.21%), omphalocele was observed in 4 (8.69%) and exophthalmos in 3 (6.52%) fetuses. Cleft lip, deformed ears and a protruding tongue was seen in one fetus (2.17%) each. One extra soft tissue growth was observed in the right hand of one
fetus and a frog head appearance was seen in one fetus (**DIAGRAM NO.14**) (**TABLE-18, 19, 20, 33**).

Multiple external malformations namely, frog head appearance, bilateral exophthalamos, cleft lip, deformed ears, webbed neck were present in one fetus of 28 weeks gestation (fetus no.2). In another fetus of 38 weeks (fetus no. 6) a flexion deformity of the vertebral column with omphalocele was observed.

On internal examination (**TABLE-21, 22**) (**Fig.71 to 80**) of 43 fetuses with anencephaly, the brain was primarily seen as a dark brown undifferentiated mass with complete absence of the cerebellum in all fetuses. In 12 fetuses (26%) cerebral hemispheres, mid brain, pons and medulla could not be identified separately. Spinal cord was normal in appearance and structure and was seen to be directly merging into this undifferentiated dark brown mass.

In 6 fetuses (13%) appearance of brain was same as above except, that the spinal cord at its cranial end continued into small part of open neural tube corresponding to the position of medulla and pons. Spinal cord otherwise was normal in appearance. In 25 (54.3%) fetuses brain appeared as an undifferentiated dark brown mass with complete absence of cerebellum as mentioned above while a well formed neural tube was seen at the upper end of a normal looking spinal cord corresponding to the medulla, pons and mid brain.

Spinal cord was seen deformed, protruding out through a defect in the cervical region in 3 fetuses (6.5%) having meningomyelocele in cervical region.

In the one fetus (2.17%) with encephalocele the brain was normal in appearance. The brain substance was seen in the encephalocele sac. Spinal cord also appeared normal. Enlarged ventricles with thinning of brain tissue was seen in the fetus with hydrocephalus (2.17%). In the fetus with meningocele
brain appeared normal. The lower part of spinal cord was however present in the meningocele sac and cauda equina was absent.

The examination of skull of the 43 fetuses with anencephaly revealed absence of skull vault in all with absence of frontal bone from the base of skull also. Anterior and middle cranial fossae were shallow, posterior cranial fossa was deep and the internal acoustic meatus were seen to be present on the top of the surface. Vertebral column was well formed throughout the length in 33 fetuses (71.7%). In three fetuses (6.5%) vertebral column was defective in cervical region. Vertebral arches were not fused posteriorly. In 5 (10.8%) fetuses vertebral column was defective in cervical and thoracic regions. Vertebral arches were also open posteriorly in cervical and thoracic regions. In 4 fetuses (8.6%) fetuses vertebral column was defective from the cervical to lumbar regions.

In one fetus with encephalocele bones of the skull vault were well formed but defect was found in the occipital bone. Vertebral column was well formed. In the fetus with meningomyelocele only, the skull was well formed and defect was observed in the lumbar and sacral regions of the vertebral column. Sacrum was absent. In the fetus with hydrocephalus (2.17%) bones of skull vault were well formed with widening of sutures. Vertebral column was also well formed.

Radiograms of these fetuses also confirmed the same bony deformities (Fig.33 to 41).

Eyeball and suprarenal glands were normal in appearance on gross examination in all fetuses (Fig.82, 83, 84, 86).

5th, 7th, 9th, 10th, 11th, 12th cranial nerves were present in 25 fetuses.

Internal malformations in the abdomino-thoracic region were seen in 12 (26%) fetuses (TABLE-23) (Fig.50 to 70). Total numbers of gut anomalies were 22. Diaphragmatic hernia was seen in 3 fetuses. In one fetus it was bilateral and in rest two
it was unilateral on left and right sides. Megacolon was seen in 4 fetuses and omphalocele was also observed in another 4 fetuses. Liver was enlarged and incorporated in all four fetuses with omphaloceles. Enlarged liver occupying entire abdominal cavity was seen in 3 fetuses. Other gut anomalies seen were spleen in right hypochondrium, small intestine on right side of abdominal cavity, appendix and caecum in left hypochondrium, superior mesenteric artery lying behind third part of duodenum, intestine adherent to under surface of liver, appendix subhepatic in position. Intestines were seen in thoracic cavity of fetuses with diaphragmatic hernia on the left side.

Kidney was seen in thoracic cavity on the left side in one fetus with other abdominal contents in thoracic cavity. Dextrocardia was present in one fetus (2%).

