

# Preliminary study on congenital anomaly in DR. Sardjito General Hospital Yogyakarta

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## ABSTRACT

**M. Mansyur Romi - A preliminary study on congenital anomalies at Dr. Sardjito General Hospital, Yogyakarta.**

**Background:** Congenital anomalies and genetic diseases tend to increase and dominate hospital admittance, especially in the pediatric wards in developed countries. The spectrum of diseases in regions with low infant mortality rate is likely to go with such tendency. It is necessary to study congenital anomalies and genetic diseases at Dr. Sardjito General Hospital, locating in a region with much lower infant mortality rate than that of the national average.

**Objective:** To know the occurrence of congenital anomalies and its pattern among DR. Sardjito General Hospital in-patients.

**Method:** An descriptive study was done on secondary data taken from data-base of the Hospital in 1998 – 2002 period. All of admittances in that period diagnosed as primary or secondary diagnosis, with Q00 – Q99 congenital malformations, deformations, and chromosomal abnormalities according to *International Classification of Diseases* (ICD), were included. The pattern of anomaly at the Hospital was compared to that of different population and period.

**Results:** There were 1968 (1070 males and 898 females) admittances with congenital anomalies at Dr. Sardjito General Hospital in 1998 – 2002. The proportion compared to the whole admittance was 2.06%. The most prevalent was Q35 – Q37 cleft lip and cleft palate (21.14%), followed by Q38 – Q45 other congenital malformations of the digestive system (18.45%), Q20 – Q28 malformations of the circulatory system (15.65%), Q50 – Q56 malformations of genital organs (12.55%), Q00 – Q07 malformations of the nervous system (11.89%), Q65-Q79: malformations and deformations of musculoskeletal system (6.40%), Q80-Q89: other congenital malformations (4.06%), Q10-Q18: malformations of eye, ear, face and neck (3.91%), Q60-Q64: malformations of the urinary system (2.54%), Q90-Q99: Chromosomal anomalies (2.44%), and Q30-Q34: malformations of the respiratory system (0.97%).

**Conclusion:** Congenital anomalies at Dr. Sardjito General Hospital were dominated by cleft lip and palate, and other congenital malformations of the digestive system. The pattern was similar to that of other regions of Indonesia, and differed from Indian and European populations

**Key words:** congenital anomalies – genetic diseases – malformations – Dr. Sardjito General Hospital

## ABSTRAK

**M. Mansyur Romi – Kajian awal terhadap anomaly congenital di RSUP Dr. Sardjito**

**Latar belakang:** Anomali kongenital dan penyakit genetik cenderung makin banyak dilaporkan dan tampak mendominasi pasien rawat inap, khususnya bangsal anak di negara maju. Di kawasan dengan angka kematian bayi rendah mungkin terjadi pergeseran ke arah pola penyakit tersebut. Perlu kajian yang membahas anomali kongenital dan penyakit genetik di RSUP Dr. Sardjito, Yogyakarta yang berada di wilayah dengan angka kematian bayi jauh di bawah rerata nasional.

**Tujuan:** Kajian ini bertujuan untuk mengetahui angka kejadian anomali kongenital dan gambaran polanya pada pasien yang dirawat di RSUP. Dr. Sardjito.

**Bahan dan Cara:** Dengan cara deskriptif kajian ini membahas data anomali kongenital dari rekam medis pasien di Instalasi Rekam Medis RS. Dr. Sardjito Yogyakarta selama 5 tahun. (1998 sampai 2002). Semua

data pasien rawat inap dengan diagnosis utama maupun sekunder yang termasuk kelompok *congenital malformations, deformations, and chromosomal abnormalities* (Q00 – Q99) menurut *International Classification of Diseases* (ICD) diikutsertakan dalam kajian ini. Pola anomali yang ada dibandingkan dengan pola dari populasi dan kurun waktu yang berbeda.

**Hasil:** Anomali kongenital yang masuk ke RS. Dr. Sardjito antara 1998 sampai 2002 tercatat 1968 kasus, terdiri atas 1070 lelaki dan 898 perempuan, dengan proporsi terhadap seluruh pasien yang dirawat terhitung 2,06%. Bibir sumbing (Q35-Q37) merupakan kasus terbanyak mencapai (21,14%), diikuti Q38-Q45: malformasi lain pada sistem digesti (18,45%), Q20-Q28: system sirkulasi (15,65%), Q50-Q56: organ genital (12,55%), Q00-Q07: sistem saraf (11,89%), Q65-Q79: muskuloskeletal (6,40%), Q80-Q89: malformasi lain-lain (4,06%), Q10-Q18: mata, telinga, wajah dan leher (3,91%), Q60-Q64: sistem urinaria (2,54%), Q90-Q99: abnormalitas kromosom, tidak masuk kelompok lain (2,44%) dan Q30-Q34: sistem respirasi (0,97%).

