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# Prevalence of congenital malformations during pregnancy in China: screening by ultrasound examination

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**Summary**

*Purpose:* To assess the prenatal prevalence of congenital malformations and the different types and to determine rate of perinatal mortality. *Design:* Cross-sectional study. *Setting:* Tertiary care centre. *Materials and Methods:* During the reporting period from August 2013 to September 2015, 6,432 ultrasound examinations were conducted in 2,832 pregnant women, out of whom 2,689 deliveries occurred in the referral center. *Results:* The authors diagnosed 119 cases with 154 congenital malformations (isolated: 82.35% cases; complex: 17.65% cases). The prenatal prevalence of congenital malformations was 54.38 for each 1,000 pregnancies, whereas the birth prevalence was 51.15 for each 1,000 births. The perinatal death rate was 35.29% (complex 73.68% and isolated 26.51%). The average maternal age of pregnant women was 29.94 years. Overall, the most widely observed congenital malformations involved circulatory system (20.78%), followed by musculoskeletal system (16.23%), followed by nervous system (12.34%), eye, ear, face, and neck (11.04%), cleft lip and cleft palate (7.79%), digestive system (7.79%), genital organs (6.49%), chromosomal abnormalities (5.84%), urinary system (4.55%), others (3.89%), and respiratory system (3.25%). *Conclusion:* The present study demonstrated that majority of perinatal deaths were due to complex congenital malformations. In turn the most common malformations included congenital heart diseases, neural tube defects, cleft lip/cleft palate, and polydactyly.

*Key words:* Congenital malformations; Fetal anomalies; Pregnancy; Prenatal diagnosis; Ultrasound.

## Introduction

Congenital malformations also referred to as birth defects or congenital anomalies/disorders are functional and/or structural, as well as single or multiple abnormalities of morphogenesis in body or organs that occur in utero and can be antenatal, during child birth or later. They result in long-term incapacity/disability, with greater influence on healthcare organization, society, individuals, and family. Although the cause of nearly half of the malformations cannot be determined, the other risk factors or causes are as follows: demographic and socioeconomic factors, infections, genetic as well as environmental factors, and nutritional status during maternity. As per recent stats, congenital anomalies contribute to 2.76 million deaths during initial four weeks of birth every year globally [1-3]. The worldwide prevalence is approximately 2% to 3% [4,5]. As per world health statistics, there was one death per 1,000 live births due to congenital malformations globally in 2000 to 2013 (ranging from 5% to 7%) among children aged below five years. In China, the estimated deaths due to congenital malformations ranged from 6% to 13% from 2000 to 2013 [6].

Proof of congenital anomalies at birth begins a complex clinical procedure focused to amend diagnostic definition, clinical/prognostic assessment, including genetic counseling, and treatment choice. Majority of congenital anomalies recognize diverse causes as well as pathogenetic pathways irrespective of similar phenotypic pattern [2, 3, 7]. Hence the diagnostic process is time-consuming and troublesome and may require long follow ups, including but not limited to imaging, phenotype analysis, anamnesis, and laboratory tests.

Ultrasound examination is advantageous in the early discovery of congenital anomalies. In populations at low risk, 17% to 35 % of sensitivity and 99% of specificity, can be observed while in populations at high risk, more than 90% sensitivity can be noted [8, 9]. The specific use of 3D ultrasound in assessment of skeletal, limb, and facial structure anomalies was demonstrated in reviews conducted by Timor-Tritsch *et al.* and Goncalves *et al.* [10, 11]. Prenatal diagnosis of congenital malformations is critical for the suitable counseling of parents regarding special needs, in utero interventions, voluntary pregnancy termination when required, intimation to neonatology team for proper care, delivery in the appropriate centre, and future prevention [9, 12]. The types as well as prevalence of congenital anomalies vary from one country to that of another and in turn from one region to that of another.

As per the present authors' knowledge, none of the studies focused on determination of the prenatal prevalence of congenital malformations in China. The major goal of the present study was to assess the prenatal prevalence and of

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congenital malformations and their different types, and to determine rate of perinatal mortality.

## Materials and Methods

This single-centre cross-sectional observational study was performed at a tertiary hospital, China over a period of two years, from August 2013 to September 2015.

