

**Review Article****Birth Defects: A Review on Global Action Plans on Maternal and Child Health Care****Siti Syairah Mohd Mutalip<sup>1,2,\*</sup>, Sharaniza Ab Rahim<sup>2</sup>, Mohd Hamim Rajikin<sup>2</sup>**<sup>1</sup>Faculty of Pharmacy, Universiti Teknologi MARA (UiTM), Puncak Alam Campus, Selangor, Malaysia<sup>2</sup>Faculty of Medicine, Universiti Teknologi MARA (UiTM), Sg. Buloh Campus, Selangor, Malaysia**Email address:**

syairah@puncakalam.uitm.edu.my (M. M. S. Syairah)

\*Corresponding author

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**Abstract:** Increasing cases of birth defects has been a worldwide problem for decades. According to the available reports, most of the birth defects were induced by exogenous factors including environmental, chemical or physical factors. As most of these problems are life-threatening and might cause lifelong disability, the concern on reducing the incidences of birth defects has been proportionally increased. This has demand for a global action plan to decrease the preventable birth defects. Present paper intended to provide a review on the global action plans through the Millennium Development Goals (MDGs) and Sustainable Development Goals (SDGs) that were set by the United Nations (UN) in relation to reducing the occurrences of birth defects.**Keywords:** Birth Defects, Maternal Health, Pregnancy, Child Care, Millennium Development Goals (MDGs), Sustainable Development Goals (SDGs)

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**1. Introduction**

Continuous increase in the reported cases of birth defects is indeed a global woe, with most of these problems is life-threatening and might cause lifelong disability [1]. The increases have caused the study of abnormal prenatal development and congenital malformations continue to be an expanding area of medical research. Based on the numerous case records, most of the birth defects are reported to be induced by exogenous factors including environmental, chemical or physical factors [2-4].

The searches for alternatives for the reduction of preventable birth defects have been going-on for decades. According to a study report by Andrew [5], the major parts of birth defects (85.3%) are preventable. Andrew also has outlined the classifications of the three levels of prevention approaches. The first approach is called the primary prevention, which refers to avoiding the cause(s) of birth defects, for example by vaccination of rubella or periconceptional supplementation with folic acid and other necessary multivitamins.

The second approach or secondary prevention is taken through the focus on the early detection followed by early effective treatment. The example of the secondary prevention is neonatal orthopedic screening which is very effective for the early detection and treatment of deformities such as congenital dislocation of the hip. Meanwhile, the third approach which is also known as the tertiary prevention refers to the complete recovery of congenital abnormalities by early surgical intervention without residual defects or minimal after effects [5].

Based on the report by [5], birth defects induced by maternal exposure to exogenous factors during pregnancy are preventable if the contributing factors can be identified and avoided. For instance, exposure to the environmental pollutants such as the endocrine-disturbing chemicals may act as hormone mimics or antagonists and causes the disruption of the normal hormonal pathways [6]. Other examples include the exposure to the unhealthy lifestyle such as smoking and consuming alcohol which may result in the generation of reactive oxygen species (ROS)-induced oxidative stress (OS) [7-9]. It has been reported that the presence of high level of OS

are the risk factor for a number of pregnancy-related disorders, such as embryonic mortality, early spontaneous abortion, fetal death, premature delivery and low birth weight [10-11].

## 2. Birth Defects

Birth defects are a worldwide problem, which is also known as ‘congenital anomalies’, ‘congenital disorders’ or ‘congenital malformations’. World Health Organization (WHO) defined birth defects as structural (physical) or functional anomalies including metabolic disorders that occur during intrauterine life and can be identified prenatally, at birth or later in life [1]. According to the National Center on Birth Defects and Developmental Disabilities (NCBDDD), United States of America (USA) (2016) [12], birth defects are structural changes in one or more body parts that are present at birth. Birth defects normally occur during the first trimester of the fetal developmental period and the defects could be of the factors of inheritance or external influences.

