eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Risk Factors of Congenital Anomalies at South Sumatra Indonesia

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ARTICLE INFO

Keywords:
Risk factors
Perinatal death
Maternal exposure
Cleft lip
Prevalence

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/bsm.v4i4.165

ABSTRACT

Introduction. A congenital anomaly is one of the leading causes of neonatal death. It is the third leading cause of newborn death in Indonesia. More than half of all congenital disabilities can't be related to a specific purpose, suggesting multiple risk factors. This study aims to identify patterns and risk factors of congenital anomalies in general hospital Dr Mohammad Hoesin Palembang.
Methods. This descriptive observational study with a cross-sectional design used 100 patients' medical records, taken at RSUP Dr Mohammad Hoesin Palembang, as samples. Missing data were complemented with a phone interview. Samples were picked using a proportional random sampling method. Collected data were counted within each category of congenital anomalies.
Results. There were 366 neonatal patients diagnosed with congenital anomalies at RSUP Dr Mohammad Hoesin Palembang in 2015. The most prevalent (44,8%) congenital defects belonged to congenital anomalies of the digestive system, followed by congenital anomalies of the circulatory system (18,6%), and cleft lip/palate (11,5%). Following risk factors were found: the history of maternal active or passive smoking (41%), maternal exposure to chemicals or solvents (31%), family member with congenital anomalies of the same category (27%), maternal drug consumption (26%), maternal infection (22%), maternal diabetes mellitus (4%), and maternal hypertension (4%).
Conclusion. History of maternal active or passive smoking was the most frequently found risk factors among patients of congenital anomalies**.**

1. Introduction

A congenital anomaly is defined as any structural, anatomical, or functional deviations present at birth[1]. It is one of the leading causes of disability in children, as well as the fourth leading cause of neonatal death in the world[2] and the third in Indonesia[3]. The incidence of congenital anomalies in Indonesia is estimated at 59,3 for every 1.000 live birth[3].

Aetiology of congenital anomalies varies widely; with around 50% cases that could not be associated with a specific cause, suggesting multifactorial involvement[4]. A lot of studies have explored the associations of congenital anomalies and various risk factors: genetic, environmental, and interactions of both elements.

Among successfully identified risk factors are maternal health conditions during pregnancy. These conditions include age, infection, diabetes, hypertension, drugs or alcohol consumption, exposure to certain chemicals, and smoking.

The high contribution of congenital anomalies towards neonatal death necessitates the identification of risk factors of congenital disabilities in each region, including Palembang. Data, especially regarding modifiable risk factors, can be decisive in efforts to prevent and reduce the incidence of a

congenital disability in Palembang. This study aims to identify risk factors of congenital disability at Dr Mohammad Hoesin General Hospital Palembang.

2. Methods

This descriptive observational study with a cross-sectional design was conducted in August-October 2016 at the Department of Medical Records, Dr Mohammad Hoesin General Hospital Palembang. Subjects were medical records of patients under 1-year-old with congenital anomalies in the period of January-December 2015. Samples were chosen using a proportional random sampling method, following proportions of congenital anomalies categories at Dr Mohammad Hoesin General Hospital Palembang. Types of congenital anomalies developed the International Classification of Disease (ICD-10), also used by the hospital medical record system. In case of missing data from medical records, phone interviews with parents were conducted

Variables in this research included congenital anomalies, family history of congenital disabilities from the same category, use of assisted reproductive technology (ART), and maternal conditions during pregnancy: infection, diabetes mellitus, hypertension, active or passive smoking, alcohol consumption, drug consumption, and exposure to chemical or solvent. These risk factors were selected based on their statistical significance in previous studies. Gathered data were then analyzed and described to identify numbers of patients with congenital anomalies, risk factors of congenital disabilities and pattern of risk factors on each category of congenital disabilities.

3. Results

There were 366 patients diagnosed with congenital anomalies at Dr.Mohammad Hoesin General Hospital Palembang in the period of January-December 2015 (Table 1).

Out of eleven categories, the congenital anomaly of the digestive system was most prevalent (44.8%), followed by a congenital disability of the circulatory system (18.6%) and cleft lip/palate (11.5%). Other noted categories were a congenital anomaly of the musculoskeletal system (9.3%) and nervous system (9%). No patient with a congenital disability of the respiratory system was found.