Every pregnant women attended in the setting had a routine ultrasound examination at gestation period between 18 and 20 weeks or later at scheduled follow-up visit. In the present study, pregnant women with issues of congenital malformations with prenatal diagnosis at or who were referred to hospital with congenital malformations were included. Included patients were examined, diagnosed, and properly counseled by specialists. The majority of the patients had more than one ultrasound examination. All the required maternal data, congenital malformation details, delivery data, neonatal results, etc, collected during diagnosis were recorded in an information sheet. Data gathering and follow up were conducted in all the units, wards, and laboratories, whenever possible.

A spontaneous abortion or miscarriage was noted if pregnancy loss occurred before 20 gestation weeks. Stillbirths were enlisted at 22 weeks or older gestational age. Neonatal death was noted up to 28 days of newborn child life. Perinatal mortality encompasses the fetal or neonatal death from 22 gestation weeks to 28 days of newborn child life. As per International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) 2010 [13], congenital malformations were classified based on the system/organ involved (circulatory, digestive, musculoskeletal, nervous, respiratory, as well as urinary systems, ear, face, eye and neck, cleft lip and cleft palate, genital organs, and others). Malformations were considered as isolated when a single system was involved, whereas complex when involvement of more than one system was observed.

Prenatal prevalence was computed from the aggregate number of pregnant women, whereas birth prevalence as well as the perinatal mortality were assessed from the number of deliveries. The Institutional ethics committee approval was acquired for the present study and patient confidentiality was strictly maintained.

Table 1. — *Maternal demographic characteristics (n=119).*

| Characteristics | | Total (n=119) |
|---|---|---|
| Maternal age, years | Mean (SD) | 29.94 (7.81) |
| | Median (range) | 28 (18-49) |
| Age category | < 25 years, n (%) | 44 (37) |
| | 25-35 years, n (%) | 41 (34.5) |
| | > 35 years, n (%) | 34 (28.6) |
| Gender | Male, n (%) | 65 (54.6) |
| | Female, n (%) | 52 (43.7) |
| | Unknown, n (%) | 2 (1.7) |
| Parity | 0, n (%) | 84 (70.6) |
| | 1, n (%) | 22 (18.5) |
| | ≥ 2, n (%) | 13 (10.9) |
| Smoking | Yes, n (%) | 21 (17.6) |
| | No, n (%) | 98 (82.4) |
| Drinking | Yes, n (%) | 16 (13.4) |
| | No, n (%) | 103 (86.6) |
| Family history | Yes, n (%) | 18 (15.1) |
| | No, n (%) | 101 (84.9) |
| Consanguinity | Yes, n (%) | 27 (22.7) |
| | No, n (%) | 92 (77.3) |

SD = standard deviation.

## Results

During the reporting period, 6,432 ultrasound examinations were conducted for 2,832 pregnant women out of whom 2,689 deliveries happened in the referral center. The remaining patients were alluded for delivery in respective referral centers and a few were lost to follow up.

Out of 2,832 pregnant women, 119 cases were diagnosed with 154 congenital malformations (isolated: 98 [82.35%] cases and complex: 21 [17.65%] cases). The prenatal prevalence of congenital malformations was 54.38 for each 1,000 pregnancies. Of 119 cases, six (5.04%) patients experienced spontaneous abortion or miscarriage, 102 (85.71%) patients delivered in the referral center, whereas 11 (9.24%) patients

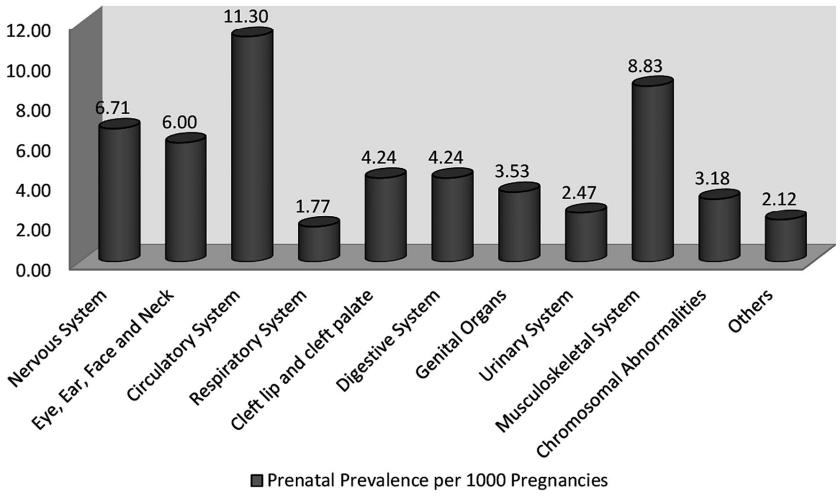


Figure 1. — Prenatal prevalence of congenital malformation based on system or organ involved is depicted.