### 2.1. Global Occurrence of Birth Defects

Birth defects have been known and recognized for decades. Occurrence of birth defects worldwide has been documented since as early as in 1948. According to a study conducted to determine the frequencies of birth defects at St. Barnabas’ Hospital in Osaka, Japan, analysis on the birth records data from 1948-1990 reported that there were 1,418 infants diagnosed with birth defects during the first week of birth, among a total number of 131,996 births during the period [13]. Another study conducted to identify the presence of congenital malformations by screening over 32,332 live-born infants over a period of two-years has reported that from a total number of 770 babies born with defects, 58 of them died during the early neonatal period [14]. A study on the occurrence of birth defects in 3000 neonates in Boulak El-Dakrou Hospital, Giza, Egypt over a duration of two-years from January 1991 until April 1993 has reported that there were 95 infants with birth defects, 39 were stillbirths and 18 babies died within the first 5 days of birth [15].

In Malaysia, the available records on birth defects occurrence were documented since 1970. The data on birth defects in Malaysia before the year of 1970 were collected in a survey by WHO (1966) involving the consecutive births in 24 centers around the world. Malaysia was one of the participating countries and data were collected from the Maternity Hospital, Kuala Lumpur [16]. According to the report issued by the Health Technology Assessment Unit, Medical Development Division, Ministry of Health, Malaysia, a study which has been carried out in 1970 at University Hospital, Kuala Lumpur reported that 66 infants out of 1404 live births are born with defects [17].

Another study on perinatal and infant mortality was carried out in 1972 at the University Hospital, Petaling Jaya, Selangor. This study reported that 27% of perinatal and infant deaths were caused by inborn defects or malformations [18]. A similar study conducted in Hospital Alor Setar, Kedah from 1st April 1984 to 31st March 1987 over a number of 19,769

live births revealed that 302 infants were found born with major birth defects [19]. Another study in Hospital Kuala Lumpur in 1996 reported on an estimation of 141 cases of major birth defects over 15,535 live birth babies [17]. The report also stated that a number of 1,055 lethal congenital malformations were recorded nationwide in the year of 1999 (unpublished data).

A study to determine the epidemiology of major birth defects in live births during perinatal period has been carried out by Thong *et al.* [20]. This study was conducted in the district of Kinta, Perak over duration of 14 months, using a population-based birth defect register. The study reported that there were 253 infants born with major birth defects in 17,720 live births, giving an incidence per 1000 live birth recorded as 14.3 [20]. Recently, a study has been conducted on the birth defects that were registered in Pulau Pinang [21]. In this study, the data were taken from the International Classification of Diseases 10 (ICD10) database from the year 1999 to 2004. The state of Pulau Pinang was divided into five major districts, namely Seberang Perai Selatan, Seberang Perai Tengah, Seberang Perai Utara, Timur Laut and Barat Daya. Analysis on the incidence of congenital anomalies indicated a total of 3985 cases of birth defects from all of the five districts, with the average annual increase of 797 cases in the state [21].

Amid the continuously growing global occurrence of birth defects, a more comprehensive report was issued by March of Dimes Birth Defects Foundation, New York, USA entitled ‘Global Report on Birth Defects: The Hidden Toll of Dying and Disabled Children’ in the year 2006 [22]. This report emphasized that an approximate of 7.9 million (which corresponds to 6% of total birth worldwide) children are born with serious birth defects of genetic or partially genetic origin every year worldwide [22]. It also reported that at least 3.3 million children under five years old died from birth defects every year. Around of 3.2 million of those who survived from birth defects may be disabled for life, perhaps with the mental, physical, auditory or visual disability [22]. A report by [1] has reported on a global estimation of 276,000 babies whom died within 4 weeks of birth were from congenital anomalies, out of 2.761 million deaths during the neonatal period in 2013.

### 2.2. Causes of Birth Defects

The incidence of birth defects affected all the races and ethnicities worldwide, however the highest and severe impacts are seen in the middle- and low income countries (MLIC). These are shown with an estimate of 94% of birth with serious defects that results on about 95% of death every year in the MLIC [22]. The increasing trends in the incidence of birth defects particularly in these countries were reported to be caused by several factors, although the causes of approximately 50% of birth defects are unknown. The causes include the factor of inheritance, maternal exposure to harmful environment as well as the complex interaction of genetic and environmental influences [22]. Besides, the huge differences in maternal health management between high- and low- or middle-income countries also influenced the risk of birth defects. Other significant risk factors including poverty, high

percentage of older mothers, greater frequency of consanguineous marriages and low survivability rate against malaria for carriers of sickle cell, thalassemia, and glucose-6-phosphate dehydrogenase (G6PD) deficiency genes were also named as risk factors leading to birth defects [22].