**Simpulan:** Anomali kongenital di RS. DR. Sardjito didominasi oleh bibir sumbing dan malformasi lain pada sistem digesti. Pola anomali mempunyai kesamaan dengan wilayah lain di Indonesia dan berbeda dengan populasi di India maupun Eropa.

## INTRODUCTION

Congenital anomalies and genetic diseases are more commonly reported along with the advance of medical knowledge. There is a paradox that the better health service that decreases the infant mortality rate the longer life expectancy of children with congenital anomalies and the greater genetic burdens, with all consequences. Because of the fact, in areas where the infant mortality rate is low, a change in health problems needs to be anticipated, one of them is the shift of disease pattern. It can be observed, for example, in the occupants of pediatric wards in North America are dominated by patients with genetic problems or congenital anomalies. The frequency of genetic disorders admitted into the pediatric ward in Seattle, United States, were: chromosomal anomalies (0.6%), single gene (3.9%), polygenic (48.9%); while in Montreal, Canada, the proportion were 0.4%, 6.9%, and 29%, respectively.<sup>1</sup> Other reports showed that in general, congenital anomalies were responsible for 50% admission to the hospital, 10% perinatal death, and 40% death in the first year of life.<sup>2</sup>

Such data in Indonesia are limited. Studies showed that the proportion of congenital abnormality cases in patients admitted to RS Ibu dan Anak Harapan Kita Jakarta in 1990-1994 were 5.21%, 6.46%, 6.79%, and 8.84%, respectively, or as a whole was 3.16%.<sup>3</sup> Eventhough the rate was lower than that in North America, apparently there had been an increased rate.

RSUP Dr Sardjito as a referral hospital and main teaching hospital in Yogyakarta which has

infant mortality rate lower than national average is assumed to have many congenital anomalies and genetic problem patients. This study is a preliminary one to reveal the pattern of congenital anomaly for 5 years, comparing the data with another period and populations, discussing various potential etiology and risk factors. With further and better studies, it is expected that the anticipation of holistic health problem dynamics are considered, including the increase in the knowledge and competence of experts, from molecular to clinical, software of policy, instruments and logistics needed for community health service, as one of the efforts to develop translational medicine.

## METHOD

This preliminary study was an analytical descriptive study using secondary data available at Dr Sardjito Hospital, Yogyakarta. Data were obtained from the database of Medical Record Unit documenting the diagnosis of congenital malformations, deformities, and chromosomal abnormalities (Q00-Q99) according to the International Classification of Diseases (ICD). The data from the last 10 years (1998-2007) were studied and classified into 2 groups, each consisted of 5 year period. All medical records of inpatients with diagnosis group of Q00-Q99, either as the main or the secondary diagnosis, for 5 first years (1998-2002) were included in this study. If data showed more than one Q category, the first diagnosis was taken. The next 5 year period (2003-2007) data were used as comparison, and would be analyzed later.

## RESULTS AND DISCUSSION

### Pattern of congenital anomaly

For 5 years, from 1998 until 2002, there were 1968 admissions to RS Dr Sardjito with diagnosis category of Q00-Q99 congenital malformations, deformations, and chromosomal abnormalities, according to the International Classification of Diseases (ICD-10). Based on the whole patients admitted in the year, the proportion of congenital anomaly was 2.06%, comprising 1070 male and 898 female patients.

The most common diseases were Q35-Q37 cleft lip and cleft palate (416 cases, 21.14%), followed by Q38-Q45 other congenital malformations of the digestive system (363 cases, 18.45%), Q20-Q28 congenital malformations of the circulatory system (308 cases, 15.65%), Q50-Q56 congenital malformations of genital organ (247 cases, 12.55%), and Q00-Q07 congenital malformations of the nervous system (234 cases, 11.89%). Other group was less than 10%.