Table 2. — *Prenatal congenital malformations (CMs) diagnosed by ultrasound.*

| Type of CM based on system or organ involved | Total | N | CM % | Prenatal prevalence (per 1,000 pregnancies) |
|---|---|---|---|---|
| Nervous system | 19 | | 12.34 | 6.71 |
| Neural tube defects | | 14 | 9.09 | 4.94 |
| Anencephalus and similar | | 4 | 2.59 | 1.41 |
| Encephalocele | | 4 | 2.59 | 1.41 |
| Spina bifida | | 6 | 3.89 | 2.12 |
| Hydrocephalus | | 3 | 1.95 | 1.06 |
| Microcephaly | | 2 | 1.29 | 0.71 |
| Eye, ear, face and neck | 17 | | 11.04 | 6.00 |
| Eye | | 7 | 4.55 | 2.47 |
| Anophthalmos | | 3 | 1.95 | 1.06 |
| Microphthalmos | | 2 | 1.29 | 0.71 |
| Congenital cataract | | 1 | 0.65 | 0.35 |
| Congenital glaucoma | | 1 | 0.65 | 0.35 |
| Ear | | 5 | 3.25 | 1.77 |
| Macrotia | | 2 | 1.29 | 0.71 |
| Microtia | | 2 | 1.29 | 0.71 |
| Pointed ear | | 1 | 0.65 | 0.35 |
| Face and neck | | 5 | 3.25 | 1.77 |
| Sinus, fistula and cyst of brachial cleft | | 2 | 1.29 | 0.71 |
| Otocephaly | | 1 | 0.65 | 0.35 |
| Pterygium colli | | 1 | 0.65 | 0.35 |
| Macrostomia | | 1 | 0.65 | 0.35 |
| Circulatory system | 32 | | 20.78 | 11.30 |
| Cardiac chambers and connections | | 10 | 6.49 | 3.53 |
| Common arterial truncus | | 4 | 2.59 | 1.41 |
| Single ventricle | | 2 | 1.29 | 0.71 |
| Transposition of great vessels | | 4 | 2.59 | 1.41 |
| Cardiac septa | | 10 | 6.49 | 3.53 |
| Ventricular septal defect | | 2 | 1.29 | 0.71 |
| Tetralogy of Fallot | | 4 | 2.59 | 1.41 |
| Atrioventricular septal defect | | 3 | 1.95 | 1.06 |
| Unspecified | | 1 | 0.65 | 0.35 |
| Pulmonary and tricuspid valves | | 3 | 1.95 | 1.06 |
| Pulmonary valve stenosis | | 1 | 0.65 | 0.35 |
| Tricuspid atresia | | 2 | 1.29 | 0.71 |
| Aortic and mitral valves | | 6 | 3.89 | 2.12 |
| Aortic valve atresia/stenosis | | 2 | 1.29 | 0.71 |
| Mitral valve anomalies | | 1 | 0.65 | 0.35 |
| Hypoplastic left heart syndrome | | 3 | 1.95 | 1.06 |
| Absence of aorta | | 2 | 1.29 | 0.71 |
| Coarctation of aorta | | 1 | 0.65 | 0.35 |
| Respiratory system | 5 | | 3.25 | 1.77 |
| Malformations of nose | | 3 | 1.95 | 1.06 |
| Malformations of lung | | 2 | 1.29 | 0.71 |
| Cleft lip and cleft palate | 12 | | 7.79 | 4.24 |
| Cleft lip | | 8 | 5.19 | 2.82 |
| Cleft palate with cleft lip | | 4 | 2.59 | 1.41 |
| Cleft palate | | 4 | 2.59 | 1.41 |
| Digestive system | 12 | | 7.79 | 4.24 |
| Esophageal atresia | | 3 | 1.95 | 1.06 |
| Duodenal atresia or stenosis | | 2 | 1.29 | 0.71 |
| Atresia of small intestine | | 2 | 1.29 | 0.71 |
| Imperforate anus | | 1 | 0.65 | 0.35 |
| Hiatus hernia | | 2 | 1.29 | 0.71 |
| Atresia of large intestine | | 2 | 1.29 | 0.71 |
| Genital organs | 10 | | 6.49 | 3.53 |
| Hypospadias | | 4 | 2.59 | 1.41 |
| Undescended testicle | | 2 | 1.29 | 0.71 |
| Indeterminate sex | | 2 | 1.29 | 0.71 |
| Absence of ovary | | 1 | 0.65 | 0.35 |
| CM of uterus and cervix | | 1 | 0.65 | 0.35 |
| Urinary system | 7 | | 4.55 | 2.47 |
| Congenital hydronephrosis | | 1 | 0.65 | 0.35 |
| Cystic kidney disease | | 2 | 1.29 | 0.71 |
| Renal agenesis | | 2 | 1.29 | 0.71 |
| CM of kidney/urinary system | | 2 | 1.29 | 0.71 |
| Musculoskeletal system | 25 | | 16.23 | 8.83 |
| Polydactyly | | 8 | 5.19 | 2.82 |
| Syndactyly | | 2 | 1.29 | 0.71 |
| Congenital diaphragmatic hernia | | 2 | 1.29 | 0.71 |
| Musculoskeletal dysplasia | | 2 | 1.29 | 0.71 |
| Gastroschisis | | 3 | 1.95 | 1.06 |
| Omphalocele | | 2 | 1.29 | 0.71 |
| Congenital scoliosis | | 1 | 0.65 | 0.35 |
| Limb reduction defects | | 1 | 0.65 | 0.35 |
| Talipes | | 4 | 2.59 | 1.41 |
| Chromosomal abnormalities | 9 | | 5.84 | 3.18 |
| Down syndrome | | 4 | 2.59 | 1.41 |
| Patau syndrome | | 3 | 1.95 | 1.06 |
| Edwards syndrome | | 2 | 1.29 | 0.71 |
| Others | 6 | | 3.89 | 2.12 |
| Moebius syndrome | | 1 | 0.65 | 0.35 |
| CM of breast | | 2 | 1.29 | 0.71 |
| CM of integument | | 2 | 1.29 | 0.71 |
| Fetal alcohol syndrome | | 1 | 0.65 | 0.35 |
| Total | 154 | | | 54.38 |