WHO through the 63rd World Health Assembly Report on Birth Defects that was issued in April 2010 has provided a detailed list of birth defects risk factors [23]. According to this report, birth defects are a diverse group of disorders that originated prenatally which can be caused by single gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens and micronutrient deficiencies. In addition, maternal infectious diseases such as syphilis and rubella also have been counted as a significant cause of birth defects in low- and middle-income countries. Moreover, poor

maternal health status including diabetes mellitus, iodine and folic acid deficiency, and exposure to recreational drugs, alcohol, tobacco are also contributing to birth defects [23].

### 2.3. Global Action Plans on Prevention of Birth Defects

A global action through an initiative named as the ‘Millennium Development Goals (MDGs) for 2015’ was set in the year 2000 by the United Nations (UN). This was established following the adoption of the UN Millennium Declaration [24]. This 15-years initiative plan was supported by all 189 UN member states at that time and at least by 23 international organizations, including WHO which committed to help achieving the MDGs by the year 2015.



**Figure 1.** The eight Millennium Development Goals (MDGs) set in the year of 2000 and to be achieved by target date of 2015. These goals ranged from halving extreme poverty to attenuating the spread of HIV/AIDS, providing universal primary education, as well as reducing child mortality and improving maternal health [24].

The MDGs emphasized on three main areas aiming to increase the living standards; (1) human capital, (2) infrastructure and (3) human rights. Human capital objective include education, nutrition and healthcare such as child mortality, HIV/AIDS, tuberculosis, malaria and reproductive health. Infrastructure objectives include access to safe drinking water, energy and modern information/communication technology. Meanwhile, human rights objectives include empowering women, reducing violence, ensuring equal access to public services and increasing security of property rights. The MDGs initiative has outlined eight international development goals as listed below and summarized in Figure 1:

1. To eradicate extreme poverty and hunger
2. To achieve universal primary education
3. To promote gender equality
4. To reduce child mortality
5. To improve maternal health

6. To combat HIV/AIDS, malaria and other diseases
7. To ensure environmental sustainability
8. To develop a global partnership for development

The world community held hands together to take action against the high occurrence of birth defects through one of the eight global goals outlined in the MDGs, which was to reduce child mortality (Goal Number 4). Going in-depth, this goal falls in the target on human capital objective, which could be achieved through proper nutrition and healthcare to both mother and infants during the early stage of pregnancy. As discussed above, the high prevalence of birth defects were reported to be mostly associated with the poor maternal health status especially during the prenatal stage. Following that, the interventions for prevention and care against birth defects was also discussed in the 63rd World Health Assembly Report on Birth Defects [23]. The suggestions are inclusive of the proper care during the three important periods of pregnancy which are the preconception period, pregnancy period and postnatal

period (Table 1).

The support towards the move in prevention of birth defects was given due emphasis where it was discussed and reported in the ‘Community Genetics Services: Report of a WHO Consultation on Community Genetics in Low- and Middle-Income Countries’ report that was issued in September 2010 [25]. The aim of the consultation was to develop an evidence-based report on community genetics services to provide health-related guidance to the low- and middle-income countries (LMIC). This was in accordance to the Action Plan for Global Strategy for the Prevention and Control of Non-Communicable Diseases (NCDs) 2008-2013 [26], which included the community genetics services in LMIC in preventing birth defects and genetic diseases at population level. The 63rd World Health Assembly Report on Birth Defects also emphasized that the occurrence of birth defects are preventable if the primary community genetics services (Figure 2) are implemented during the initial stage of pregnancy [23].

Community genetics services include activities for the

diagnosis, care and prevention of birth defects and genetic diseases at the community level [27-29] that would help to maximize the chances for having healthy and normal babies. The activities include the clinical and laboratory diagnosis of birth defects and genetic diseases (cytogenetic analyses, DNA testing, biochemical assays and others), pre-conception care, prenatal screening, prenatal and pre-implantation genetic diagnoses, carrier and newborn screening, genetics counseling and population genetic screening. These activities are implemented in different need and importance in the primary, secondary and tertiary levels of care (Figure 2) [25].