TABLE 1. The list of congenital anomaly according to ICD-10 in DR Sardjito Hospital 1998-2002

No.	Congenital Anomaly	♂	♀	Total	(%)
1.	<i>Q35 – Q37 Cleft lip and cleft palate</i>	217	199	416	21.14
2	<i>Q38 – Q45 Other congenital malformations of the digestive system</i>	205	158	363	18.45
3	<i>Q20 – Q28 Congenital malformations of the circulatory system</i>	135	173	308	15.65
4	<i>Q50 – Q56 Congenital malformations of genital organ</i>	201	46	247	12.55
5	<i>Q00 – Q07 Congenital malformations of the nervous system</i>	107	127	234	11.89
6	<i>Q65 – Q79 Congenital malformations and deformations of the musculoskeletal system</i>	73	53	126	6.40
7	<i>Q80 – Q89 Other congenital malformations</i>	30	50	80	4.06
8	<i>Q10 – Q18 Congenital malformations of eye, ear, face and neck</i>	41	36	77	3.91
9	<i>Q60 – Q64 Congenital malformations of the urinary system</i>	24	26	50	2.54
10	<i>Q90 – Q99 Chromosomal anomalies</i>	23	25	48	2.44
11	<i>Q30 – Q34 Congenital malformations of the respiratory system</i>	14	5	19	0.97
Total		1070	898	1968	100

In 1990-1994, in Ibu & Anak Harapan Kita Hospital, there were 2442 cases of congenital abnormalities, or 6.78% of all patients. Based on similar diagnosis classification, Q35-Q37 cleft lip and cleft palate was in the second position (19.5%) after Q38-Q45 other congenital malformations of the digestive system (24.15%). The next positions

were Q65-Q79 congenital malformations and deformations of the musculoskeletal system (14.67%), Q20-Q28 congenital malformations of the circulatory system (14.12%), and Q50-Q56 congenital malformations of genital organ (10.54%). Based on the birthrate in this hospital, the proportion of congenital anomaly was 3.16%.<sup>3</sup>

TABLE 2 The frequency of congenital anomaly according to ICD-10 in Harapan Kita Hospital

The pattern of congenital anomalies in DR Sardjito Hospital, with cleft lip and palate as the most common, was similar with the observation in Manado, although the next position in the list was different, that is, talipes, multiple malformation, anal atresia, omphalocele, and congenital heart diseases. This data were of babies born in Gunung Wenang Hospital in 5 year period, which showed a total incidence of congenital malformations of 0.9% and 0.5%, some of them were in major category.<sup>4</sup> In RS Pirngadi Medan in 1981-1984, there were 77 cases of congenital anomalies from 15.185 births (0.51%), and the most common were pes equinovarus (7 cases, 9.1%), labiognathopalatoschisis, hydrocephalus, and anencephalus, each was 6 cases (7.7%).<sup>5</sup>

A study in South India in September 1989 until December 1992 included 12.797 births, it was found a total incidence of 3.7%, consisted of 3.2% in liveborns and 15.7% in stillbirths. The anomalies were musculoskeletal cases (9.69 per 1000), cutaneous (6.33 per 1000), genitourinary (5.47 per 1000), gastrointestinal (5.47 per 1000), central nervous system (3.99 per 1000), and cardiac anomalies (2.03 per 1000). Musculoskeletal, cutaneous, and genito-urinary malformation cases were commonly found in live births, while gastrointestinal and central nervous system malformations were commonly found in stillbirths. In the study, antenatal infection and drug consumption were not found as significant causal factors of defects.<sup>6</sup> In Indira Gandhi Medical College, Shimia, in 5 year period study covering 10,100 births,

there were 180 babies with congenital malformations, with overall incidence of 1.78%. In 311 stillbirths, there were 47 cases (15.1%), while in livebirths 1.3%. The most common malformations were central nervous system (40%), followed by musculoskeletal system (23.8%), while the less common was genitourinary system (3.8%). In this study malformations were more

often found in babies with birthweight < 2500 gm

1 Q38 – Q45 Other congenital malformations of the digestive system  
 2 Q15 – Q37 Cleft lip and cleft palate  
 3 Q65 – Q79 Congenital malformations and deformations of the musculoskeletal system  
 4 Q20 – Q28 Congenital malformations of the circulatory system  
 5 Q50 – Q56 Congenital malformations of genital organ  
 6 Q00 – Q07 Congenital malformations of the nervous system  
 7 Q90 – Q99 Chromosomal anomalies  
 8 Q60 – Q64 Congenital malformations of the urinary system  
 9 Q80 – Q89 Other congenital malformations  
 10 Q10 – Q19 Congenital malformations of eye of ear, face and neck  
 11 Q30 – Q34 Congenital malformations of the respiratory system

1.	Total	25%
2.	Cardiac defect	17%
3.	Limb anomalies	15%
4.	Chromosomal syndromes	15%
5.	Urinary system	15%
6.	Central nervous system and neural tube	10%
7.	Oral cleft	6%