were either alluded for delivery in respective referral centers or were lost to follow up. During the study period, 2,522 patients delivered with 129 congenital malformations. The birth prevalence of congenital malformations was 51.15 for each 1,000 births.

The perinatal death rate was 35.29% (36 stillborn and neonatal deaths out of 102 cases). The perinatal death rate with complex congenital malformation was 73.68% (14 out of 19 patients) and isolated congenital malformation was 26.51% (22 out of 83 patients).

The average maternal age (SD) of pregnant women was 29.94 (7.81) years. The fetuses were 65 (54.6%) males, 52 (43.7%) females, and two (1.7%) were of unknown sex. The maternal demographic characteristics including age, age category, gender of fetus, parity, smoking, drinking, family history, and consanguinity are presented in Table 1.

Overall, the most widely observed congenital malformations involved circulatory system (n=32, 20.78%) with a prenatal prevalence of 11.3 for each 1,000 pregnancies. In the circulatory system, defects related to cardiac chambers and connections and cardiac septa were mostly seen (6.49% each). The second common congenital malformations involved musculoskeletal system (n=25, 16.23%) followed by nervous system (n=19, 12.34%), eye, ear, face and neck (n=17, 11.04%), cleft lip and cleft palate (n=12, 7.79%), digestive system (n=12, 7.79%), genital organs (n=10, 6.49%), chromosomal abnormalities (n=9, 5.84%), urinary system (n=7, 4.55%), others (n=6, 3.89%), and respiratory system (n=5, 3.25%), respectively. Further information regarding prenatal congenital malformations is demonstrated in Table 2. Prenatal prevalence of congenital malformation based on system or organ involved is depicted in Figure 1.

## Discussion

Since the emergence of ultrasonography in the decade of 1960, there was a rise in the total sum of pregnancy imaging studies. Considerable improvements in magnification imaging as well as signal processing enhanced the capacity to envision anatomy of embryos and fetuses. Variations with respect to critical practice regarding frequency and ultrasonography performance during pregnancy exist. Developments in imaging, for example magnetic resonance imaging and echocardiography, have adjoined to early fetal evaluation in certain specific cases. The capabilities to hearten a high risk pregnant woman regarding ordinary fetal discoveries, and to give exhaustive counseling/guidance with the choice to terminate in instances of unequivocally suspected deadly or significant anomalies, have moved to the advance in gestational age from the prenatal diagnosis [14].