There were more male patients (62%) than females. Patients' birth weight ranged from 1.9 kg to 4.2 kg, while birth length ranged from 41 cm to 51 cm. The majority of patients fell within average birth weight (91%), and standard birth length categories (70%) Summary of congenital anomaly patients' characteristics are present in Table 2.

Most genetic and environmental risk factors included at the beginning of this research were found, except for alcohol consumption and the use of assisted reproductive technology (Table 3). History of maternal active or passive smoking was the most frequently found risk factors (41%). In comparison, the least was the history of maternal diabetes mellitus (4%) and a history of maternal hypertension during pregnancy (4%). More than half of the patients were recorded having multiple risk factors (Table 4).

Nine patients were recorded having a congenital anomaly of the nervous system, with diagnoses anencephaly, encephalocele, congenital hydrocephalus, atresia of foramina Magendie and Luschka (Dandy-Walker syndrome), and spina bifida. Maternal exposure to chemical or solvent, usually occupational, was the most common risk factor (55.6%), closely followed by infection (44.4%) and active or passive smoking (33.3%). Six out of nine patients had multiple risk factors (Table 5). Eighteen patients were recorded having a congenital anomaly of the circulatory system, with diagnoses double outlet right ventricle, discordant ventriculoarterial connection, ventricular septal defect, atrial septal defect, aortic valve stenosis, patent ductus arteriosus, atresia of the pulmonary artery, and stenosis of the pulmonary artery. The most common risk factor was each family history (33.3%) and drug consumption (33.3%), followed by active or passive

smoking (27.8%) and hypertension during pregnancy (22.2%). More than half of the patients had multiple risk factors (Table 6). Eleven patients were recorded having a congenital anomaly of cleft lip and cleft palate. History of active and passive smoking was most frequent (81.8%), followed by family history (63.6%) and exposure to chemical or solvent (36.4%). Most patients had multiple risk factors (Table 7).

There were 45 patients recorded having congenital anomaly of the digestive system, mostly with diagnoses anal atresia with or without fistula and Hirschsprung's disease. History of active or passive smoking was most frequent (40%), followed by exposure to chemical or solvent (35.6%) and drug consumption (28.9%). Close to half of the patients had multiple risk factors (Table 8). Nine patients were recorded having a congenital anomaly of the musculoskeletal system, with diagnoses polydactyly, craniosynostosis, microcephaly, congenital diaphragmatic hernia, exomphalos, and gastroschisis. Maternal drug consumption was most frequent (44.4%), followed by active or passive smoking (33.3%), and exposure to chemical or solvent. Four out of nine patients had multiple risk factors (Table 9).

Three patients were recorded having congenital anomaly of the genital organ, with diagnosis hypospadias. Risk factors found on these patients were active or passive smoking (66.7%), family history (33.3%), and exposure to chemical or solvent (33.3%). Only one patient had multiple risk factors.

Two patients were recorded having congenital anomaly of the urinary system, with diagnoses congenital vesica-ureter-renal reflux and atresia and stenosis of urethra and bladder. A history of maternal infection was found on one patient.

Only one patient, diagnosed with congenital cataract, included within the inherent anomaly of the eye, ear, face, and neck. History of maternal infection, namely rubella, was found. There was also only one patient, diagnosed with congenital ichthyosis, included within other congenital anomalies. History of maternal active or passive smoking and drug consumption were found.

One patient was included within chromosomal abnormality, with diagnosis Down syndrome. No risk factor found on the patient.