Summarizing various dysmorphology was difficult because of several constraints, including: different nomenclature, variability, difference in

severity affecting the phenotype, age effect, expansion and contraction.<sup>9</sup> Based on the above discussion, the proportion of congenital anomaly in RS Dr Sardjito in 1998-2002 based on inpatients was 2.06%, while in RSIA Harapan Kita in 1990-1994 was 6.78%. Possible factors affecting this result was the more general scope of patients in RS Dr Sardjito compared to RS Harapan Kita who admitted mothers and children only. A more urban life pattern in Jakarta compared to in Yogyakarta needs to be studied, although there was an increase in proportion each year in Jakarta, while in Yogyakarta, the increase was not observed. In Indonesian population, admitted into RS Harapan Kita and RS Dr Sardjito, the anomaly of gastrointestinal system and cleft lip and palate were the most common (around 40%), while circulation system anomaly was around 15%. In Indian population, the anomalies of musculoskeletal and nervous system were more common. European population was dominated by heart defects (25%), while cleft lip and palate was only 6%. This difference is probably caused by various factors, including the etiology and existence of risk factors, and its relationship with critical window in current growth and development process.

Concerning the etiology and risk factors, congenital anomaly as an abnormality known since the ancient times can be traced in paleopathology studies. Palatoschisis was noted in Nubian residence more than 3000 years ago and in ancient

Eskimo, talipes was found in the skeletons from ancient Egypt more than 4500 years ago.<sup>10,11,12</sup> The understanding of its etiology has revolutionized from mystic irrational to the latest scientific explanations developing to the molecular level.

In pregnancy, a unique event is occurred, affecting all biochemical, physiological, and anatomical processes. Exposure of xenobiotic factors and natural agents may change the growth and development process with consequences probably obvious since birth and/or all through life; the consequences can be cured partly or wholly, but may also caused a fixed defect. Organogenesis occurs in a short period, that is : 10 days (day 6-15) in rat 22 day pregnancy, 13 days (day 6-19) in rabbit 29 day pregnancy, and 7 weeks (7 x 7 = 49 days, that is, day 9-58) in human 9 month pregnancy. Generally, only this short growth and development stage is susceptible to the induction of malformations.<sup>13</sup>

Congenital anomaly is a broad concept, including all types of structural and functional defects. Structural abnormality can be classified into malformations, malformation syndromes, deformations, and disruptions. Functional anomaly may be caused by the hormonal imbalance while the babies in growth and developmental stage since pregnancy which caused health consequences several years later, various congenital disorders while in intrauterine stage also caused congenital anomaly.<sup>14</sup>

TABLE 4. Definitions and examples of classic cases of each anomalies.<sup>15</sup> (Seller, 2004).

Category	Definition	Example
Malformasi	Local growth and development anomaly in the morphogenesis stage or stage in which	Isolated cleft spina bifida, septal defect
Malformasi	Some various congenital disorders while in intrauterine stage also caused congenital anomaly. <sup>14</sup>	Trisomi 21
Deformation	The abnormalities of form or structure of the body part after or at the time of its normal morphogenesis	Club foot, oligohydramn
Disruption	The abnormalities or apparent damage of part of the body that has been normally grown or potentially able to grow normally	Missing limb

Congenital anomaly is caused by genetic and or environmental factors in growth and development process since pregnancy. Generally, it was known that most congenital anomalies have genetic background. The role of environment as the causal factor has been known more commonly found (2-37%). Drugs, radiation, infection, and alcohol were believed as the etiology in 6-8% of cases.<sup>15</sup> The variations may be explained by the difference in the definition of “environment”. Some expert

considered environment in broad meaning, that is, every non-genetic factor increasing the risk of congenital anomaly in exposed individual, consisted of biological factors (such as rubella infection), physical factors (X ray, ionizing radiation), and chemical agents (such as drugs used in pregnancy). Some other experts limited the environment definition on chemical and physical exposures in the air, water, soil, and food.