On Histological examination (Fig. 87 to 127), there was appropriate development of suprarenal glands in terms of presence of all components of the glandular tissue in all fetuses. There was marked hyalinization present in the cortex of suprarenal gland of one fetus.

Development of eye ball was normal with respect to the presence of all its components. Histology of retina showed presence of all layers. Histology of iris and ciliary body was normal.

Microscopic appearance of brain in the 43 fetuses with anencephaly was reminiscent of an angioma, consisting of venous vessels of varying caliber interspersed with connective tissue and islets of nervous tissue which mainly comprised of scattered nerve cells, astroglial cells and cavities lined by ependyma. Undifferentiated neural tube was seen in 31 (67.3%) fetuses showing cluster of nerve cells, cavities, large blood vessels and white matter. Surface of the brain was lined by columnar epithelium.

A well-formed trigeminal ganglion was seen in 10 (21.7%) fetuses. Histology of enlarged liver from four fetuses showed dilated
blood vessels and marked aggregation of lymphocytes. Histology of gall bladder appeared normal in these four fetuses.

Detailed history from each mother of the affected fetus (as mentioned in material method) revealed the following facts. Mothers of all 46 dead fetuses were not registered at any time for antenatal check up. The maternal age ranged from 18 years to 35 years. 63% mothers were 20 or less than 20 years of age. 17.39% were of age between 21 to 25 years, 10.86% were between 26 to 30 years and only 8.69% were above 30 years (DIAGRAM NO.5) (TABLE-25). Cut of these 46, 28 (60.8%) mothers were primi gravida, 8 (17.36%) 2nd gravida, 5 (10.86%) 3rd gravida and 5 (10.86%) were 4th gravida (DIAGRAM NO.9) (DIAGRAM NO.15) (TABLE-28, 34).

40 mothers (87%) belonged to rural background and 6 (13%) were residents of urban area (DIAGRAM NO.6) (TABLE-26). 45 mothers (97.8%) belonged to low socioeconomic strata (class III, IV and V), only 1 belonged to (class II), that is, middle socioeconomic strata (DIAGRAM NO.8) (TABLE-27).

41 mothers (89.13%) were illiterate, 4 had studied till 8th standard and only one was a graduate (10.86%) (DIAGRAM NO.7) (TABLE-26).

All were housewives except one who was labourer (TABLE-12, 26).

17 mothers (37%) conceived in summer, 21 (47%) in winter and 4 each (8%) in autumn and spring (DIAGRAM NO.4) (TABLE-24). None of the mothers gave a history of intake of any vitamins or folic acid during the periconceptional period and during pregnancy.

None of them provided any positive history of consanguinity, alcohol and tobacco intake, infection during pregnancy, chemical exposure, drug intake, radiation exposure, trauma, hormone intake or anesthesia during pregnancy. None gave any history
suggestive of any cause of anoxia to fetus during pregnancy except that one had fever at 8 weeks of pregnancy, other had history of fall from tree at 28 weeks of pregnancy. One mother mentioned history of some unknown chemical exposure during pregnancy (TABLE-13, 14, 15, 16).

Only 5 mothers (10.8%) were non vegetarian, rest 41 (89%) were vegetarian with a staple diet consisting of peanuts, ground nuts, cereals, mainly rice and pulses all through the pregnancy (TABLE-16).

37 mothers (80.4%) consumed ground water and 9 (19.5%) gave history of intake of tap water (TABLE-16). Only one mother out of the 18 multi gravida interviewed gave a positive past history of delivery of an anencephaly baby at 36 weeks (TABLE-12).

Legitimacy of the child could not be accurately obtained as only 29 women came forward with the answer to this question, all being legitimate (TABLE-12).

At admission maternal hemoglobin varied from 7.5-10 gm%. 41 patients (89%) had normal delivery either spontaneous or induced while 5 (10.8%) underwent cesarean section for various obstetric reasons (DIAGRAM NO.10) (TABLE-13, 29).

Water samples were collected from the respective three regions, Anand, Godhara, Ahmedabad and tested with inductively coupled plasma and ion selective electrode methods. The trace elements detected were, Zinc 1-31 μg/l, Fluorine 0.44-0.59mg/l, Calcium 31.40-59.90mg/l, Sodium 22.20-162mg/l, Magnesium 8.29-75.20mg/l, Iron 0-0.61mg/l. No traces of Cadmium and Lead were detected in any of the water samples (TABLE-35).