In 2015, after 15 years of Millennium Development Goals implementation has come to its end, the progress report has shown an uneven data, particularly in places such as in Africa, least developed countries, landlocked developing countries and small island developing States, where some of the Millennium Development Goals remain off-track, in particular those related to maternal, newborn and child health and to reproductive health [30].

**Table 1.** Interventions of Birth Defects Prevention or Treatment during the Three Important Periods of Pregnancy as Suggested by [23].

Preconception Care	Pregnancy Care	Newborn Infant and Child Care
<ol style="list-style-type: none"> <li>1. Family planning                             <ol style="list-style-type: none"> <li>a) Introducing women to the concept of reproductive choice</li> <li>b) Reducing the total number of children born with a birth defect</li> <li>c) Reducing the proportion of mothers of advanced maternal age, which reduces the birth prevalence of autosomal trisomies, particularly Down syndrome</li> <li>d) Allowing women with affected children the option of not having further children</li> </ol> </li> <li>2. Preconception screening and counseling                             <ol style="list-style-type: none"> <li>a) Using family history taken in primary health care facilities to identify individuals at risk of having affected children</li> <li>b) Undertaking carrier screening for common recessive disorders (e.g. thalassemia and sickle cell disorders)</li> </ol> </li> <li>3. Optimizing women’s diet before and throughout pregnancy                             <ol style="list-style-type: none"> <li>a) Promoting the use of salt fortified with iodine to prevent iodine deficiency disorder</li> <li>b) Promoting the use of a staple food fortified with folic acid and of supplementary multivitamins with folic acid to prevent neural tube defects and other malformations</li> <li>c) Promoting avoidance of alcohol, tobacco and cocaine</li> <li>d) Promoting and ensure an adequate general diet (e.g. with sufficient proteins, calories, iron)</li> </ol> </li> <li>4. Preventing and treating teratogen-induced infections before and throughout pregnancy for infections like:                             <ol style="list-style-type: none"> <li>i. Syphilis</li> <li>ii. Rubella</li> </ol> </li> <li>5. Optimizing preconception maternal health and treatment for                             <ol style="list-style-type: none"> <li>a) Insulin-dependent diabetics</li> <li>b) Women on treatment for epilepsy</li> <li>c) Women on treatment with warfarin</li> </ol> </li> </ol>	<ol style="list-style-type: none"> <li>1. Antenatal screening for                             <ol style="list-style-type: none"> <li>a) Rhesus status</li> <li>b) Syphilis</li> <li>c) Individuals at risk of having children with birth defects using a family history</li> <li>d) Down syndrome (advanced maternal age; maternal serum screening; early ultrasound scanning)</li> <li>e) Neural tube defects (maternal serum screening)</li> <li>f) Major malformations (ultrasound fetal anomaly scanning (18+ weeks gestation))</li> <li>g) Carriers of common recessive disorders (e.g. thalassemia and sickle cell disorders)</li> </ol> </li> <li>2. Prenatal diagnosis                             <ol style="list-style-type: none"> <li>a) Ultrasound</li> <li>b) Amniocentesis</li> <li>c) Chorionic villus biopsy</li> </ol> </li> <li>3. Fetal treatment for                             <ol style="list-style-type: none"> <li>a) Syphilis</li> <li>b) Fetal anemia with intrauterine transfusion</li> </ol> </li> </ol>	<ol style="list-style-type: none"> <li>1. Newborn infant examination – referring to the practice of clinically examining all newborn infants for birth defects by trained examiners</li> <li>2. Newborn infant screening                             <ol style="list-style-type: none"> <li>a) Congenital hypothyroidism</li> <li>b) Phenylketonuria</li> <li>c) Cystic fibrosis</li> <li>d) Others (as dictated by each country’s need and circumstances)</li> </ol> </li> <li>a) Medical treatments such as:                             <ol style="list-style-type: none"> <li>i. Neonatal jaundice in G6PD deficiency and Rhesus incompatibility</li> <li>ii. Treatment and care for children with blood disorders such as sickle-cell disorder, thalassemia, etc.</li> <li>iii. Treatment of some inborn errors of metabolism</li> <li>iv. Care of children with cystic fibrosis</li> </ol> </li> <li>3. Surgery, such as the correction of:                             <ol style="list-style-type: none"> <li>i. Simple congenital heart defects</li> <li>ii. Cleft lip and palate</li> <li>iii. Club foot</li> <li>iv. Congenital cataracts</li> </ol> </li> <li>3. Rehabilitation and palliative care; as appropriate</li> </ol>