Anatomy in addition to pathophysiology of fetus can contrast from that of the infant, pediatric as well as adult population, hence a reasonable comprehension and learning of this is crucial. Experience of personnel, imaging, and maternal attributes impact reporting accuracy of fetal malformations, specifically in late first trimester. Imaging skills and high expenses with regards to equipment as well as time enhance identification rates. The existence of related malformations and risk factors for fetal anomalies (e.g., family history, smoking, drinking, consanguinity, obesity, etc) paves for more focused attention, thereby enhancing the accuracy of results [14-17]. Various systematic reviews and studies demonstrated greater identification rates of anomalies prior to 24 weeks, particularly major malformations. Many organizations inferred that ultrasonography at previable 2$^{nd}$ trimester ought to be routinely offered and specific guidelines have to be followed [8, 14, 18, 19]. A study conducted by Reddy *et al.* stressed on the fact that no less than one ultrasound study ought to be offered to every single pregnant women somewhere around 18 and 20 weeks [15]. Early finding of extensive variety of fetal malformations can be determined via transvaginal and/or transabdominal examinations during 11 to 14 gestation weeks [16, 20-22].

The perinatal death rate was higher with complex congenital malformations, was firmly associated to maternal age, and the multifaceted nature of the malformations. The present study was clinically based and hence does not constitute the actual prevalence in China. This information ought to invigorate future research and coordinated effort for more precise and outright reporting of congenital malformations in China. The prenatal prevalence of congenital malformations was 54.38 for each 1,000 pregnancies whereas the birth prevalence was 51.15 for each 1,000 births. The most widely observed congenital malformations involved circulatory system, followed by musculoskeletal and nervous systems, and so on. The rates of consanguinity, smoking, drinking, and family history are 22.7%, 17.6%, 13.4%, and 15.1%, respectively. The determination of congenital malformations has enhanced significantly in the previous few years which is majorly attributed to innovations in ultrasound technology and skilled personnel. This may clarify the expanded number of cases as of now being analyzed contrasted with the past, which thus mirrors a greater prenatal prevalence of congenital malformations.

In studies specific to prevalence of congenital malformations in China demonstrated the following results: average incidence reported from 1997 to 2011 in Henan province of China was 86.2 cases per 10,000 births with majority of neural tube defects [23]; data from 2000 to 2010 in Hainan province of China showed rising trend of birth defects prevalence with 77.99 cases in 2000 to 98.93 cases per 10,000 births in 2010 (polydactyly, cleft lip, hydrocephalus, congenital heart diseases, and limb defects as the most common malformations) [24]; average incidence reported from 2009 to 2010 in five countries/cities in Gansu province was 7.49%, with most common defects being congenital heart disease, neural tube defects/pigmented nevus, and hydrocephalus [25]; prevalence of 156.1 cases per 10,000 births was reported in population based survey performed from 2005 to 2008 in Inner Mangolia, China (with higher prevalence of neural tube defects and congenital heart disease) [26]; data from 2006 to 2012 in Tongzhou district of Beijing showed prevalence of 12.62% birth defects (congenital heart diseases, polydactyly, cleft lip/palate, neural tube defects, and external ear malformation as the most defects) [27]. The present study nearly showed similar results with congenital heart diseases, neural tube defects, cleft lip/cleft palate, and polydactyly as the frequent malformations.

There is developing proof of connection between prenatal maternal ecological exposures and raised risk of congenital malformations. All the more particularly, many epidemiological studies showed that exposure during pregnancy to environmental factors, such as air pollutants (e.g. NO2, PM10, and SO2), tobacco smoke, and contaminated water is altogether connected with an increased risk for congenital mal-

formations [28-31]. Maternal age, consanguinity, drinking, smoking and family history, parity, socioeconomic status, etc were also considered to be risk factors for congenital malformations in many studies [23-27]. The higher prenatal prevalence in current study can be attributed to aforementioned factors.

It is noteworthy that not all pregnant women who were diagnosed by ultrasonography had delivered in the referral center and hence the false positive, as well as false negative results are not known. However, current results demonstrated the ultrasound as robust diagnostic tool with skilled personnel.

## Conclusion

The present study demonstrated that majority of perinatal deaths were due to complex congenital malformations. The most frequently reported congenital malformations involved circulatory system followed by musculoskeletal system and nervous system. In turn the most common malformations included congenital heart diseases, neural tube defects, cleft lip/cleft palate, and polydactyly. Continued efforts are required in order to improve maternal as well as child healthcare via information sharing, health education, and preventive measures.

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