Table 1. Distribution of Congenital Anomalies

Category	n	%
Nervous system	33	9
Eye, ear, face, neck	2	0.5
Circulatory system	68	18.6
Respiratory system	-	-
Cleft lip/palate	42	11.5
Digestive system	164	44.8
Genital organs	12	3.3
Urinary system	7	1.9
Musculoskeletal system	34	9.3
Other	2	0.5
Chromosomal	2	0.5
Total	366	100

Table 2. Characteristics of Congenital Anomalies Patients

Characteristic	n (100)	%
Sex		
Male	61	61
Female	39	39
Birth weight Category		
Very Low Birth Weight (<1,5 kg)	-	-
Low Birth Weight (<2,5 kg)	8	8
Average Birth Weight (2,5-4 kg)	91	91
Considerable Birth Weight (>4 kg)	1	1
Birth length Category		
Low Birth Length (<48 cm)	70	70
Standard Birth Length (48-52 cm)	30	30
Considerable Birth Length (>52 cm)	-	-

Table 3. Risk Factors of Congenital Anomalies

Risk Factor	n (100)	%
Genetic		
Family history	27	27
Environmental		
Infection	22	22
Diabetes mellitus	4	4
Hypertension during pregnancy	4	4
Active or passive smoking	41	41
Alcohol consumption	-	-
Drug consumption	26	26
Exposure to chemical or solvent	31	31
Assisted Reproductive Technology	-	-

Table 4. Number of Risk Factors Found on Patients

Number of Risk Factors	n (100)	%
No risk factor	12	12
Single risk factor	35	35
Multiple risk factor	53	53

Table 5. Risk Factors of Congenital Anomaly of Nervous System

Risk Factor	n (9)	%
Genetic		
Family history	1	11,1
Environmental		
Infection	4	44,4
Diabetes mellitus	1	11,1
Hypertension during pregnancy	-	-
Active or passive smoking	3	33,3
Alcohol consumption	-	-
Drug consumption	2	22,2
Exposure to chemical or solvent	5	55,6
Assisted Reproductive Technology	-	-
Multiple Risk Factors	6	66,7

Table 6. Risk Factors of Congenital Anomaly of Circulatory System

Risk Factor	n (18)	%
Genetic		
Family history	6	33,3
Environmental		
Infection	3	16,7
Diabetes mellitus	2	11,1
Hypertension during pregnancy	4	22,2
Active or passive smoking	5	27,8
Alcohol consumption	-	-
Drug consumption	6	33,3
Exposure to chemical or solvent	2	11,1
Assisted Reproductive Technology	-	-
Multiple Risk Factors	10	55,6

Table 7. Risk Factors of Congenital Anomaly *Cleft Lip and Cleft Palate*

Risk Factor	n (11)	%
Genetic		
Family history	7	63,6
Environmental		
Infection	3	27,3
Diabetes mellitus	-	-
Hypertension during pregnancy	-	-
Active or passive smoking	9	81,8
Alcohol consumption	-	-
Drug consumption	-	-
Exposure to chemical or solvent	4	36,4
Assisted Reproductive Technology	-	-
Multiple Risk Factors	9	81,8

Tabel 8. Risk Factors of Congenital Anomaly of the Digestive System

Risk Factor	n (45)	%
Genetic		
Family history	10	22,2
Environmental		
Infection	8	17,8
Diabetes mellitus	1	2,2
Hypertension during pregnancy	-	-
Active or passive smoking	18	40
Alcohol consumption	-	-
Drug consumption	13	28,9
Exposure to chemical or solvent	16	35,6
Assisted Reproductive Technology	-	-
Multiple Risk Factors	21	46,7

Tabel 9. Risk Factors of Congenital Anomaly of the Musculoskeletal System

Risk Factor	n (9)	%
Genetic		
Family history	2	22,2
Environmental		
Infection	2	22,2
Diabetes mellitus	-	-
Hypertension during pregnancy	-	-
Active or passive smoking	3	33,3
Alcohol consumption	-	-
Drug consumption	4	44,4
Exposure to chemical or solvent	3	33,3
Assisted Reproductive Technology	-	-
Multiple Risk Factors	4	44,4

4. Discussions

The most prevalent categories of congenital anomaly, on descending order, were a congenital anomaly of the digestive system (44.8%), a congenital disability of the circulatory system (18.6%), and cleft lip and cleft palate (11.5%). This distribution is similar to the results of the study conducted at Dr Pirngadi General Hospital Medan, which found a congenital anomaly of the gastrointestinal system most prevalent (66.7%). However, the second and third most common inherent ways were of central nervous and cardiothoracic system respectively[5].