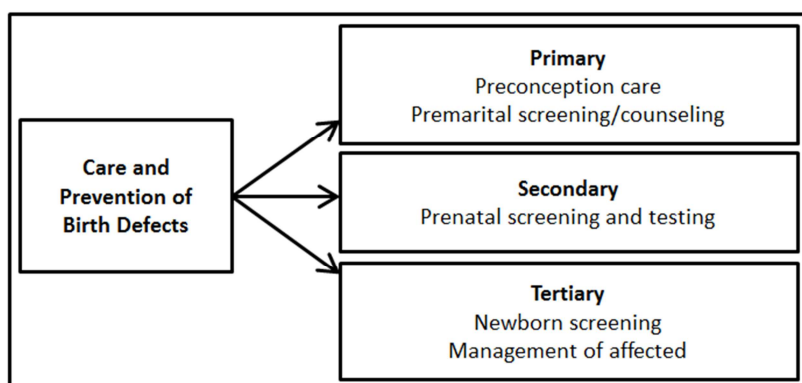


Figure 2. Activities of community genetics services in different levels of care and treatment of birth defects and genetic diseases.

Table 2. The 17 Sustainable Development Goals (SDGs) as outlined in the new resolution [30].

Sustainable Development Goals
Goal 1 End poverty in all its forms everywhere
Goal 2 End hunger, achieve food security and improved nutrition and promote sustainable agriculture
Goal 3 Ensure healthy lives and promote well-being for all at all ages
Goal 4 Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all
Goal 5 Achieve gender equality and empower all women and girls
Goal 6 Ensure availability and sustainable management of water and sanitation for all
Goal 7 Ensure access to affordable, reliable, sustainable and modern energy for all
Goal 8 Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all
Goal 9 Build resilient infrastructure, promote inclusive and sustainable industrialization and foster innovation
Goal 10 Reduce inequality within and among countries
Goal 11 Make cities and human settlements inclusive, safe, resilient and sustainable
Goal 12 Ensure sustainable consumption and production patterns
Goal 13 Take urgent action to combat climate change and its impacts*
Goal 14 Conserve and sustainably use the oceans, seas and marine resources for sustainable development
Goal 15 Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss
Goal 16 Promote peaceful and inclusive societies for sustainable development, provide access to justice for all and build effective, accountable and inclusive institutions at all levels
Goal 17 Strengthen the means of implementation and revitalize the Global Partnership for Sustainable Development

Following this, the UN committees have recommitted themselves for realization of all the MDGs, including the off-track places. This is to be done in particular by providing focused and scaled-up assistance to the least developed countries and other countries in special situations with the relevant support programs. Hence, the new transformative '2030 Agenda for Sustainable Development' has been set up in September 2015, outlining 17 Sustainable Development Goals (SDGs) targeting for the next 15 years. This new resolution was built based on the previous MDGs to complete all of the targets that have not been achieved [30]. All of the 17 goals outlined in the new resolution are shown in Table 2.

In the new SDGs, the aim to accomplish the target of reducing the maternal, newborn, child and reproductive health falls under Goal 3 (Ensure healthy lives and promote well-being for all at all ages). Under this goal, some of the specific outlined targets on the maternal, newborn, child and reproductive health are [30]:

1. By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births
2. By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under 5 mortality to at least as low

as 25 per 1,000 live births

3. By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being
4. Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol
5. By 2030, ensure universal access to sexual and reproductive health-care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programs
6. Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all

### 3. Conclusion

Based on the MDGs and the SDGs objectives, it is clearly indicated that the issues of maternal, newborn, child and reproductive health are among the major global concerns. As discussed in this review, the suggestions on the interventions and preventions against the occurrences of birth defects as

outlined in Table 1 showed that the preconception period is the most crucial time for prevention of malformations (primary level of care).

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