TABLE 5. Chemical agents and exposure conditions associated with congenital anomaly in humans<sup>14</sup>

1. Chemical agents
<ul style="list-style-type: none"> <li>● Pharmaceuticals, for example: DES, thalidomide, warfarin</li> <li>● Hair colouring agents</li> <li>● Pesticides</li> <li>● Non-pesticide endocrine disrupter (ED, for example: bisphenol A, phthalate, vinyl chloride, TCDD)</li> <li>● Heavy metal (Pb, Hg, Cd, As, Cr and Ni)</li> <li>● Organic solvents, for example: styrene</li> </ul>
2. Exposure conditions associated to congenital anomaly
<ul style="list-style-type: none"> <li>● Drink water (heavy metals, nitrates, chlorinated agents)</li> <li>● Residence near dangerous waste disposal</li> <li>● Pesticides in farming or gardening area</li> <li>● Air pollution</li> <li>● Food contamination (dioxin, PCB)</li> <li>● Disasters (Hiroshima, Minamata, Chernobyl)</li> </ul>

Various study results on potentially teratogenic agents were summarized from electronic and printed sources. The discussions include: i). cigarettes have a role in the occurrence of heart defects, neural tubes defect, oral-facial cleft and club foot,<sup>16</sup> ii). lithium medication was considered decreasing the risk, iii). glucocorticoids are related to facial cleft, iv) trimetophrim, v). methimazole syndrome.<sup>17,18</sup> In infertile couples, either in treatment or not, there was a higher congenital malformation prevalence; but the association with hormonal therapy is needed to be studied further.<sup>19</sup> There was also reports suggested that certain diets, toxin exposure, endocrine disrupting chemicals (EDC), and insecticides had roles in the incidence of congenital anomaly.<sup>13,20,21</sup>

Another factor often discussed was hyperthermia as teratogenic source. The threshold of temperature for teratogenic effect of hyperthermia in mammalian is considered ~1.5°C

over the core values for a long exposure, and probably for ~5 minutes or more in 4°C temperature increase. Various pathogenic mechanisms leading to defects in development suggested include cell death and cell proliferation deceleration, disruption of normal gene activity, vascular disruption, destruction of cell membrane and intracellular structures, and enzyme inhibition. Usually, the effect of heat is received directly by embryo and foetus in the uterus, the defect is not caused by maternal reaction to toxic exposure, although the maternal reaction has an effect on foetal response.<sup>22,23,24</sup> Other data showed that pregnant rats who exposed to hyperthermia would have pathological change in their placenta, and this might be responsible for the growth and development disorders.<sup>25</sup>

The previous discussion generally analyzed various evidence obtained from experimental studies. Several reports from clinical studies are summarized in the TABLE 6.

TABLE 6. Malformation types reported from clinical studies<sup>14,15</sup>

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Infectious agents

1. rubella: before 10 weeks pregnancy: cataract and heart defect; 10-16 weeks pregnancy, hearing loss and retinopathy
2. varicella : extremity hypoplasia, microcephaly, chorioretinitis
3. CMV : hydrocephalus, periventricular calcification, neurological problems
4. toxoplasmosis : hidrocephalus, microcephaly, cerebral calcification

Maternal diseases

1. insulin-dependent diabetes : macrosomy, caudal regression syndrome, neural tube defect, heart defect, especially VSD and transposition of great arteries
2. phenylketonuria (with no diet control): microcephaly, micrognathia, heart defect, mental retardation
3. folate deficiency : neural tube defect, cleft lip and palate
4. epilepsy : cannot be differentiated from teratogenic effect of treatment

Physical agents

1. radiation : high dose on foetus in midterm until the end of pregnancy would cause microcephaly
2. hyperthermia: neural tube defect, particularly anencephaly, microcephaly, microphthalmia, cleft lip and palate; difficult to differentiate from another agents of hyperpyresis.

Drugs

1. diethylstilbestrol: female – vaginal adenosis; male – micropenis, hypospadias, cryptorchidism
  2. warfarin: nose hypoplastic and bone dysplasia, choanal atresia, microcephaly, hydrocephalus
  3. phenytoin: brachicephaly, cleft lip and palate, kuku and finger hypoplasia, short neck, hirsutism
  4. retinoic acid (vitamin A congeners): hydrocephalus, microcephaly, heart defect, especially conotruncal malformation, aortal arc hypoplasia, microtia/anotia, micrognathia, urogenital anomaly
  5. alcohol: microcephaly, ‘long face’, ‘flat lip’, short distal finger, heart defect, mental retardation
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## CONCLUSION

In this study, the proportion of congenital anomaly in RS Dr Sardjito inpatients was 2.06%. The most common anomalies were cleft lip and palate (21.14%), followed by other malformations in gastrointestinal system (18.45%). This pattern is similar to another conditions in other areas in Indonesia, but different with the pattern in India and Europe. This difference needs to be studied further to find out the possible etiology and risk factors, so that an appropriate management may be developed.

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