Meanwhile, the results differ from report by WHO South-East Asia Regional Office in 2013, which stated that most prevalent congenital anomaly found among countries of South and South-East Asia was heart defect, followed by neural tube defect[6].

Similarities and differences compared to those studies may be influenced by local genetic or environmental factors, suggesting similar predisposing factors in the Indonesian population and variance from South and South-East Asia in general. Possible different factors include racial distribution, sociocultural behaviours and exposure to teratogens. Another explanation is there had been a shift of prevalence between the years both study were conducted.

More than half (53%) of patients in this study were reported having multiple risk factors. This finding is consistent with another source that around 50% of cases of congenital anomaly could not be traced to a single specific cause[4]. The most common risk factors of congenital disability found in this study are the history of maternal active or passive smoking, family history, and exposure to chemicals.

The history of a family member having congenital anomaly from the same category represents the genetic risk factor. It was the most common risk factor among patients with a congenital disability of the circulatory system (33.3%), tying with drug consumption, and also found in almost two-thirds of patients with cleft land/or cleft palate. A previous study found a significant association between family history and incidence of congenital heart defect[7], as also between family history and cleft lip and palate[8]. There is also a case report regarding the interaction of both genetic and environmental factors with the incidence of cleft lip within a family[9].

The tendency for a specific congenital anomaly occurring on multiple members of a family indicates an underlying genetic susceptibility. These genetic factors may act alone or, more likely, interact with various environmental risk factors to induce

anomaly, possibly through altering gene expression on embryonic tissue and thus changing normal organogenesis processes[10].

Maternal active or passive smoking is the most common risk factor, found in nearly all categories of a congenital anomaly; the highest is in cleft lip and cleft palate (81.8%), genital organ (66.7%), and digestive system (40%). A systematic review and meta-analysis study found a statistically significant association between smoking and the congenital anomaly of various system[11]. Both active and passive smoking were already identified, having a significant association with the incidence of cleft lip and cleft palate[11,12]. Maternal smoking was also considered to have a significant association with gastrointestinal defects and anal atresia[11]. On an interesting note, some studies found a significant association between paternal smoking and cleft lip and cleft palate, hypospadias, and the congenital anomaly of digestive system[8,13,14,15,16,17], suggesting epigenetic effects on male germ cells.

Exposure to chemical or solvent was found in 31% of patients and was the most common risk factor in the congenital anomaly of the nervous system. Previous studies identified a significant association between several chemicals and solvents and the incidence of congenital anomaly[18,19]. Chemicals and solutions that were considered risk factors include glycol ethers, chlorine, nitrate, various pesticides, organophosphates, and heavy metals. Industrial solvents and chemicals were found to be a risk factor for neural tube defect[20], although there was no significant increase in risk for combined chemical exposure[21].

Maternal infection and drug consumption were found in 26% and 22% of patients, respectively. Drug consumption was also the most common risk factor in the congenital anomaly of the circulatory (33.3%) and musculoskeletal system (44,4%). Infections had long been known as teratogens[20]. Rubella, for example, can cause congenital cataracts, which is very likely the explanation for the congenital cataract patient in this study. Several drugs had also been known for their teratogenic effects[20]. Drug consumption, along with family history and maternal smoking, were found to be significant risk factors for congenital heart defects[7]. Drug consumption was also found to be significantly associated with the inherent anomaly of the musculoskeletal system[22].

Maternal hypertension during pregnancy was found only in the congenital anomaly of the circulatory system. This finding is consistent with the results of a case-control study in the Netherlands which found that maternal hypertensive disorder has a significant association with several congenital anomalies; most of them are congenital heart defects[23].

5. Conclusion

There were 366 patients with a congenital anomaly at Dr Mohammad Hoesin General Hospital Palembang in the period January-December 2016. Most frequent congenital disabilities were a congenital anomaly of the digestive system, followed by the inherent defect of the circulatory system, and cleft lip and cleft palate. The most common risk factors were a history of maternal active or passive smoking, followed by exposure to chemical or solvent and family history.

The most common factor in each category was as follow the history of maternal active or passive smoking (cleft lip and/and palate, digestive system, and genital organ), exposure to chemical or solvent (nervous system), family history (circulatory system), and drug consumption (circulatory and musculoskeletal system.

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