Congenital Malformations to Birth Defects – The Indian Scenario

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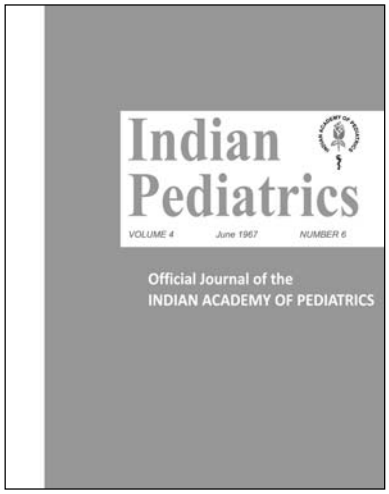
The June 1967 issue of *Indian Pediatrics* published three research papers (clinico-radiological profile in measles, congenital malformations in newborns and patterns of pulmonary tuberculosis) along with the other usual features. We selected the study on congenital malformations for this write-up as it seemed to herald a shift of academic interest to issues other than growth, nutrition and infectious diseases in children. As congenital anomalies are seen by pediatricians in all settings, we shall also trace the evolution of this field over the last five decades and discuss its clinical relevance.



THE PAST

The study: This prospective longitudinal study by Saifullah, *et al*. [1] was a collaborative effort of the departments of Pediatric Surgery, Pediatrics and Gynecology and Obstetrics of PGIMER, Chandigarh, India [1]. The primary objective was to determine the magnitude of congenital malformations in a pre-decided sample size of a thousand live- and still-births. A stringent study protocol was followed in which antenatal, obstetric, maternal and family history was obtained for consecutive births. Details of exposure to drugs, irradiation, trauma or infections; nutrition, amniotic fluid quantity, recurrent fetal loss and family history of malformations were ascertained. This was followed by an in-depth clinical examination at birth and after 6-8 weeks. Peripheral blood smear was examined for neutrophilic nuclear lobe count and presence of drumsticks (considered to be an indirect indicator of chromosomal aberrations). Over a period of 8 months, 36 infants were found to have 43 malformations (3.6%) that included 5 with multiple defects, and 9 in 30 stillbirths. These were organized by system and distribution in descending order as follows: central nervous system 1.2% (meningomyelocele 5, anencephaly 4, hydrocephalus 3); musculoskeletal system 0.8% (polydactyly 3, talipes 2, syndactyly 1, achondroplasia 1 and thumb ring constriction 1), cardiovascular system 0.6% (single umbilical artery 2, tricuspid atresia 1, transposition of great vessels 1, atrial septal defect 1, ventricular septal defect 1); skin 0.6% (pinna malformation 3, single nostril 1, extensive nevus 1, hemangioma 1); digestive system 0.5% (esophageal atresia with tracheoesophageal fistula 2, imperforate anus 2, hare lip and cleft palate 1); urogenital system 0.5% (accessory nipples 3, hypospadias 1, chordee 1). The stillbirths mainly displayed CNS anomalies (anencephaly, meningocoele, hydrocephalus and achondroplasia). The mean nuclear lobe count was significantly reduced in babies with malformations in contrast to those without (2.28 *versus* 3.12, $P<0.05$); no drumsticks were found. Malformations were four times more common in stillbirths (71 out of 561). A higher number of anomalies were observed in low birth weight babies, especially those small for gestational age. There was no significant difference in congenital malformations according to maternal age, birth order, gender, or maternal undernutrition or anemia. The authors concluded that the importance of recognizing anomalies was timely surgical correction of fatal defects resulting in better survival, identification of potentially preventable environmental teratogens, and as an indicator of other associated anomalies.

Historical background and past knowledge: Congenital malformations have afflicted human beings since the dawn of time. This is attested by prehistoric anthropological evidence and written records dating nearly 5000 years ago. In the early 19th century, anatomists, embryologists and pathologists meticulously described and categorized congenital malformations to determine patterns of inheritance. This was followed by epidemiological studies that examined magnitude and

probable associations. Indian studies have reported local incidence rates ranging from 0.3% to 3.6% [2-5], the most recent being 2.3% [6]. A much higher incidence (22%) was reported from the Lahore birth cohort where consanguinity in the study population was 46% [7]. The central nervous, gastrointestinal and cardiovascular systems are the most commonly affected. Various maternal high risk factors identified include maternal fever or certain drugs in the first trimester, diabetes mellitus, preeclampsia and antepartum hemorrhage. In the last few decades, the focus of research has shifted to developing increasingly sophisticated modalities for establishing etiology and prenatal diagnosis that has set the stage for *in-utero* fetal surgery.

THE PRESENT

Over the years, evolving knowledge has lead to a paradigm shift from ambiguous descriptions to structured nomenclature. A congenital malformation is defined as a developmental defect of a body part originating during embryogenesis. Major anomalies are those that are severe enough to interfere with function or cause death without medical or surgical intervention whereas minor anomalies are those that result in only cosmetic impairment. The clinical significance of the latter are that they may be harbingers of concealed anomalies. Malformations need to be differentiated from deformations (abnormalities of shape or form due to abnormal mechanical forces *in-utero* like oligohydramnios); disruptions (defects that occur when an extrinsic factor interferes with normal morphogenesis like an amniotic band); and dysplasias (intrinsic abnormal tissue formation during morphogenesis). In the United States, the National Birth Defects Prevention Network define a birth defect as any condition that includes malformations, chromosomal abormalities, functional defects, metabolic defects, neurodevelopmental disorders, and complications related to prematurity [8]. The commonest birth defects are congenital heart defects, neural tube defects, blood disorders (*e.g*., thalassemia, sickle cell disease), Down syndrome and Glucose-6-phosphate dehydrogenase deficiency.

Annually 3.3 million deaths are associated with birth defects, mainly major anomalies. More than 90% of infants with a serious birth defect are born in low- and middle-income countries, which lack adequate antenatal diagnostic and postnatal corrective services [9]. In contrast, in high-income countries, many receive palliative treatment and live with chronic disability [10].

There are many challenges that exist in the Indian scenario. Till recently, India lacked dedicated national surveillance systems for birth defects. Though the Rashtriya Bal Swasthya Karyakram is still in the fledgling stage, it is envisioned that national data will be generated by early identification of certain birth defects. A major challenge that will emerge with increased detection and referral is being able to provide timely corrective surgery when warranted. Currently the ratio of skilled personnel to population is extremely low. Out of the 1% live newborns with congenital heart disease that result in 10% infant mortality, less than 2% receive life-saving surgery [11]. Hence developing a parallel program aimed at capacity building is essential. Till tertiary level fetal screening becomes easily available, affordable and accessible to all pregnant mothers at risk, the only option is relying on more basic community based preventive health measures like preconception care and improving the health of women of reproductive age group. Fetal surgery is still a distant dream!

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